SI

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1 Introduction

1.1 About structural identifiability

The aim of this research project is to study the structural idendentifiability of models composed by a sistem of ODEs. In the general framework, we have:

$$\begin{cases} \mathbf{x}'(t) = f(\mathbf{k}, \mathbf{x}(t), \mathbf{u}(t)) \\ \mathbf{y}(t) = g(\mathbf{k}, \mathbf{x}(t), \mathbf{u}(t)) \end{cases} . \tag{1}$$

where $\mathbf{x}$(t) are the state variables (a priori unknown), f and g some rational functions (known), $\mathbf{k}$ the parameters (unknown), $\mathbf{u}$(t) the input variables (known) and $\mathbf{y}$(t) what we can measure, called the output variables. Given a possible solution of the model, an output preserving transformation is another solution of the model with possible different parameters and state variable functions. Being a solution of the model implies that the output ($\mathbf{y}(t)$, i.e. what we can observe, remains the same, so a priori we cannot say which solution is the correct one, that is, which solution truly describes what is happening in the system the model is trying to explain.

We say that a parameter k is identifiable if its value can be determined from $\mathbf{y}$(t) and $\mathbf{u}$(t) for generic values of $\mathbf{k}$ and initial conditions. In particular, k is globally identifiable if it is uniquely determined, while it is locally identifiable if it is determined up to finitely many values.

1.2 StructuralIdentifiability.jl

Throughout the project, we will use the StructuralIdentifiability Julia package, which contains functions such as $assess\_identifiability$, that identifies, for a given model, if each parameter is globally identifiable, locally identifiable or non-identifiable, or $find\_identifiable\_functions$, that, for a given model, find the functions that are invariant for an output preserving transformation.

1.3 Two compartments model

We start by doing an example of a simple linear model which is not uniquely identifiable. Consider

$$\begin{cases} x_1'(t) = -ax_1(t) + bx_2(t) \\ x_2'(t) = -bx_2(t) \\ y(t) = x_1(t) \end{cases} . \tag{2}$$

We can see this system as a model for two compartments, where the water flows from the second to the first at a rate $bx_2(t)$ and then it flows outside the first at a rate $ax_1(t)$. The only thing we can measure is the level of water in the first compartment and we want to find the parameters a, b and the level of water in the second in function of the time. Using $assess\_identifiability$ we find that both a and b are locally identifiable, while using $find\_identifiable\_functions$ we find that the identifiable functions are $a + b$ and $a \times b$. From this we deduce that, if (a, b) are valid parameters, then the only possible transformation is (b, a). The question we pose is: if the first solution is given by the set of initial conditions/parameters (x_1*, x_2*, a, b), then, what are the possible values for the initial condition $\widetilde{x_2}*$ associated with the new parameters $\widetilde{a} = b$ and $\widetilde{b} = a$ In this case, we can easily solve the system of ODEs, since it is linear, knowing that the solution is $\mathbf{x}(t) = e^{At}\mathbf{x}(0)$, where A is the matrix that describes the system. In order to find e^{At} we just need to diagonilize A and we have $e^{At} = Se^{Dt}S^{-1}$, where S is the matrix made of the eigenvectors of A. Now, since we want that the output is preserved, we impose that $x_1(t) = \widetilde{x_1}(t)$, where the latter is the solution of the ODE with inverted parameters. In this equation the time dependence cancels out and therefore we can solve for the only parameter $\widetilde{x_2}*$, obtaining $\widetilde{x_2}* = \frac{a}{b}(x_1 * + x_2*) - x_1*$.
Another possible and more general way to solve it, would be to use the power series expansion of $x_1(t)$ and $\widetilde{x_1}(t)$ centered at 0, and then find in this case $\widetilde{x_2}*$ that sets the derivatives equal. This can be done by getting recursively the derivatives from what we have in the system. In this case, it is sufficient to get only the first derivative, imposing $-ax_1 * + bx_2* = -bx_1 * + a\widetilde{x_2}*$ and then getting the same result as before. This implies that this relation is a necessary condition, and we should check ??? numerically ??? that it indeed gives the same output $x_1(t)$ (otherwise we are not sure about the equality of the higher order derivatives).

1.4 Epidemics with treatment

We now consider a more complex model,an epidemics which incorporates the strategies applied for disease control, such as quarantine or vaccination. The total population N(t) is divided into susceptible S(t), infectious I(t), and recovered R(t). Moreover T(t) represents the number of people under treatment meauseres. Since R(t) can be easily deduced from $N(t) - S(t) - I(t)$ we don't consider it in the analysis. The output variables are instead N and T. Therefore, our model is:

$$\begin{cases} S' = -\beta\frac{IS}{N} - \beta\delta\frac{ST}{N} \\ I' = \beta\frac{IS}{N} + \beta\delta\frac{ST}{N} - (\alpha+\gamma)I \\ T' = \gamma I - \nu T \\ N' = 0 \end{cases}. \tag{3}$$

We can use now $find\_identifiable\_functions$, with the parameter $with_states = true$ in order to find the invariants of the model that consider also the state variables. We find 8 invariants (notice that we have 9 parameters), that are: $N, T, \gamma S, \beta S, \nu+\delta\gamma, \nu+\gamma+\alpha, \gamma I+\gamma T+\alpha T$. We write the system of eight equations poning, for each invariant, invariant(original parameters) = invariant(new parameters); we can already notice that we may have a degree of freedom for the output preserving transformations, we have one variable more than the number of equations. We can try to solve the system and, from the equations related to $\nu+\delta\gamma$ and to $\nu+\gamma+\alpha$, multiplying the second one by $\widetilde{\nu}$ (we are assuming it is different from 0 for now) and subtracting the first from the second, we obtain a quadratic equation in $\widetilde{\nu}$ which give us two possibilities: either $\widetilde{\nu} = \nu$ or $\widetilde{\nu} = \alpha+\gamma$. We solve the system in the two cases and we obtain two families of