**PESTER**

**Introduction**

Pester is a way to generate the files needed to execute the PEST parameter estimation program: <http://www.pesthomepage.org/>

For a given simulation model, PEST determines the vector of parameter values that provides the best fit to a set of experiments. This is achieved using the Levenberg-Marquardt algorithm, a least squares method, with multiple model invocations. For each experiment there is an input file and a rule for extracting the relevant model predictions (to be compared with the experimental observations) from the output file. For each adjustment made to the parameter vector a set of input files is generated containing these parameter values, and a set of model runs (one for each experiment) is submitted. The relevant output values are extracted from the output files and the objective function value is computed as the sum of squares of (prediction – observation).

The spreadsheet facilitates setting up the files for PEST.

**Start sheet**

Base path. This is the location of all files (input and output) involved in the parameter fitting.

# of experiments. Each experiment has its own input file, generated from its template file.

Input template files. The list of template files used to generate the input files.

View template file #. This button loads the template file for the selected number into the ‘Input\_data’ sheet.

Write files. This button generates all the files need to run PEST.

**Experiment\_data**

This sheet holds all the experimental observations that will be used in the fitting. Each observation set occupies a row, and is identified by the experiment tag and the time (hour). At each time point there can be up to 6 output variable measurements. The output variable IDs are selected from the drop-down list at the top of each ID column. (The drop-down lists are populated from the list on the ‘ID\_options’ sheet.) A missing experimental measurement is indicated by the value -1.

The user must provide two additional pieces of information for each ID column (i.e. for each output variable):

a short tag, no more than 5 characters (this is used in the PEST files), and

a weight to be used to multiply the squared errors for this variable.

If an experiment is to be used in the parameter fitting a ‘Y’ must appear next in the ‘Used (Y/N)’ column for the first observation, otherwise an ‘N’ will ensure that this experiment is ignored.

The data in the sheet can be saved to the file provided as ‘Experiment data file’ by clicking the ‘Save data’ button, and the sheet can be populated from the named file by clicking the ‘Load data’ button.

**Parameter\_data**

Up to 10 parameters can be fitted simultaneously. The number of parameters to be fitted is the number in the cell under ‘# of params’, and the parameter names are specified in the 2nd row. Each name must correspond exactly to the name used in the input file (i.e. in the template file). Names are case-sensitive. In each column, after the parameter name there must appear a short tag, then the initial guess, minimum and maximum values for the parameter.

Parameter data can be saved to the named file or loaded from is by clicking the ‘Save parameters’ and ‘Load parameters’ buttons.

**Input\_data**

This sheet, which is for reviewing the template files, is populated when the ‘View template file #’ button is clicked on the start sheet. Note: this sheet is for viewing files only, changing data here will not change the template file, which must be created using a text editor.

**ID\_options**

This sheet holds the list of output variable names. These names correspond to the names used in the model output file, \*\_ts.out. This list should be set up once and changed only when the model outputs are changed. The first entry in the list must be blank, and is used to clear an ID on the ‘Experiment\_data’ sheet. The ‘Update’ button is used to repopulate the drop-down lists when the list is changed.

**Creating a template file**

Each template file is used to create input files for a specific experiment, therefore the number of template files must correspond to the number of experiments in the ‘Experiment\_data’ sheet. Each template file has a name based on the experiment name used in the first column of the ‘Experiment\_data’ sheet. If the experiment tag is ‘E123’ the template file name is ‘E123.tpl’.

The template file is created from an example of an input file by making two changes:

1. The line

ptf $

is added at the start of the file. (Note that this line is not displayed in the ‘Input\_data’ sheet when the template file is viewed.)

2. In the lines where the parameter names occur, the parameter value is replaced by the parameter tag (as specified in the ‘Parameter\_data’ sheet) bracketed by ‘$’. For example, where the parameter ‘GLUCOSE\_MM\_KM’ is to be fitted, and it has been given the tag ‘g\_km’, the input file line

220 GLUCOSE\_MM\_KM Michaelis-Menten Km

is replaced by

$ g\_km $ GLUCOSE\_MM\_KM Michaelis-Menten Km

(Here the total number of characters between the ‘$’ signs is 16.)

In every iteration of the PEST solver the input file for an experiment simulation is created by replacing the string ‘$ g\_km $’ by the current parameter test value. Note that the character used to bracket the tag is specified in the first line in the file, and that this must be a character that does not appear anywhere else in the input file.

**Method of solution**

In solving for the optimum vector of parameter values, PEST repeatedly evaluates the objective function for different vectors (p1, p2, …), where the values p1, p2,… are chosen to enable estimates of the rate of change of the objective with respect to each parameter. The parameter values are inserted into the template files to generate a set of input files, which are then used in a set of model runs (one for each experiment). For each model run the output values corresponding to the experimental observations are extracted from the output file, and the objective function is computed as the weighted sum of squares of errors, summed over the experiments.

The spreadsheet is currently set up to process the data in the folder ‘example’.

**Running PEST**

After the PEST input files have been created (i.e. the ‘Write files’ button is clicked), PEST is invoked. One of the files created is the PEST control file. The file name is the model name (e.g. ‘monolayer\_m’) followed by ‘.pst’. PEST can be invoked at the command line in the folder where the files were created, e.g.

pest monolayer\_m.pst

Alternatively, clicking the ‘Submit’ button achieves the same result.

Full details of the solver run can be seen in the ‘.rec’ file, and in particular the optimum parameter values are in the ‘OPTIMISATION RESULTS’ section, e.g.:

OPTIMISATION RESULTS

Parameters ----->

Parameter Estimated 95% percent confidence limits

value lower limit upper limit

g\_vmax 1.269579E-16 1.161459E-16 1.377699E-16

g\_km 211.125 140.608 281.642