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A Workflow for Structural Identifiability Analysis in Pumas

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ICC033

What is Structural Identifiability?

Structural identifiability analyzes whether model parameters can be uniquely estimated from input-output data under ideal conditions.

- **Perfect (noise-free) observations**
- **Infinite time horizon**
- **Known model structure**
- **Known initial conditions**

It's **a theoretical property** of the model structure, independent of actual data quality.

Why check for Structural Identifiability?

Identifiability is a **pre-estimation diagnostic that** checks if the data can inform the model

Common Pitfalls Without Analysis

- **Non-Convergence:** Optimizers "wander" or stall in flat likelihood regions.
- **Initial Value Sensitivity:** Different starting points yield different final estimates.
- **Inflated Uncertainty:** Massive RSE% **Implausible Estimates:** To compensate for unresolved parameters.
- **The "Good Fit" Trap:** Accurate predictions from incorrect parameters.

Interpreting the Identifiability

Result	Interpretation
Globally Identifiable	Safe to estimate (unique solution)
Locally identifiable	A finite number of values produce the same output (finite solutions)
Non-identifiable	Cannot estimate (infinite solutions)

Pumas Structural Identifiability Workflow

Step 1. Extract the ODE System using ModelingToolkit

Step 2: Define What Is/Can be Measured

Step 3: Pass ODEsStructuralIdentifiability function

- The core analysis package implements algorithms to determine identifiability [2].

Step 4: Result Organization (DataFrames)

Step 5: Visualization (AlgebraOfGraphics + CairoMakie)

Step 6: Interpret Results

Step 7: Reparameterization: Finding What IS Identifiable

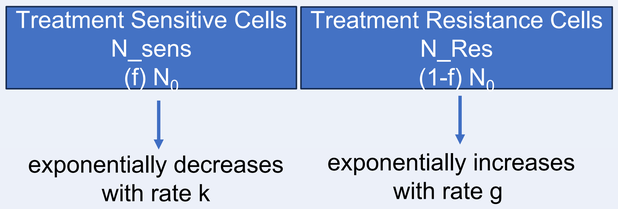
It **acts as a "stress test"** for model equations before parameter estimation phase

Example : 3-Parameter Tumor Burden Model

A patient undergoes chemotherapy for lung cancer, with **tumor size monitored** via CT scans over time.

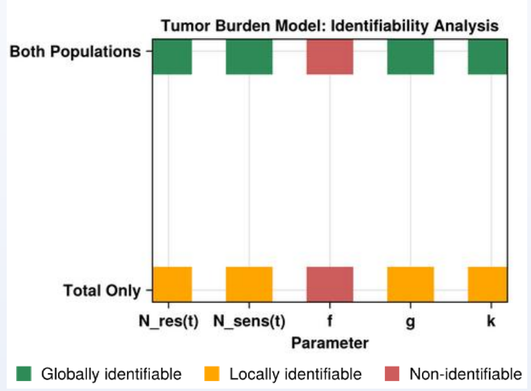
Model [1] describing tumor dynamics during cancer chemotherapy, consists of :

- f — Fraction of cells that are treatment-sensitive (0 to 1)
- g — Growth rate of resistant cells (1/day)
- k — Death rate of sensitive cells under treatment (1/day)



Can rate of cell death (k) and regrowth (g) be **estimated from total tumor size measurements alone**?

Results



Measuring Both Populations

- g and k are **globally identifiable**
- f is STILL non-identifiable

It's a structural issue

Only total tumor burden measured

- g and k are locally identifiable.
- f is completely non-identifiable!

Reparameterization Analysis : What is identifiable ?

- **g - k**: The difference between growth and death rates is identifiable
- **g × k**: The product of growth and death rates is identifiable

Conclusions

- **Identifiable Composites**: g and k are only locally identifiable individually; the net rate difference (g−k) and the geometric mean (g×k) are globally identifiable.
- **Clinical Interpretation:** The net tumor behavior can be determined (overall growth vs. shrinkage) even if the underlying individual rates remain unresolved.
- **Measurement Constraints:** Sensitive and resistant cell fractions (f) remain non-identifiable from total tumor volume alone.

Recommendations

- Build Model → Check for Identifiability → Fix Structural Issues → Estimate.
  - Strategic Reparameterization
  - Incorporate Prior Knowledge
  - Optimize Experimental Design
  - Follow up with practical identifiability on actual data [3,4].

References

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