S4 Text. Definition and algorithm for identifiability analysis.

Structural identifiability

Suppose we are given a dynamical system of the following abstract form

\[ \frac{dX}{dt} = f(X(t), \Theta, u(t)) \]
\[ y(t) = g(X(t), \Theta, u(t)), \] (1)

where \( X = (X_1, \cdots, X_n) \) represents the state variables, \( y = (y_1, \cdots, y_m) \) represents the observables, \( \Theta = (\theta_1, \cdots, \theta_k) \) contains the parameters to identify, and \( u(t) \) represents the input variable to the system. A parameter set \( \Theta \) is called structurally identifiable if

\[ g(X(t), \Theta, u(t)) = g(X(t), \Phi, u(t)) = \Phi \] (2)

for every \( \Phi = (\phi_1, \cdots, \phi_k) \) in the same space as \( \Theta \). A single parameter \( \theta_i \in \Theta \) is called structurally identifiable if

\[ g(X(t), \Theta, u(t)) = g(X(t), \Phi, u(t)) \implies \theta_i = \phi_i. \] (3)

The structural identifiability, defined above, is referred to as global identifiability in [1–4]. Global identifiability is stronger than the so-called local identifiability, which only requires Eq. (2) or Eq. (3) to hold in a neighbourhood \( \mathcal{N}(\Theta) \) of \( \Theta \). Structural identifiability analysis is usually conducted before the fitting of the model and it does not rely on any data. We perform the structural identifiability analysis using the software SIAN [56], which is based on differential algebra and Taylor series expansion. Detailed documentations on the theory behind the software can be found in [5], and information regarding the algorithm can be obtained from [6]. We also checked structural identifiability using the software GenSSI 2.0 [7], which is based on the Lie derivatives of ODE models.

Practical identifiability and correlation matrix

A parameter is called practically identifiable if it can be uniquely determined from the discrete data points instead of the structure of the equation. A structurally identifiable parameter may not be practically identifiable given the noise and limited measure points in the data. Unlike structural identifiability, there is no consistent definition of practical identifiability in the literature. Nevertheless, several methods including correlation matrix methods have been proposed to describe practical identifiability quantitatively [8, 9].

Statistical correlation can be used to describe some of the practical non-identifiability phenomena. Specifically, one can use the Fisher Information Matrix (FIM) to calculate the correlation matrix of \( \Theta \) in Eq. (1). FIM is defined as:

\[ F = \sum_{i=1}^{T} S_i^T V^{-1} S_i, \] (4)

where \( V \) is covariance matrix of the measurements error. \( S_i = \frac{\partial \tilde{y}(t_i)}{\partial \Theta} \) is the sensitivity matrix at time \( t_i \), which can be calculated by solving the adjoint equation:

\[ \frac{dS_i}{dt} = \frac{\partial g(X(\cdot), \Theta)}{\partial X}(t_i) S_i + \frac{\partial g(X(\cdot), \Theta)}{\partial \Theta}(t_i) \] (5)

using automatic differentiation libraries. It is proved that the correlation matrix is equal to \( F^{-1} \) by the Cramér–Rao theorem [10]. Once the correlation matrix is obtained, one
can determine whether a parameter is identifiable by checking whether it is correlated with the other parameters. If $\theta_i$ is strongly correlated with $\theta_j$, then neither of these parameters is practically identifiable because they cannot be uniquely determined from the data.

References


