

# SUPPLEMENTARY INFORMATION

## DETAILED INSTRUCTIONS ON SETTING UP THE COPASI GUI FOR PROFILE LIKELIHOOD CALCULATIONS

- 1) Perform parameter estimations using COPASI.
  - a. Configure the 'Parameter Estimation' task as shown in Figure S1.
  - b. Map variables to experimental data file (Figure S2). Example data file is shown in 'Data.txt'.
  - c. Define a report to collect the parameter estimates and SSR values (Figure S3 and S4)
  - d. Create a repeat item in the scan task to perform multiple parameter estimations as per the instructions in Figure S5. The output should be a parameter estimation results file. The absolute path to this file can be used as input to the keyword argument 'result\_files' of the `pydentify.Multi_Profile_Likelihoods` class.
  - e. To speed the estimation process, several identical COPASI files can be setup with different report file names and run simultaneously. These data files can be placed in a subfolder on their own and the absolute path to this folder can be used as input to the `results_dir` keyword argument of the `pydentify.Multi_Profile_Likelihoods` class.

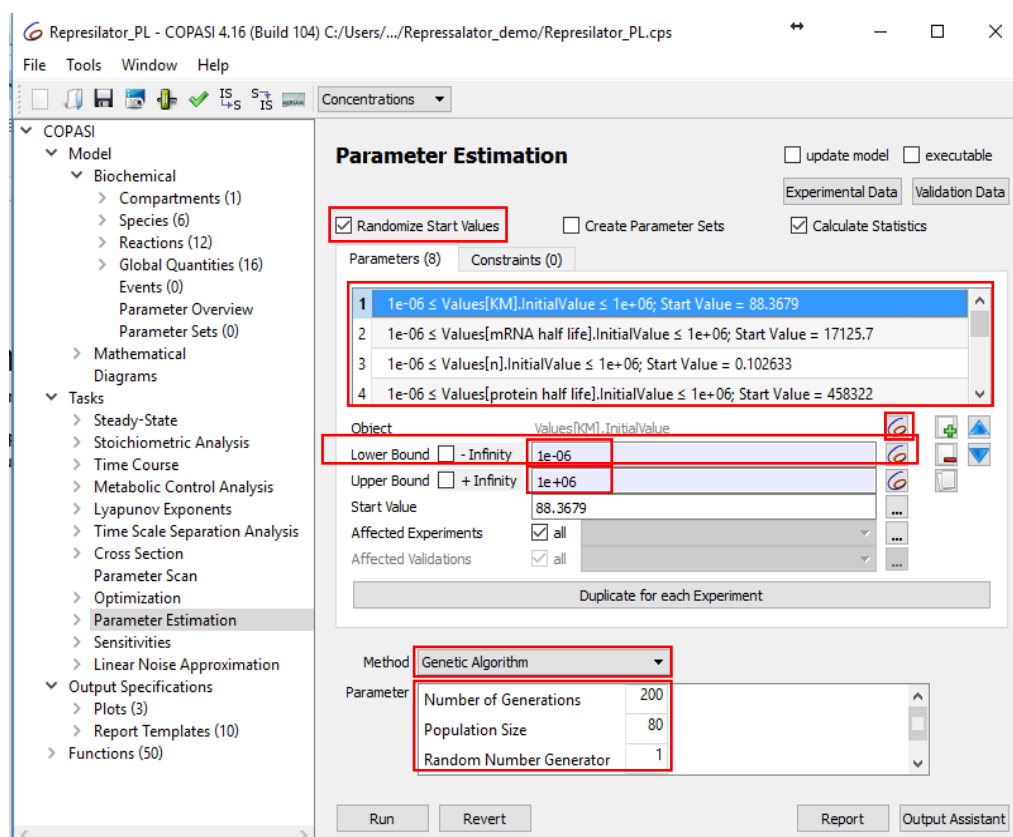


Figure S1: Configure COPASI for parameter estimation. 1) Choose estimated variables from the list given by pressing the COPASI icon by the 'Object' box. Select 'Randomize Start Values'. 2) Choose upper and lower boundaries for the optimization of each parameter; 3) pick a global optimization algorithm and set optimization parameters for that algorithm (algorithm details are in the COPASI manual).

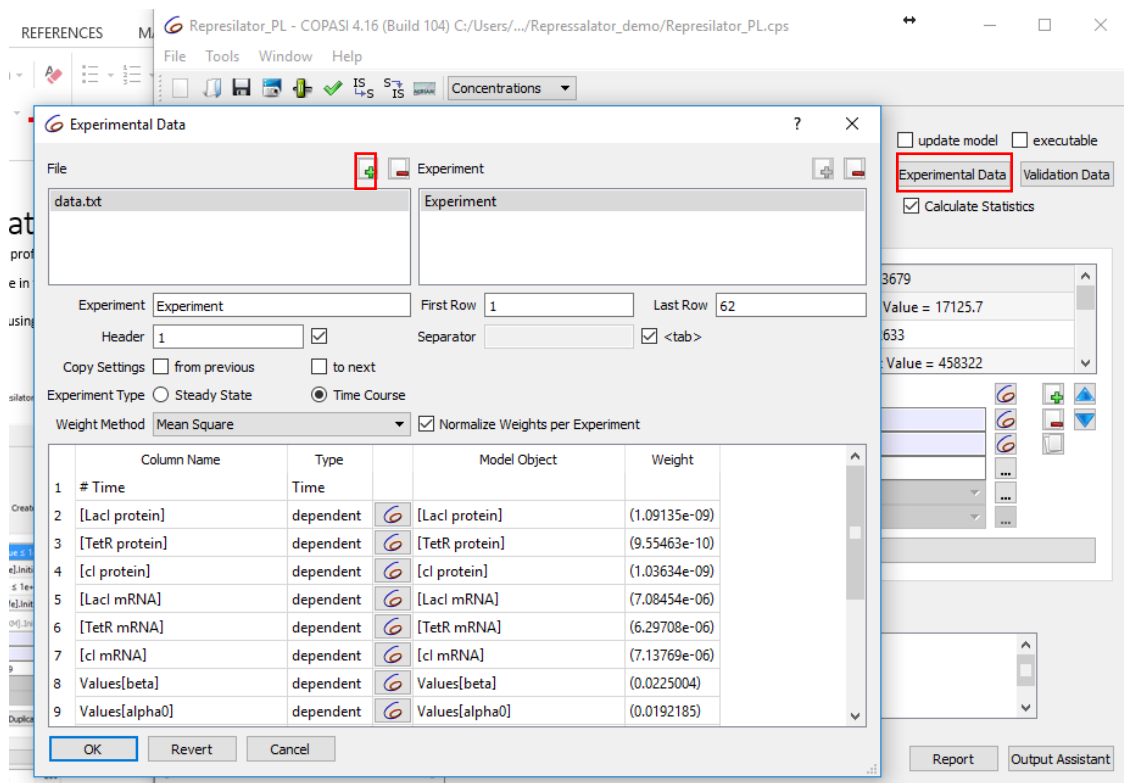


Figure S2: Mapping data to variables. Click the 'Experimental Data' button, then the green cross to select a data file and map variables to experimental data.

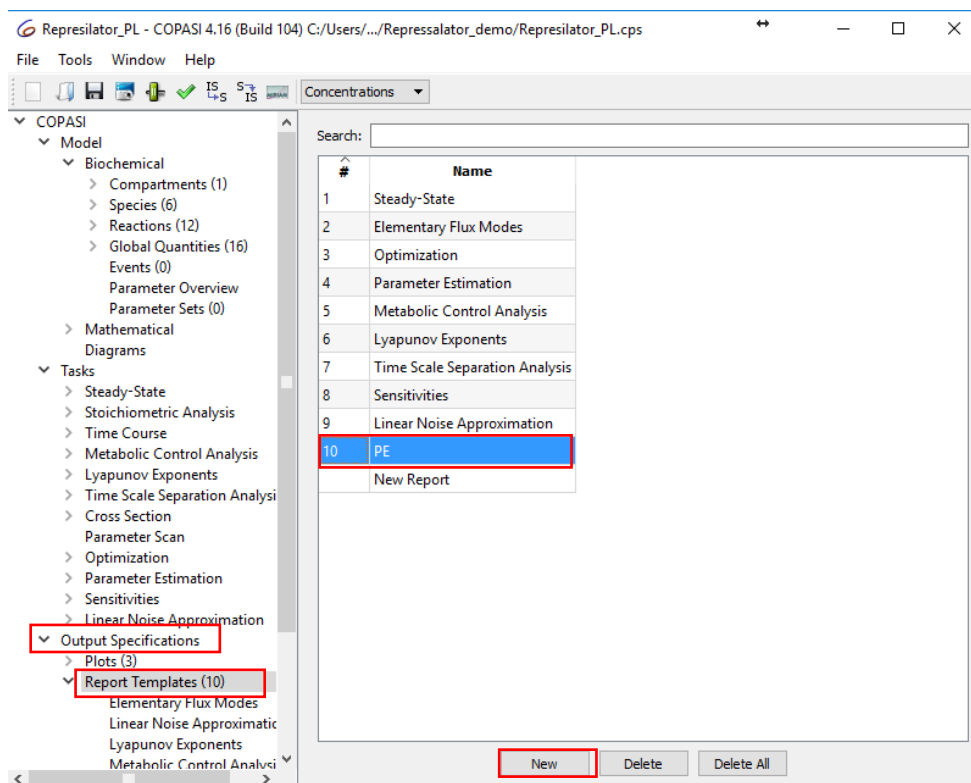


Figure S3: Create new report. Go to 'Output Specifications' then 'Report Templates'. Select 'New' name the report.

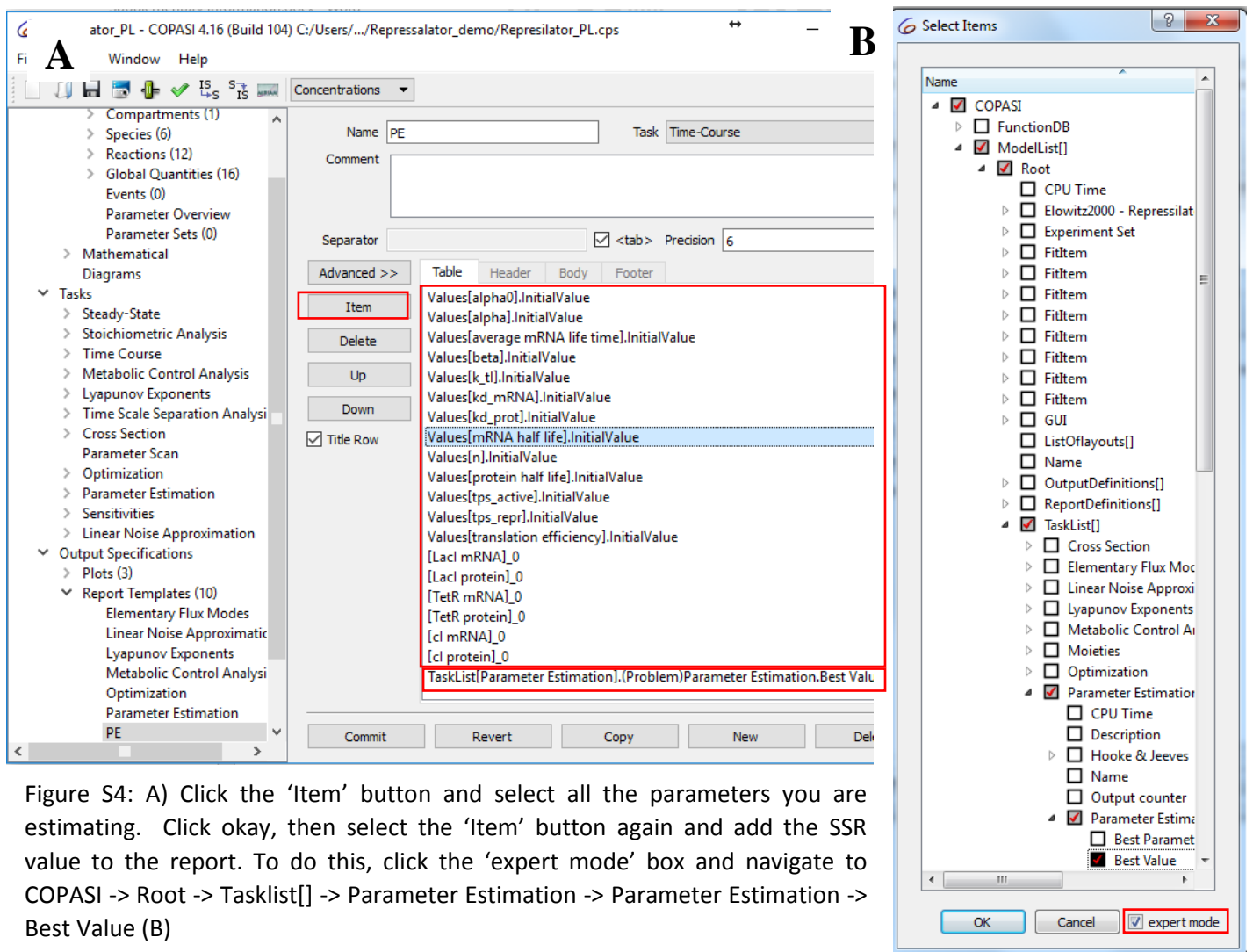


Figure S4: A) Click the 'Item' button and select all the parameters you are estimating. Click okay, then select the 'Item' button again and add the SSR value to the report. To do this, click the 'expert mode' box and navigate to COPASI -> Root -> Tasklist[] -> Parameter Estimation -> Parameter Estimation -> Best Value (B)

- 2) Make a copy of your COPASI file and put it in a subdirectory with the data files used for estimation. Ensure no other text files are present in this directory.
- 3) Rename your reactions  $v_1, \dots, v_p$  for  $i = 1$  to number of parameters ( $p$ ) (Figure S6). This is a requirement if you are estimating local parameters (i.e. those not defined in the global variables).
- 4) Create a new report from COPASI's 'output specifications'. Name it 'LikelihoodProfile' as shown in Figure S7). This time the report should contain two items, a single arbitrary estimated parameter and the SSR (best value) (SSR location described in Figure S4B)
- 5) Set up the parameter estimation task as shown in Figure S8.
- 6) Set up the scan task as shown in Figure S9.

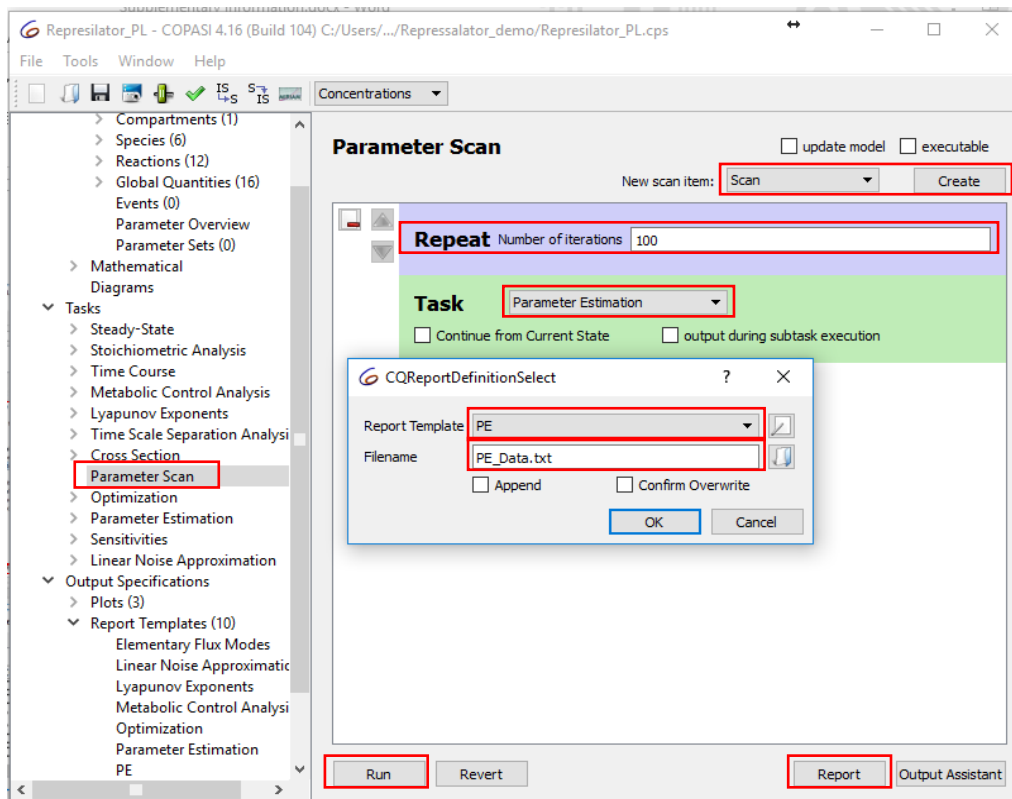


Figure S5: Configure scan task to run multiple parameter estimations. Select 'Repeat' from drop down list labelled 'New scan item' and click create. Choose number of parameter estimations runs, set Task to 'Parameter Estimation', use the report template defined in Figure S4 to collect the results and press 'Run'

The screenshot shows the COPASI software interface with the 'Reactions' table open. The table has columns for '#', 'Name', 'Reaction', and 'Rate Law'. The 'Name' column is highlighted, and the reactions are listed with their corresponding rate laws.

#	Name	Reaction	Rate Law
1	v1	"LacI mRNA" ->	Function for degradation of LacI transcripts
2	v2	"TetR mRNA" ->	Function for degradation of TetR transcripts
3	v3	"cl mRNA" ->	Function for degradation of CI transcripts
4	v4	-> "LacI protein"; "LacI mRNA"	Function for translation of LacI
5	v5	-> "TetR protein"; "TetR mRNA"	Function for translation of TetR
6	v6	-> "cl protein"; "cl mRNA"	Function for translation of CI
7	v7	"LacI protein" ->	Function for degradation of LacI
8	v8	"TetR protein" ->	Function for degradation of TetR
9	v9	"cl protein" ->	Function for degradation of CI
10	v10	-> "LacI mRNA"; "cl protein"	Function for transcription of LacI
11	v11	-> "TetR mRNA"; "LacI protein"	Function for transcription of TetR
12	v12	-> "cl mRNA"; "TetR protein"	Function for transcription of CI

Figure S6: Relabel reaction names

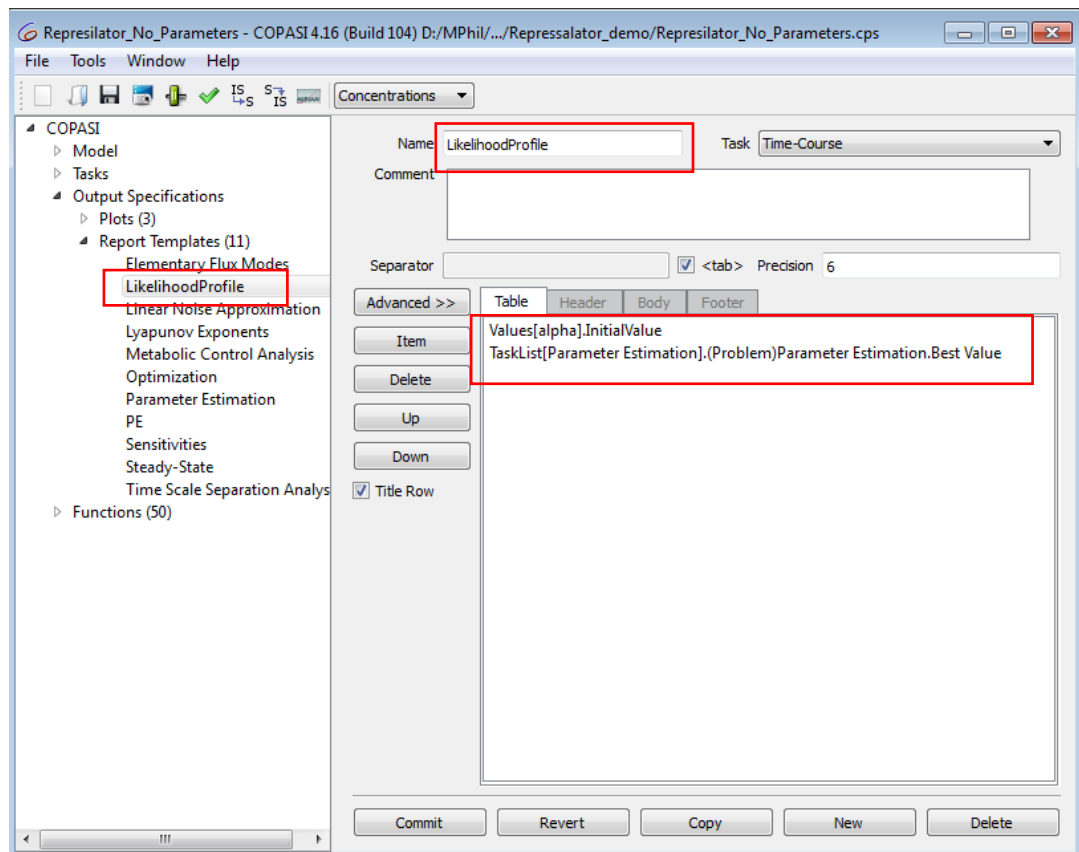


Figure S7: Define a report to collect results. Name it 'LikelihoodProfile'

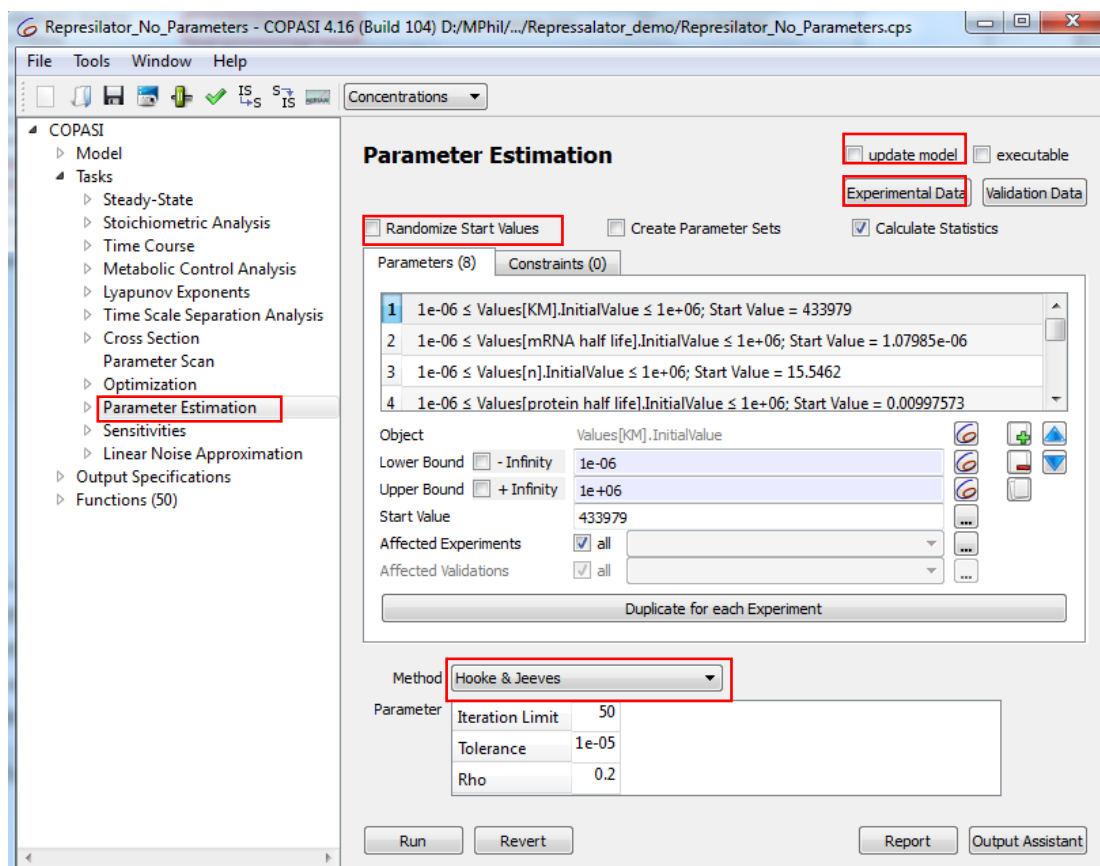


Figure S8: Set up the parameter estimation task. Uncheck the 'Randomize Start Values' and 'update model' boxes. Set the method to Hooke & Jeeves with default parameter values for the algorithm. Double check observable variables are still mapped to experimental data.

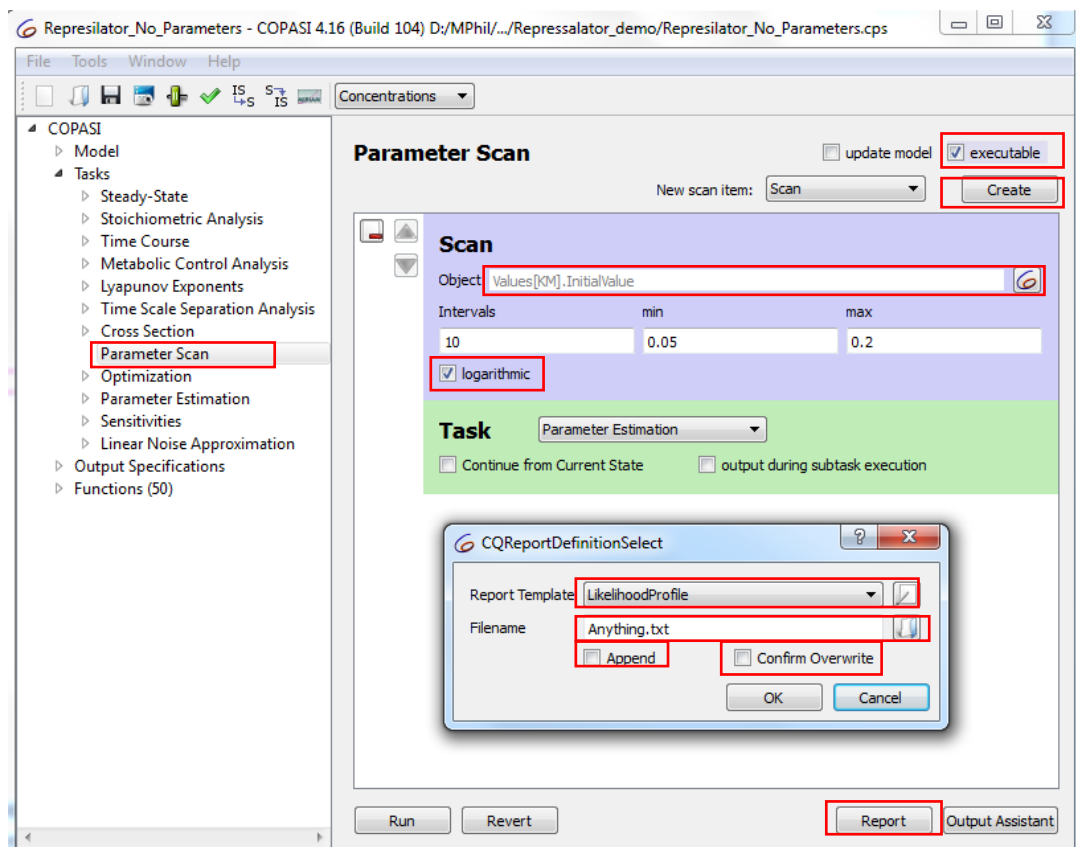


Figure S9: Set up the scan task. Create a scan item and choose any estimated parameter. Check the 'logarithmic' box and select 'Parameter Estimation' as the task. Use the 'LikelihoodProfile' report template defined earlier by clicking the 'Report' button. Name it anything and uncheck both 'Append' and 'Confirm Overwrite' boxes. Click 'OK' and check the 'executable' box in the top right hand corner to enable running this task using command line COPASI (CopsiSE).