Identifiability of Linear Compartment Models

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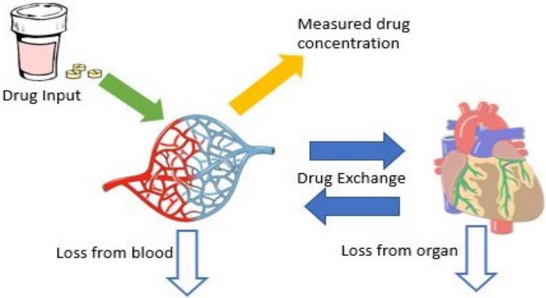
Outline

- Introduce Identifiability
- Process to Determine Identifiability
- Effects of Removing/Adding a Leak

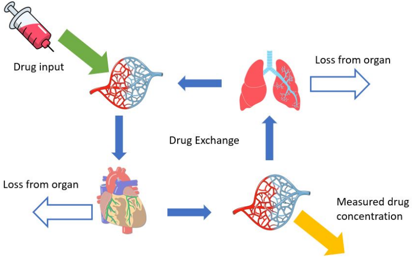
Background

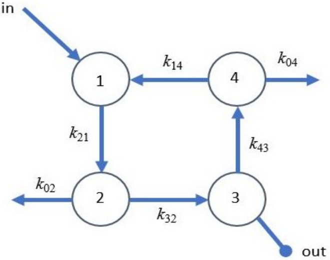
Definition

Identifiability seeks to determine which unknown parameters of a model can be recovered from the given input-output data.
A model is **unidentifiable** if some parameters cannot be determined given the input-output data.



Linear Compartment Models





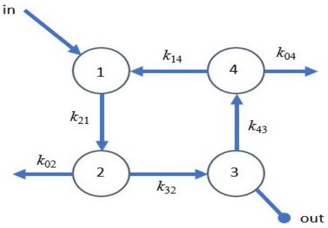
Goal

Recover the parameters k_{ij}.

Process

The Compartmental Matrix:

$$A = \begin{bmatrix} -k_{21} & 0 & 0 & k_{14} \\ k_{21} & -k_{02} - k_{32} & 0 & 0 \\ 0 & k_{32} & -k_{43} & 0 \\ 0 & 0 & k_{43} & -k_{04} - k_{14} \end{bmatrix}$$



Proposition (Meshkat, Sullivant, Eisenberg 2015)

$$\det(\partial I - A)y_3 = \det((\partial I - A)_{13})u_1$$

$$y_3^{(4)} + (c_1)y_3^{(3)} + (c_2)y_3^{(2)} + (c_3)y_3^{(1)} + (c_4)y_3 = u_1^{(2)} + (c_5)u_1^{(1)} + (c_6)u_1$$

$c_1 = k_{02} + k_{04} + k_{14} + k_{21} + k_{32} + k_{43}$
$c_2 = k_{02}k_{04} + k_{02}k_{14} + k_{02}k_{21} + \cdots$
$c_3 = k_{02}k_{04}k_{21} + k_{02}k_{14}k_{21} + k_{02}k_{04}k_{43} + \cdots$

$c_4 = k_{21}k_{43}(k_{02}k_{04} + k_{02}k_{14} + k_{04}k_{32})$
$c_5 = k_{21}k_{32}$
$c_6 = k_{21}k_{32}(k_{04} + k_{14})$

Define the map $\mathbb{R}^6 \to \mathbb{R}^6$ as:
$(k_{01}, k_{04}, k_{14}, k_{21}, k_{32}, k_{43}) \to (c_1, c_2, c_3, c_4, c_5, c_6)$

Process

$$J = \begin{array}{cc} \begin{array}{c} c_1 \\ c_2 \\ \vdots \\ c_4 \\ c_5 \\ c_6 \end{array} & \left[\begin{array}{cccc} 1 & 1 & 1 & \cdots \\ k_{02}+k_{04}+k_{14}+k_{32}+k_{43} & k_{02}+k_{21}+k_{32}+k_{43} & k_{04}+k_{14}+k_{21}+k_{43} & \cdots \\ \vdots & \vdots & \vdots & \vdots \\ k_{02}k_{04}k_{43}+k_{02}k_{14}k_{43}+k_{04}k_{32}k_{43} & k_{02}k_{21}k_{43} & k_{04}k_{21}k_{43}+k_{14}k_{21}k_{43} & \cdots \\ k_{32} & 0 & 0 & \cdots \\ k_{32}(k_{04}+k_{14}) & k_{21}k_{32} & 0 & \cdots \end{array} \right] \\ & \begin{array}{cccc} k_{21} & k_{14} & k_{02} & \cdots \end{array} \end{array}$$

Proposition (Meshkat, Sullivant, Eisenberg 2015)

Identifiable $\iff$ Jacobian matrix of coefficient map has full rank

The Jacobian matrix has full rank if the determinant is a non-zero polynomial.

In the previous example :

$$\det(J) = -k_{21}^3 * k_{32}^2 * k_{43} * (k_{21} - k_{43}) * (k_{02} - k_{21} + k_{32}) * (k_{02} + k_{32} - k_{43})$$

Yes - this model is identifiable.

Research Question: Effects of Model Operations

Removing a Leak

If a model is identifiable and a leak is removed - is the resulting model identifiable?

Adding a Leak

If a model is unidentifiable and a leak is added - is the resulting model unidentifiable?

Preliminary Results

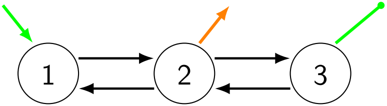
Lemma

Let $\mathcal{M}$ be a linear compartment model with $Leak = \emptyset$ and coefficients c_i. Let $\widetilde{\mathcal{M}}$ be the linear compartment model formed by adding a single leak $k_{0\ell}$ to $\mathcal{M}$. The coefficients of the model with the leak $\tilde{c}_i$ have the form:

$$\tilde{c}_i = c_i + k_{0\ell}(x)$$

where x is some combination of k_{ij}'s.

Preliminary Results

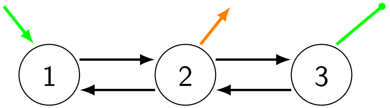


Recall: $\det(\partial I - A)y_3 = \det((\partial I - A)_{13})$

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

$$(\partial I - \widetilde{A}) = \begin{bmatrix} \frac{d}{dt} + k_{21} & -k_{12} & 0 \\ -k_{21} & \frac{d}{dt} + k_{02} + k_{12} + k_{32} & -k_{23} \\ 0 & -k_{32} & \frac{d}{dt} + k_{23} \end{bmatrix}$$

Preliminary Results



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$$(\partial I - \widetilde{A}) = \begin{bmatrix} \frac{d}{dt} + k_{21} & -k_{12} & 0 \\ -k_{21} & \frac{d}{dt} + k_{02} + k_{12} + k_{32} & -k_{23} \\ 0 & -k_{32} & \frac{d}{dt} + k_{23} \end{bmatrix}$$

$$\det(\partial I - \tilde{A})\Big|_{k_{0j}=0} = \det(\partial I - A)$$

$$\tilde{c}_i\Big|_{k_{0j}=0} = c_i \text{ for all } i$$

$$\tilde{c}_i = c_i + k_{0j}(x)$$

Preliminary Results

Lemma

Let $\mathcal{M}$ be a linear compartment model with $Leak = \emptyset$. If $\mathcal{M}$ has r coefficients in the input-output equation, then the model $\widetilde{\mathcal{M}}$ obtained by adding a single leak $k_{0\ell}$ to compartment-ℓ has exactly $r + 1$ coefficients.

Preliminary Results

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Let $\mathcal{M}$ be a linear compartment model with $Leak = \emptyset$. If $\mathcal{M}$ has r coefficients in the input-output equation, then the model $\widetilde{\mathcal{M}}$ obtained by adding a single leak $k_{0\ell}$ to compartment-ℓ has exactly $r + 1$ coefficients.

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

$$\det(A) = 0$$

$$(\partial I - \widetilde{A}) = \begin{bmatrix} \frac{d}{dt} + k_{21} & -k_{12} & 0 \\ -k_{21} & \frac{d}{dt} + k_{02} + k_{12} + k_{32} & -k_{23} \\ 0 & -k_{32} & \frac{d}{dt} + k_{23} \end{bmatrix}$$

$$\det(\widetilde{A}) \neq 0$$

Preliminary Results

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Let $\mathcal{M}$ be a linear compartment model with $Leak = \emptyset$. If $\mathcal{M}$ has r coefficients in the input-output equation, then the model $\widetilde{\mathcal{M}}$ obtained by adding a single leak $k_{0\ell}$ to compartment-ℓ has exactly $r + 1$ coefficients.

$(\partial I - A)_{13}$

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

$\det(A) = 0$

$\det(A_{13}) \neq 0$

$(\partial I - \widetilde{A})_{13}$

$$(\partial I - \widetilde{A}) = \begin{bmatrix} \frac{d}{dt} + k_{21} & -k_{12} & 0 \\ -k_{21} & \frac{d}{dt} + k_{02} + k_{12} + k_{32} & -k_{23} \\ 0 & -k_{32} & \frac{d}{dt} + k_{23} \end{bmatrix}$$

$\det(\widetilde{A}) \neq 0$

$\det(\widetilde{A}_{13}) \neq 0$

Adding a Leak

Theorem (Adding a Single Leak)

If model $\mathcal{M}$ is unidentifiable because there are **more parameters than coefficients** *- then the model $\widetilde{\mathcal{M}}$ formed by adding a leak (at any compartment) will be* **unidentifiable**.

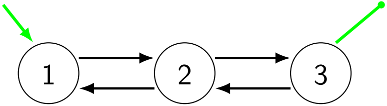


Figure Catenary model, input = 1, output = 3, no leaks.

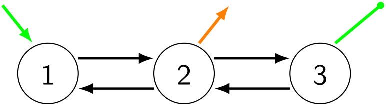


Figure Catenary model, input = 1, output = 3, leak = 2.

$$y_3^{(3)} + (c_{y_1})y_3^{(2)} + (c_{y_2})y_3^{(1)} = (c_{u_1})u_1$$

$c_{y_1} = k_{12} + k_{21} + k_{23} + k_{32}$
$c_{y_2} = k_{12}k_{23} + k_{21}k_{23} + k_{21}k_{32}$
$c_{u_1} = k_{21}k_{32}$

3×4 Jacobian matrix

$$y_3^{(3)} + (\tilde{c}_{y_1})y_3^{(2)} + (\tilde{c}_{y_2})y_3^{(1)} + (\tilde{c}_3)y_3 = (c_{u_1})u_1$$

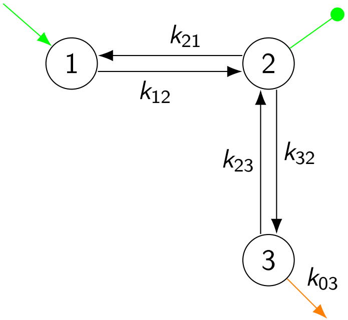
$\tilde{c}_{y_1} = k_{02} + k_{12} + k_{21} + k_{23} + k_{32}$
$\tilde{c}_{y_2} = k_{02}(k_{21} + k_{23} + k_{32}) + k_{12}k_{23} + k_{21}k_{23} + k_{21}k_{32}$
$\tilde{c}_{y_3} = k_{02}k_{21}k_{23}$
$c_{u_1} = k_{21}k_{32}$

4×5 Jacobian matrix

Removing a Leak

Theorem (Removing a Single Leak (pending))

Let $\widetilde{\mathcal{M}}$ be a strongly connected linear compartment model with $|In| = |Out| = |Leak| = 1$. If $\widetilde{\mathcal{M}}$ is locally identifiable, then so is the model $\mathcal{M}$ obtained by removing the leak.



$$\begin{aligned}
\tilde{c}_{y_1} &= c_{y_1} + k_{03} \\
\tilde{c}_{y_2} &= c_{y_2} + k_{03}(k_{12} + k_{21} + k_{32}) \\
\tilde{c}_{y_3} &= k_{03}(k_{21}k_{32})
\end{aligned}$$

$$\begin{aligned}
\tilde{c}_{u_1} &= c_{u_1} + k_{03}(0) \\
\tilde{c}_{u_2} &= c_{u_2} + k_{03}(-k_{21})
\end{aligned}$$

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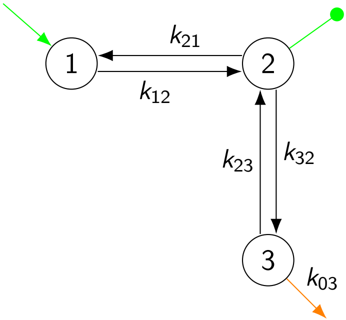

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&\boxed{\tilde{c}_{y_3} = k_{03}(k_{21}k_{32})}
\end{aligned}$$

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\tilde{c}_{u_1} &= c_{u_1} + k_{03}(0) \\
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\end{aligned}$$

Removing a Leak

- **Goal:** Show that $\det(J_{\widetilde{\mathcal{M}}}) \neq 0 \Rightarrow \det(J_{\mathcal{M}}) \neq 0$

$$J_{\mathcal{M}} = \begin{array}{c|c|} c_{y_1} & \\ \vdots & \boxed{\dfrac{\partial c_{y_i}}{\partial k_{ij}}} \\ c_{y_r} & \\ c_{u_1} & \\ \vdots & \boxed{\dfrac{\partial c_{u_i}}{\partial k_{ij}}} \\ c_{u_m} & \\ & \cdots k_{ij} \cdots \end{array} \qquad \widetilde{J_{\mathcal{M}}} = \begin{array}{c|c|c|} c_{y_1} & & \\ \vdots & \boxed{\dfrac{\partial c_{y_i}}{\partial k_{ij}} + k_{03}(\cdots)} & \\ c_{y_r} & & \\ c_{y_{r+1}} & \boxed{\text{either } 0 \text{ or } k_{03}(\cdots)} & a \\ c_{u_1} & & \\ \vdots & \boxed{\dfrac{\partial c_{u_i}}{\partial k_{ij}} + k_{03}(\cdots)} & \\ c_{u_m} & & \\ & \cdots k_{ij} \cdots & k_{03} \end{array}$$

$$J_{\mathcal{M}} = \begin{bmatrix} 1 & 1 & 1 & 1 \\ k_{23} + k_{32} & k_{23} & k_{21} & k_{12} + k_{21} \\ -1 & 0 & 0 & 0 \\ -k_{23} & 0 & 0 & -k_{21} \end{bmatrix}$$

$$J_{\widetilde{\mathcal{M}}} = \begin{bmatrix} 1 & 1 & 1 & 1 & 1 \\ k_{23} + k_{32} + k_{03} & k_{23} + k_{03} & k_{21} + k_{03} & k_{12} + k_{21} & k_{12} + k_{21} + k_{32} \\ k_{03}k_{32} & 0 & k_{03}k_{21} & 0 & k_{21}k_{32} \\ -1 & 0 & 0 & 0 & 0 \\ -k_{23} - k_{03} & 0 & 0 & -k_{21} & -k_{21} \end{bmatrix}$$

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$$\widetilde{J_{\mathcal{M}}} = \begin{array}{c|c|c|} c_{y_1} & & \\ \vdots & \boxed{\dfrac{\partial c_{y_i}}{\partial k_{ij}} + k_{03}(\cdots)} & \\ c_{y_r} & & \\ c_{y_{r+1}} & \text{either 0 or } k_{03}(\cdots) & a \\ c_{u_1} & & \\ \vdots & \boxed{\dfrac{\partial c_{u_i}}{\partial k_{ij}} + k_{03}(\cdots)} & \\ c_{u_m} & & \\ & \cdots k_{ij} \cdots & k_{03} \end{array} \qquad c_{y_{r+1}} = k_{03}(a)$$

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$$J_{\widetilde{\mathcal{M}}} = \begin{bmatrix} 1 & 1 & 1 & 1 & 1 \\ k_{23} + k_{32} + k_{03} & k_{23} + k_{03} & k_{21} + k_{03} & k_{12} + k_{21} & k_{12} + k_{21} + k_{32} \\ k_{03} k_{32} & 0 & k_{03} k_{21} & 0 & k_{21} k_{32} \\ -1 & 0 & 0 & 0 & 0 \\ -k_{23} - k_{03} & 0 & 0 & -k_{21} & -k_{21} \end{bmatrix} \qquad c_{y_3} = k_{03}(k_{21} k_{32})$$

Removing a Leak

- **Goal:** Show that $\det(J_{\widetilde{\mathcal{M}}}) \neq 0 \Rightarrow \det(J_{\mathcal{M}}) \neq 0$

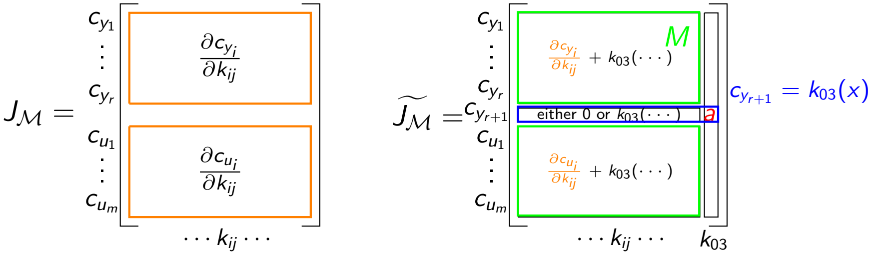
$$J_{\mathcal{M}} = \begin{array}{c}c_{y_1}\\ \vdots\\ c_{y_r}\\ c_{u_1}\\ \vdots\\ c_{u_m}\\ \\ \end{array}\begin{array}{c}\left[\begin{array}{c}\boxed{\dfrac{\partial c_{y_i}}{\partial k_{ij}}}\\ \boxed{\dfrac{\partial c_{u_i}}{\partial k_{ij}}}\end{array}\right]\\ \cdots k_{ij} \cdots\end{array} \qquad \widetilde{J_{\mathcal{M}}} = \begin{array}{c}c_{y_1}\\ \vdots\\ c_{y_r}\\ c_{y_{r+1}}\\ c_{u_1}\\ \vdots\\ c_{u_m}\\ \\ \end{array}\begin{array}{cc}\left[\begin{array}{c|c}\boxed{\dfrac{\partial c_{y_i}}{\partial k_{ij}} + k_{03}(\cdots) \quad M} & \\ \boxed{\text{either } 0 \text{ or } k_{03}(\cdots)} & \boxed{a}\\ \boxed{\dfrac{\partial c_{u_i}}{\partial k_{ij}} + k_{03}(\cdots)} & \end{array}\right] & \\ \cdots k_{ij} \cdots & k_{03}\end{array} \quad c_{y_{r+1}} = k_{03}(a)$$

$$J_{\mathcal{M}} = \begin{bmatrix} 1 & 1 & 1 & 1 \\ k_{23}+k_{32} & k_{23} & k_{21} & k_{12}+k_{21} \\ -1 & 0 & 0 & 0 \\ -k_{23} & 0 & 0 & -k_{21} \end{bmatrix}$$

$$J_{\widetilde{\mathcal{M}}} = \begin{bmatrix} 1 & 1 & 1 & 1 & 1 \\ k_{23}+k_{32}+k_{03} & k_{23}+k_{03} & k_{21}+k_{03} & k_{12}+k_{21} & k_{12}+k_{21}+k_{32} \\ \boxed{k_{03}k_{32}} & \boxed{0} & \boxed{k_{03}k_{21}} & \boxed{0} & \boxed{k_{21}k_{32}} \\ -1 & 0 & 0 & 0 & 0 \\ -k_{23}-k_{03} & 0 & 0 & -k_{21} & -k_{21} \end{bmatrix} \quad c_{y_3} = k_{03}(k_{21}k_{32})$$

Removing a Leak

- **Goal:** Show that $\det(J_{\widetilde{\mathcal{M}}}) \neq 0 \Rightarrow \det(J_{\mathcal{M}}) \neq 0$



$$J_{\mathcal{M}} = \begin{array}{c} c_{y_1} \\ \vdots \\ c_{y_r} \\ c_{u_1} \\ \vdots \\ c_{u_m} \end{array} \begin{bmatrix} \boxed{\dfrac{\partial c_{y_i}}{\partial k_{ij}}} \\ \boxed{\dfrac{\partial c_{u_i}}{\partial k_{ij}}} \end{bmatrix} \quad \cdots k_{ij} \cdots$$

$$\widetilde{J_{\mathcal{M}}} = \begin{array}{c} c_{y_1} \\ \vdots \\ c_{y_r} \\ c_{y_{r+1}} \\ c_{u_1} \\ \vdots \\ c_{u_m} \end{array} \begin{bmatrix} \dfrac{\partial c_{y_i}}{\partial k_{ij}} + k_{03}(\cdots) \quad M & \\ \text{either 0 or } k_{03}(\cdots) & a \\ \dfrac{\partial c_{u_i}}{\partial k_{ij}} + k_{03}(\cdots) & \end{bmatrix} \quad \cdots k_{ij} \cdots \quad k_{03}$$

$c_{y_{r+1}} = k_{03}(x)$

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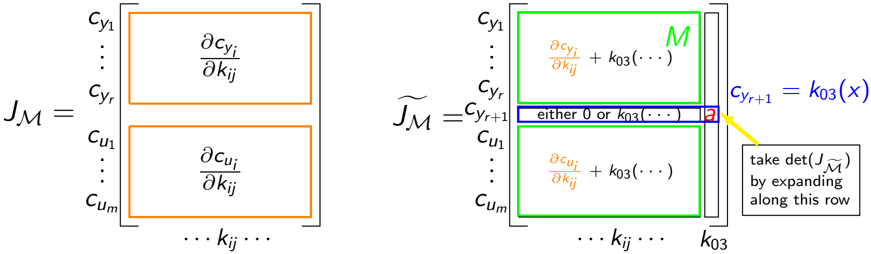
Removing a Leak

- **Goal:** Show that $\det(J_{\widetilde{\mathcal{M}}}) \neq 0 \Rightarrow \det(J_{\mathcal{M}}) \neq 0$



$$J_{\mathcal{M}} = \begin{array}{c} c_{y_1} \\ \vdots \\ c_{y_r} \\ c_{u_1} \\ \vdots \\ c_{u_m} \end{array} \left[\begin{array}{c} \boxed{\dfrac{\partial c_{y_i}}{\partial k_{ij}}} \\ \boxed{\dfrac{\partial c_{u_i}}{\partial k_{ij}}} \end{array} \right] \qquad \cdots k_{ij} \cdots$$

$$\widetilde{J_{\mathcal{M}}} = \begin{array}{c} c_{y_1} \\ \vdots \\ c_{y_r} \\ c_{y_{r+1}} \\ c_{u_1} \\ \vdots \\ c_{u_m} \end{array} \left[\begin{array}{c|c} \boxed{\dfrac{\partial c_{y_i}}{\partial k_{ij}} + k_{03}(\cdots) \quad M} & \\ \boxed{\text{either 0 or } k_{03}(\cdots)} & \boxed{a} \\ \boxed{\dfrac{\partial c_{u_i}}{\partial k_{ij}} + k_{03}(\cdots)} & \end{array} \right] \qquad \cdots k_{ij} \cdots \quad k_{03}$$

$c_{y_{r+1}} = k_{03}(x)$

take $\det(J_{\widetilde{\mathcal{M}}})$ by expanding along this row

$$J_{\mathcal{M}} = \begin{bmatrix} 1 & 1 & 1 & 1 \\ k_{23} + k_{32} & k_{23} & k_{21} & k_{12} + k_{21} \\ -1 & 0 & 0 & 0 \\ -k_{23} & 0 & 0 & -k_{21} \end{bmatrix}$$

$$J_{\widetilde{\mathcal{M}}} = \begin{bmatrix} 1 & 1 & 1 & 1 & 1 \\ k_{23} + k_{32} + k_{03} & k_{23} + k_{03} & k_{21} + k_{03} & k_{12} + k_{21} & k_{12} + k_{21} + k_{32} \\ \xcancel{k_{03}k_{32}}\ 0 & 0 & \xcancel{k_{03}k_{21}}\ 0 & 0 & k_{21}k_{32} \\ -1 & 0 & 0 & 0 & 0 \\ -k_{23} - k_{03} & 0 & 0 & -k_{21} & -k_{21} \end{bmatrix}$$

Removing a Leak

Goal

Show $\det(J_{\widetilde{\mathcal{M}}}) \neq 0 \Rightarrow \det(J_{\mathcal{M}}) \neq 0.$

$$J_{\mathcal{M}} = \begin{array}{c|c|}
c_{y_1} & \\
\vdots & \dfrac{\partial c_{y_i}}{\partial k_{ij}} \\
c_{y_r} & \\
c_{u_1} & \\
\vdots & \dfrac{\partial c_{u_i}}{\partial k_{ij}} \\
c_{u_m} & \\
 & \cdots k_{ij} \cdots
\end{array}$$

$$\widetilde{J_{\mathcal{M}}} = \begin{array}{c|c|c|}
c_{y_1} & M & \\
\vdots & \frac{\partial c_{y_i}}{\partial k_{ij}} + k_{03}(\cdots) & \\
c_{y_r} & & \\
c_{y_{r+1}} & \text{either } 0 \text{ or } k_{03}(\cdots) & a \\
c_{u_1} & & \\
\vdots & \frac{\partial c_{u_i}}{\partial k_{ij}} + k_{03}(\cdots) & \\
c_{u_m} & & \\
 & \cdots k_{ij} \cdots & k_{03}
\end{array}$$

$c_{y_{r+1}} = k_{03}(x)$

$\neq 0$

Removing a Leak

Goal

Show $\det(J_{\widetilde{\mathcal{M}}}) \neq 0 \Rightarrow \det(J_{\mathcal{M}}) \neq 0.$

$$J_{\mathcal{M}} = \begin{array}{c|c|} c_{y_1} & \\ \vdots & \frac{\partial c_{y_i}}{\partial k_{ij}} \\ c_{y_r} & \\ \hline c_{u_1} & \\ \vdots & \frac{\partial c_{u_i}}{\partial k_{ij}} \\ c_{u_m} & \\ & \cdots k_{ij} \cdots \end{array}$$

$$\widetilde{J_{\mathcal{M}}} = \begin{array}{c|c|c|} c_{y_1} & & \\ \vdots & \frac{\partial c_{y_i}}{\partial k_{ij}} + k_{03}(\cdots) \quad M & \\ c_{y_r} & & \\ \hline c_{y_{r+1}} & \text{either } 0 \text{ or } k_{03}(\cdots) & a \\ \hline c_{u_1} & & \\ \vdots & \frac{\partial c_{u_i}}{\partial k_{ij}} + k_{03}(\cdots) & \\ c_{u_m} & & \\ & \cdots k_{ij} \cdots & k_{03} \end{array}$$

$c_{y_{r+1}} = k_{03}(x)$

$\neq 0$

$$\text{Know: } \det(J_{\widetilde{\mathcal{M}}})\Big|_{k_{03}=0} = 0 + 0 + \cdots + 0 \pm a \cdot (\det(M|_{k_{03}=0})) \\ = a \cdot (\det(J_{\mathcal{M}}))$$

Removing a Leak

Goal

Show $\det(J_{\widetilde{\mathcal{M}}}) \neq 0 \Rightarrow \det(J_{\mathcal{M}}) \neq 0.$

$$J_{\mathcal{M}} = \begin{array}{c|c|}
\begin{matrix} c_{y_1} \\ \vdots \\ c_{y_r} \end{matrix} & \boxed{\dfrac{\partial c_{y_i}}{\partial k_{ij}}} \\
\begin{matrix} c_{u_1} \\ \vdots \\ c_{u_m} \end{matrix} & \boxed{\dfrac{\partial c_{u_i}}{\partial k_{ij}}} \\
 & \cdots k_{ij} \cdots
\end{array}$$

$$\widetilde{J_{\mathcal{M}}} = \begin{array}{c|c|c|l}
\begin{matrix} c_{y_1} \\ \vdots \\ c_{y_r} \end{matrix} & \boxed{\dfrac{\partial c_{y_i}}{\partial k_{ij}} + k_{03}(\cdots) \quad M} & & \\
c_{y_{r+1}} & \boxed{\text{either } 0 \text{ or } k_{03}(\cdots)} & a & \begin{matrix} c_{y_{r+1}} = k_{03}(x) \\ \neq 0 \end{matrix} \\
\begin{matrix} c_{u_1} \\ \vdots \\ c_{u_m} \end{matrix} & \boxed{\dfrac{\partial c_{u_i}}{\partial k_{ij}} + k_{03}(\cdots)} & & \\
 & \cdots k_{ij} \cdots & k_{03} &
\end{array}$$

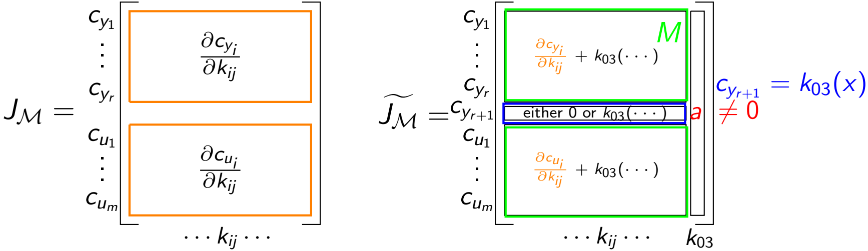
$$\text{Know: } \det(J_{\widetilde{\mathcal{M}}})\Big|_{k_{03}=0} = 0 + 0 + \cdots + 0 \pm a \cdot (\det(M|_{k_{03}=0}))$$
$$= a \cdot (\det(J_{\mathcal{M}}))$$

Key: $k_{03} \nmid \det(J_{\widetilde{\mathcal{M}}})$

Removing a Leak

Goal

Show $\det(J_{\widetilde{\mathcal{M}}}) \neq 0 \Rightarrow \det(J_{\mathcal{M}}) \neq 0.$



$$J_{\mathcal{M}} = \begin{array}{c|c|} c_{y_1} & \\ \vdots & \frac{\partial c_{y_i}}{\partial k_{ij}} \\ c_{y_r} & \\ c_{u_1} & \\ \vdots & \frac{\partial c_{u_i}}{\partial k_{ij}} \\ c_{u_m} & \\ & \cdots k_{ij} \cdots \end{array}$$

$$\widetilde{J_{\mathcal{M}}} = \begin{array}{c|c|c|} c_{y_1} & & \\ \vdots & \frac{\partial c_{y_i}}{\partial k_{ij}} + k_{03}(\cdots) \quad M & \\ c_{y_r} & & \\ c_{y_{r+1}} & \text{either } 0 \text{ or } k_{03}(\cdots) & a \\ c_{u_1} & & \\ \vdots & \frac{\partial c_{u_i}}{\partial k_{ij}} + k_{03}(\cdots) & \\ c_{u_m} & & \\ & \cdots k_{ij} \cdots & k_{03} \end{array}$$

$c_{y_{r+1}} = k_{03}(x)$

$\neq 0$

$$\text{Know: } \det(J_{\widetilde{\mathcal{M}}})\Big|_{k_{03}=0} = 0 + 0 + \cdots + 0 \pm a \cdot (\det(M|_{k_{03}=0}))$$

$$= a \cdot (\det(J_{\mathcal{M}}))$$

Key: $k_{03} \nmid \det(J_{\widetilde{\mathcal{M}}})$ Then: $\det(J_{\widetilde{\mathcal{M}}})\Big|_{k_{03}=0} \neq 0 \Rightarrow \det(J_{\mathcal{M}}) \neq 0$

Thank You

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