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► **To cite this version:**

François Lemaire, Louis Roussel. Parameter Estimation with Integral Elimination. Differential Algebra and Related Topics XII, Apr 2024, Kassel, Germany. . hal-04576171

HAL Id: hal-04576171

<https://hal.science/hal-04576171v1>

Submitted on 15 May 2024

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Parameter Estimation with Integral Elimination

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Integral Equation Modeling

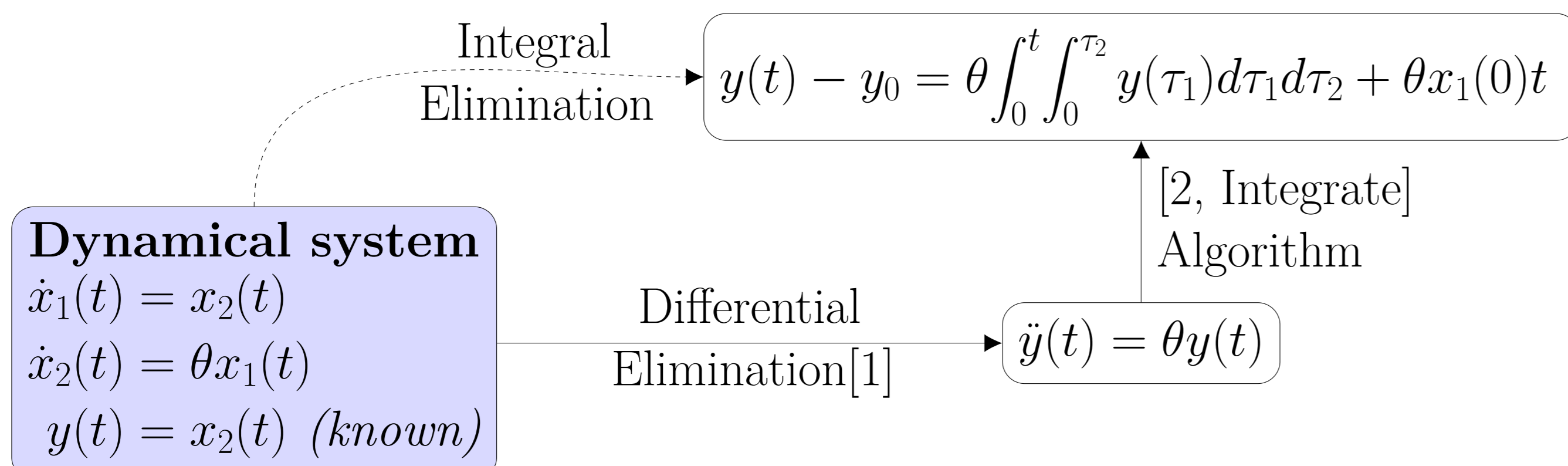


Figure: Modeling, elimination and [2, Integrate] algorithm.

Many models (such as the SIR epidemiology model) consist of non-linear differential equations, involving unknown numerical parameters. Recent work investigates the treatment of integro-differential equations i.e. equations involving both derivation and integration operators. The introduction of integral equations helps to increase the expressiveness of the models, improve the estimation of parameters and reduce the size of the intermediate equations.

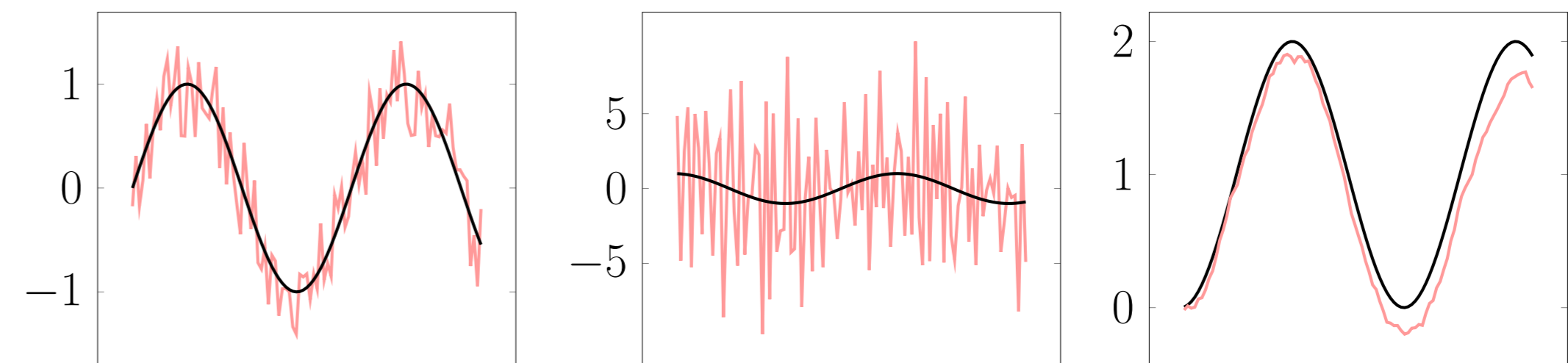
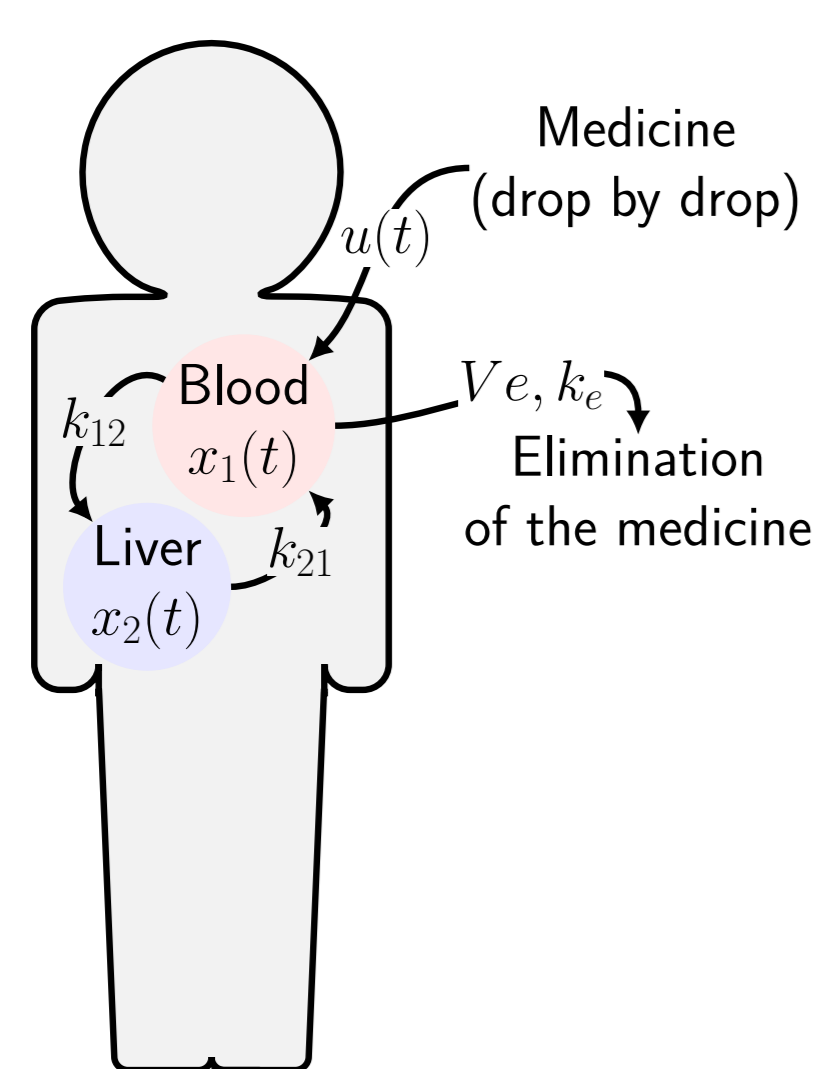


Figure: A signal, its derivative and its integral (with noise in red).

Experiment and Method



$$\begin{cases} \dot{x}_1(t) = -k_{12}x_1(t) + k_{21}x_2(t) - \frac{V_e x_1(t)}{k_e + x_1(t)} + u(t) \\ \dot{x}_2(t) = k_{12}x_1(t) - k_{21}x_2(t) \\ y(t) = x_1(t) \end{cases}$$

- $u(t)$: medicine (drop by drop). We simplify by taking $u(t) = 0$.
- $x_1(t)$: amount of medicine in the blood (known and noisy).
- $x_2(t)$: amount of medicine in the liver (unknown).

Goal: Compare the quality of estimation between integral (with exponentials) I/O equations and differential I/O equations on the academical example

- 1 Consider 5 different I/O equations
- 2 Generate noisy solutions $y(t)$ from chosen parameter values
- 3 For each I/O equation p : Estimate the parameter values by minimizing the following error using CMA-ES [4] optimization algorithm.

$$E(k_{12}, k_{21}, k_e, V_e) = \frac{1}{N} \sum_{i=0}^{N-1} p(t_i)^2$$

We used a 4 points scheme to estimate the signal derivatives and the Simpson rule for estimating integrals.

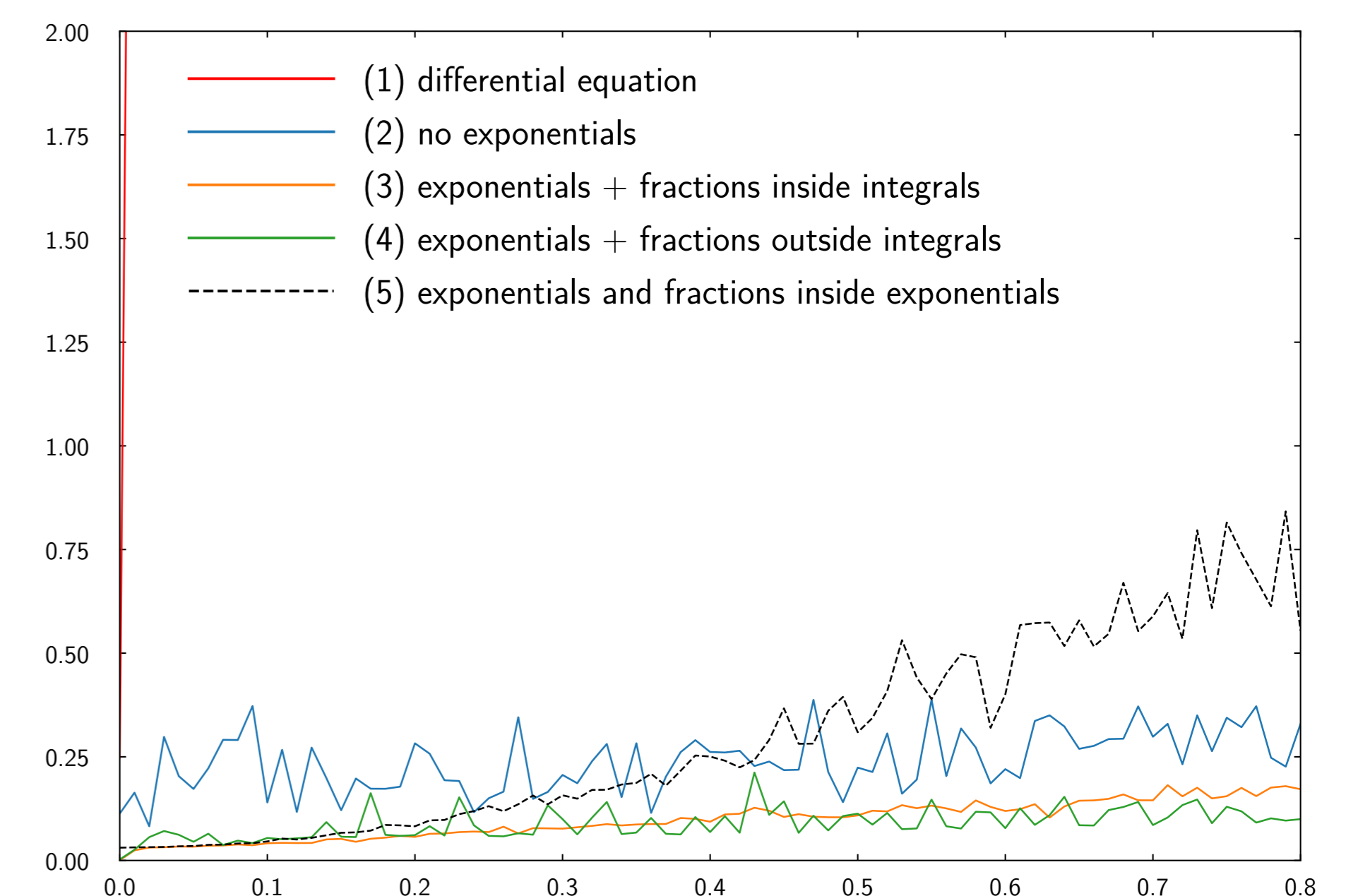
Parameter estimation:

Compute the parameter values from experimental data

Results

- (1) $V_e k_{21} k_e y + V_e k_{21} y^2 + V_e k_e y + k_{12} k_e^2 y + 2k_{12} k_e y y + k_{12} y^2 y + k_{21} k_e^2 y + 2k_{21} k_e y y + k_{21} y^2 y + k_e^2 y + 2k_e y y + y^2 y$
- (2) $k_{21} V_e \int \frac{y}{k_e + y} + (k_{12} + k_{21}) \int (y - y_0) - V_e \int \left(\frac{y}{k_e + y} - \frac{y_0}{k_e + y_0} \right) - y_0 t + y - y_0$
- (3) $-y + y_0 - k_{12} \int y - \int \frac{V_e y}{k_e + y} + \left(\frac{V_e y_0}{k_e + y_0} + y_0 + k_{12} y_0 \right) \int e^{-k_{21} t} + k_{21} k_{12} \int \left(e^{-k_{21} t} \int e^{k_{21} t} y \right) - y^2 + y_0^2 - 2k_e y + 2k_e y_0 - 2k_e k_{12} \int y - 2k_{12} \int y^2 - 2V_e \int y + 2k_e \left(\frac{V_e y_0}{k_e + y_0} + y_0 + k_{12} y_0 \right) \int e^{-k_{21} t}$
- (4) $+ 2 \left(\frac{V_e y_0}{k_e + y_0} + y_0 + k_{12} y_0 \right) \int y e^{-k_{21} t} + 2k_e k_{21} k_{12} \int \left(e^{-k_{21} t} \int e^{k_{21} t} y \right) + 2k_{21} k_{12} \int \left(y e^{-k_{21} t} \int e^{k_{21} t} y \right)$
- (5) $-y e^{\int (k_{12} + \frac{V_e}{k_e + y})} + y_0 + \left(\frac{V_e y_0}{k_e + y_0} + y_0 + k_{12} y_0 \right) \int e^{\int (k_{12} + \frac{V_e}{k_e + y})} e^{-k_{21} t} + k_{12} k_{21} \int \left(e^{\int (k_{12} + \frac{V_e}{k_e + y})} e^{-k_{21} t} \int e^{k_{21} t} y \right)$

Figure: Estimation of parameters k_{12} , k_{21} , V_e , k_e and y_0 (for integral equations). On the x-axis, the standard deviation σ used to produce the white gaussian noise added to the signal $y(t)$. On the y-axis, the average value, for 50 different simulations, of the relative error.



Example Treated with our Integral Elimination Prototype

$$\begin{cases} \dot{S} = \mu - \beta_I S I - \beta_W S W - \mu S + \alpha R \\ \dot{I} = \beta_W S W + \beta_I S I - \gamma I - \mu I \\ \dot{W} = \zeta (I - W) \\ \dot{R} = \gamma I - \mu R - \alpha R \\ y_1 = \kappa I \end{cases}$$

Differential I/O equation:

- I/O differential equation and identifiability studied in [3] using StructuralIdentifiability package in Julia.
- 9Mo: Sum of 209 350 terms containing y_1^{10} , \dot{y}_1^{10} , \ddot{y}_1^8 , \ddot{y}_1^5 , \ddot{y}_1^4

The integral I/O equation is much smaller:

$$\begin{aligned} & -\alpha \beta_W \gamma \zeta \int (u_{i0} u_{i2} \int v_{i0} y_1 \int u_{i1} v_{i2} \int v_{i1} y_1) - \alpha \beta_I \kappa r_0 \int (u_{i2} y_1 \int u_{i1} v_{i2}) - \alpha \beta_W \gamma \kappa w_0 \int (u_{i0} u_{i2} \int u_{i1} v_{i2} \int v_{i1} y_1) \\ & - \beta_I \kappa \mu \int (u_{i2} y_1 \int v_{i2}) - \alpha \beta_W \gamma \zeta \int (u_{i0} u_{i2} \int u_{i1} v_{i2} \int v_{i0} y_1) - \beta_W \kappa \zeta s_0 \int (u_{i0} u_{i2} \int v_{i0} y_1) - \alpha \beta_W \kappa^2 r_0 w_0 \int (u_{i0} u_{i2} \int u_{i1} v_{i2}) \\ & - \alpha \beta_W \kappa \zeta r_0 \int (u_{i0} u_{i2} \int u_{i1} v_{i2} \int v_{i0} y_1) - \alpha \beta_W \kappa \zeta r_0 \int (u_{i0} u_{i2} \int v_{i0} y_1 \int u_{i1} v_{i2}) - \beta_W \kappa^2 s_0 w_0 \int (u_{i0} u_{i2}) - \beta_W \kappa^2 \mu w_0 \int (u_{i0} u_{i2} \int v_{i2}) \\ & - \beta_W \kappa \mu \zeta \int (u_{i0} u_{i2} \int v_{i0} y_1 \int v_{i2}) - \alpha \beta_W \gamma \zeta \int (u_{i0} u_{i2} \int u_{i1} v_{i2} \int v_{i0} y_1 \int v_{i1} y_1) - \beta_I \kappa s_0 \int (u_{i2} y_1) - \beta_W \kappa \mu \zeta \int (u_{i0} u_{i2} \int v_{i2} \int v_{i0} y_1) \\ & - \alpha \beta_I \gamma \int (u_{i2} y_1 \int u_{i1} v_{i2} \int v_{i1} y_1) + \gamma \kappa \int (y_1) - \kappa^2 I_0 + \kappa \mu \int (y_1) + \kappa y_1 = 0 \end{aligned}$$

$$\begin{cases} v_{i0} = e^{\zeta} \int 1 \\ v_{i1} = e^{(\alpha + \mu) \int 1} \\ v_{i2} = e^{(\mu \int 1 + \frac{\beta_I}{\kappa} \int y_1 + \frac{\beta_W}{\kappa} \int y_1 - \frac{\beta_W}{\kappa} e^{-\zeta \int 1} (\int y_1 e^{\zeta \int 1}))} \\ \quad \times e^{(\frac{\beta_W w(0)}{\zeta} - \frac{\beta_W w(0)}{\zeta} e^{-\zeta \int 1})} \\ u_{i0} v_{i0} = u_{i1} v_{i1} = u_{i2} v_{i2} = 1 \end{cases}$$

Conclusion

The experiment shows that modeling with integral equations seems promising for parameter estimation even with equations involving exponentials. We obtained promising results on non-trivial examples with our integral elimination prototype.

This work has been partially supported by the THIA ANR Program « AI_PhD@Lille », from the French National Research Agency, grant ANR-20-THIA-0014.

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