**Workshop XX: Algorithm to assess local structural identifiability**

Professor: Ricardo Pérez C.

Authors: Sofía Breton, Felipe Guzmán & José Tomás Suazo

In this workshop, you are required to analyze the **structural identifiability** of two different dynamic models. Each model must be represented using the algorithm discussed during the lectures. While it is not necessary to include the code in the final written report, **your Colab Notebook will be reviewed**, so it must be **well-structured, clearly commented, and properly organized.**

For each model, make sure to include the following:

* **Clear and well-formatted** plots that are easy to interpret. Each figure must include descriptive titles, axis labels, and legends. Use appropriate formatting (e.g., font sizes, line styles, colors) to enhance readability.
* A **concise yet thorough discussion** of the results obtained, explaining their implications regarding the identifiability of the model parameters.
* Ensure that **all labels and annotations are legibl**e, and plots are presented in a way that supports the interpretation of your findings.

# **Cell Growth in a Bioreactor Setup**

Wanika et al. (2024) based their work of [*Structural and Practical Identifiabilty*](https://jbioleng.biomedcentral.com/articles/10.1186/s13036-024-00410-x) on the earlier work of Yongky et al. (2015) which focused on [*Continiuous Culture of Mammalian Cells*](https://pubmed.ncbi.nlm.nih.gov/25676211/). In their analysis, Wanika proposed a simplified version of the original model and performed a comparative evaluation of model performance with and without fixed parameters. Moreover, they used experimental data to verify practical identifiability.

The simplified model is:

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In this model, the parameters are:

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| --- | --- | --- |
| **Parameter | Unit** | **Description** | **Nominal Value** |
|  | Consumption rate of glucose | 0.032 |
|  | Production rate of lactose | 0.020 |
|  | Maximum growth rate of cells | 0.078 |
|  | Saturation constant of glucose | 0.221 |
|  | Inhibition constant of  lactate | 10.954 |

Considering that all the parameters are unknown and all the states are observed, answer the following questions:

1. Analyze the model dynamics with all parameters free. Perform a Monte Carlo analysis and present the following results:

* A plot of the last column of the matrix V,
* The mean absolute value of the last column of V (i.e., mean of |V\_last|),
* The log₁₀ of the singular values obtained during the Monte Carlo simulations.

Based on these results, discuss the identifiability of the model.

Is it necessary to fix one or more parameters to achieve structural identifiability? Justify your answer.

1. Compare the model dynamics with the experimental data. Present the simulation results alongside the experimental data for visual comparison.

Do the model predictions resemble the experimental data? If not, what strategies could be applied to improve the fit between the model and the experimental observations? Provide a brief discussion based on your results.

1. Analyze the model dynamics with one parameter, or a combination of them, fixed. Compare the results with those obtained when all parameters were free.

Does fixing parameters improve structural identifiability or the fit to experimental data?

If not, what alternative strategies could be proposed to improve model performance or identifiability? Justify your answer based on the analysis. Does the model improve the results?

*Note: consider this constants and initial values: .*

# **Erythroblast Growth Inhibition**

Wanika et al. (2024) also based their work of [*Structural and Practical Identifiabilty*](https://jbioleng.biomedcentral.com/articles/10.1186/s13036-024-00410-x) on the earlier work of Glen et al. (2018) which focused on Mechanistic model of erythroblast growth inhibition. In their analysis, Wanika proposed a new version of the original model and performed a comparative evaluation of model performance with and without fixed parameters. Moreover, they used experimental data to verify practical identifiability.

The simplified model is:

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In this model, the parameters are:

|  |  |  |
| --- | --- | --- |
| **Parameter | Unit** | **Description** | **Nominal Value** |
|  | Growth rate | 0.057 |
|  | Inhibitor decay rate | 0.005 |
|  | Inhibitory sensitivity | 2.6 |
|  | Threshold | 3.4 |

Considering that all the parameters are unknown and all the states are observed, answer the following questions:

1. Analyze the model dynamics with all parameters free. Perform a Monte Carlo analysis and present the following results:

* A plot of the last column of the matrix V,
* The mean absolute value of the last column of V (i.e., mean of |V\_last|),
* The log₁₀ of the singular values obtained during the Monte Carlo simulations.

Based on these results, discuss the identifiability of the model.

Is it necessary to fix one or more parameters to achieve structural identifiability? Justify your answer.

1. Compare the model dynamics with the experimental data. Present the simulation results alongside the experimental data for visual comparison.

Do the model predictions resemble the experimental data? If not, what strategies could be applied to improve the fit between the model and the experimental observations? Provide a brief discussion based on your results.

1. Analyze the model dynamics with one parameter, or a combination of them, fixed. Compare the results with those obtained when all parameters were free.

Does fixing parameters improve structural identifiability or the fit to experimental data?

If not, what alternative strategies could be proposed to improve model performance or identifiability? Justify your answer based on the analysis. Does the model improve the results?

*Note: consider these constant and initial values: .*