HOW TO PREPARE THE INPUT FILE OF DAISY FOR CHECKING IDENTIFIABILITY

In the directory MOD, available to the user, there are some examples of DAISY input files together with their corresponding output files.

The user can use these input files as templates.

Case 1: No initial conditions are given (i.e. identifiability with generic initial conditions)

ATTENTION: users of the previous version of DAISY, just need to complete the input file by adding the TWO red lines found below.

Open a text file and write the following instructions in **bold**.
Comment lines are labeled with %.

WRITE "MODEL OF …"$

% B_ is a reserved name used to denote the vector of the (non constant) input, output and state variables. Note that the components should be ordered as follows: first the input and then the output followed by the states. Names of the variables can be freely chosen by the user. For example:

B_:={u1, y1, y2, x1, x2}$

% The following instruction defines the components of vector B_ as time-depending variables:

FOR EACH EL_ IN B_ DO DEPEND EL_,T$

% Please note: Constant inputs must not be listed in vector B_, but directly included in the model equations.

% B1_ is a reserved name used to indicate the vector of unknown parameters. For example:

B1_:={p21, p12, vmax, km}$

% If there are constraints relating the parameters or some parameters are known, instructions such as "LET" can be used and the user must delete from vector B1_ the known or constrained parameters. For example:

LET p12=p21$ %then vector B1_ becomes **B1_={p21, vmax, km}**

% or, if p12 is known:

LET p12=alpha$** (or **let p12=5$) %then vector B1_ becomes **B1_={p21, vmax, km}**

% Please note:
a) only integer values are allowed

b) If constraints as, for example, p12=p21=km are present, these must be inserted as follows:

LET p12=p21, km=p21$ %(then vector B1_ becomes **B1_={p21, vmax})**

% NU_, NY_ and NX_ are reserved to indicate the number of inputs, outputs and states included in vector B_. Thus the number of the B_ components should be equal to NU_ + NY_ + NX. For example:

NU_:=1$
NY_:=2$
NX_:=2$

% Please note: if the model has no input just write **NU_:=0**.

% C_ is a reserved variable name used to indicate the system of **POLYNOMIAL or RATIONAL** first order differential equations describing the model:

C_:={df(x1, t)=-(p21+vmax/(km+x1))*x1+p12*x2+u1,
df(x2, t)=p21*x1-p12*x2,
y1=x1,
y2=x2}$

% Note that algebraic (i.e. non differential) equations are allowed. In this case the additional algebraic variables have also to be included in the B_ vector and the number NX_ has to be correctly incremented.

% Choose an integer value (seed_) >> of the number of unknown parameters. The subroutine "random" will choose, in a random way in the interval [1, seed_], the numerical values corresponding to each component (model unknown parameter) of vector B1_. % For example:

SEED_:=35$

% Invoke the procedure that calculates the characteristic set:

DAISY()$

% Complete the input file with:

END$

% No comment lines can be written after the end of the file.

WARNING

1. Names of the variables reserved for the REDUCE language cannot be used for defining the variables of the above input file.
2. To verify the genericity of the vector parameter value, the user has to repeat the test by starting from different seed values.

Case 2: identifiability with given (known) initial conditions

DAISY can be used to check the identifiability of the model by including, when available, the known values of some, or all, initial conditions.

In principle this requires to verify an additional structural property of the model: the *accessibility from the given initial conditions* [2]. To check accessibility the model should be affine in the input function [3]. This is verified in many biological models where the input usually appears additively.

A system which is accessible from the given initial conditions poses no problem and can be dealt with according to the instructions described below.

In particular, after calling the procedure "DAISY()$" (before the instruction "END$" in the end line), the **numerical (integer) or symbolic**[1] values of the given initial conditions must be inserted with instructions such as "IC:=…" and the subroutine CONDINIZ needs to be called.
The complete instruction, for our example, is:

IC_:={ X1=a, X2=3}$

CONDINIZ()$

% Please note that, in general, it is not necessary to provide all the initial conditions values, but only some of them. If the user provides the initial conditions of only some of the state variables, DAISY will automatically provide the missing initial conditions of the state variables xi by assigning them an unknown symbolic value xi_0**.**

% Please note that in case of algebraic-differential model, the user must assign to ALL initial conditions a known value, not only to some of them. These known values must satisfy the algebraic equation of the model at time 0.

% Complete the input file with:

END$

% Remember that no comment lines can be written at the end of the file.

Call this file e.g. EXAMPLE-IC.TXT and save it in C:\MOD\.

Note that if the system is not accessible from the given initial conditions, the user may have to implement a model reduction procedure to arrive at a reduced model which is accessible from the given initial conditions. Suggestions on how to deal with this case are reported in the APPENDIX.

[1] If the user only assumes known the initial condition, but without fixing a specific value.

APPENDIX: Model accessibility from given initial conditions

This Appendix provides some rudimentary notions which should help the reader understanding what may go wrong when the system is started from given initial conditions (i.e. from non generic initial conditions).

The user not interested in these details may safely skip it.

Accessibility from a given initial state, is a concept of geometric nonlinear control theory. For a formal treatment of this concept see [3]. It means that from a given initial state one can reach, by using suitable input functions, all points in an open sphere of full dimension *n* in the state space.

If the system is accessible from the given initial condition, the space where the state trajectories evolve cannot be shrunk or reduced. In other words the *dimension* of the model cannot be reduced.

Non accessible systems can be of two kinds:

1. *Systems which are not accessible from some initial state*: then there must be a lower dimensional algebraic manifold in the state space containing the initial conditions and the state evolution must take place on this manifold. This submanifold is described by algebraic equation(s) which should be added to the set of differential equations of the original system (which will then describe a manifold of solutions of smaller dimension). DAISY run on this enlarged set of equations and provides the correct identifiability results.
2. *Systems which are globally non-accessible*: i.e. one can never reach all states in a sphere of full dimension *n no matter where it is started from*. In this case some differential equations of the system are redundant irrespective of initial conditions; i.e. some equations are combinations of the others and the actual dimension of the system is smaller than the number of original differential equations. In this case, if the system is accessible from initial conditions belonging to the submanifold of the actual dimension of the system, there are no problems in verifying identifiability [4]: DAISY run on the set of the original model differential equations and provides the correct identifiability answer; if the system is

not accessible from initial conditions belonging to this submanifold, the algebraic equation(s) describing it should be added to the set of differential equations of the original system, as in case 1.

For systems globally non-accessible however it is often possible to define a more parsimonious model with fewer state variables. In particular, the user can manipulate the model to derive a static *algebraic* (non-differential) set of equations relating the state and (possibly) input variables. This set of algebraic equations describes the submanifold in the n-dimensional space, where *all* possible solutions of the system must evolve. Often the reduced (algebraic differential) model can be found by inspection. Systematic procedures to find it are described in [3].

Note that an algebraic differential system is always globally non-accessible, since the algebraic (non-differential) equations of the system describe a submanifold in the n-dimensional space, where all possible solutions of the system must evolve. In this case, as already written in the above input file instructions, one should just check that the given initial conditions values satisfy the above algebraic set of equations (i.e. the initial state actually belongs to the submanifold).

REFERENCES

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3. Sontag ED (1998) Mathematical control theory. 2nd edn. Springer, Berlin.
4. D'Angiò, L., Saccomani, M.P., Audoly, S., G. Bellu. Identifiability of nonaccessible nonlinear systems. In Positive Systems, Lecture Notes in Control and Information Sciences, R. Bru, S. Romero-Vivó, Eds., Springer-Verlag, Berlin Heidelberg, Germany, 389:269-277, 2009. DOI: 10.1007/978-3-642-02894-6_26.