Review: To be or not to be an identifiable model. Is this a relevant question in animal science modelling?

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**Supplementary material S1**

**Three methods for performing structural identifiability analysis of dynamic models**

This section describes briefly three methods for testing structural identifiability in dynamic models. Consider the model described by the following ordinary differential equations

(1)

where is the time, is the vector of state variables, is the vector of model observables, and isthe vector of external stimuli (input vector). The equations contain a set of parameters defined by the vector, and **f,** **g** are vector functions.

*Laplace Transform*

If the model in Eq. (1) is linear, a classical approach for testing its structural identifiability is via the analysis of the transfer function of the model resulting from the Laplace transformation ([Bellman and Astrom, 1970](#_ENREF_1)). The transfer function matrix is defined by

(2)

where is the argument of the Laplace domain, and are the Laplace transforms of the observables () and inputs ().

Once is written in canonical form, we can proceed to write the transfer function matrix for two parameters sets . Further, by establishing the relation we can derive a set of equations translating the identities of the coefficients of and .

If the solution for the set of equations is unique for , that is , the model is structurally identifiable.

For illustration, let us consider the following single-input and single-output (SISO) model

(3)

with parameters and the input . The observable is the state variable . By applying the Laplace transform, we obtain

(4)

where correspond respectively to the state variable and the input variable in the Laplace domain. The model observable in the Laplace domain is . The transfer function is given by

(5)

The identity equations are

(6)

(7)

From Eq. (6) and Eq. (7), we can conclude that the parameter is uniquely identifiable while the parameters are nonidentifiable since Eq. (7) have infinite solutions.

Many examples of identifiability analysis for linear compartmental models are presented in [Carson *et al.*, 1983](#_ENREF_2).

*Taylor series expansion*

This approach was developed by [Pohjanpalo, 1978](#_ENREF_5). It assumes that the vector functions **f,** **g** in Eq. (1) are continuously differentiable in their arguments, implying that the state and the observable vectors can have infinitely many time derivatives. The development of the Taylor series of the observable in the model described by Eq. (1) results

(8)

Let us denote

(9)

Since the observable vector is a unique function of time, all its derivatives () are unique and known. The structural identifiability of the model is determined from the analysis of the equations of the successive derivatives evaluated at two parameters sets . The model is structurally identifiable if

(10)

where is at least the number of unknown parameters.

As example, consider the following model

(11)

With parameters and the input . The model has two state variables and one observable that corresponds to the state variable . By developing the successive derivatives of , we obtain

(12)

(13)

(14)

The model is globally identifiable. The parameter can be uniquely obtained from the coefficient , and subsequently can be uniquely recovered from .

*Generating series*

This method was developed by [Walter and Lecourtier, 1982](#_ENREF_7) and it is conceptually similar to the Taylor series approach. Consider the model described by the following ordinary differential equations

(15)

where () and **g** are analytic, implying that the model observables can be expanded in series with respect to time and the model inputs. The coefficients of the series are and the successive Lie derivatives evaluated at

(16)

where is the Lie derivative of **g** along **f**, defined by

(17)

with the number of state variables.

Analogous to the Taylor series, let the vector of the series coefficients. The model is structurally identifiable if ([Walter and Pronzato, 1996](#_ENREF_8)).

(18)

As example, consider again the model in Eq. (11), which can be written as

(19)

where , ,

The first Lie derivative operators are

(20)

(21)

The coefficients of the series are the following Lie derivatives

(22)

(23)

From the coefficient in Eq. (22), it is deduced that is identifiable. From Eq. (23), we obtain that is identifiable.

Finally, the interested reader is referred to recent literature on structural identifiability methods and their comparison ([Chis *et al.*, 2011](#_ENREF_3); [Miao *et al.*, 2011](#_ENREF_4); [Raue *et al.*, 2014](#_ENREF_6)).

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