15 August 2011

KinGUII
Manual for the Graphical User Interface

Manual Version: 0.15
KinGUII Version: 2.2011.811.11535
KinGUII Viewer Version: 2.2011.811.11502

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1 Introduction

KINGUI 2 is a software tool for determining kinetic parameters from results of environmental fate studies, e.g. aerobic soil degradation, by fitting respective mathematical models to the observed data. It consist of two parts, first a package of numerical methods for the actual calculations, implemented in R (R language for statistical computing and graphics, http://www.r-project.org/), and second a graphical user interface for project administration, parameterization of the optimization runs and result evaluation.

The optimization workflow and the evaluation of results is optimized to account for the requirements given by the FOCUS Report on Estimating Persistence and Degradation Kinetics (EC Document Reference Sanco/10058/2005, version 2.0, June 2006). Thus it provides all kinetic models recommended in this report and by default does the standard statistical evaluations requested.

In Version 2 KINGUI allows the choice between different optimization algorithms. In particular the estimation of parameter confidence intervals is much improved as compared to the previous version by providing the methods Iteratively Reweighted Least Squares (IRLS) and Markov Chain Monte Carlo (MCMC).

1.1 Workflow

- Create ‘R’-script files (with the GUI or with a simple text editor like notepad^{++})
- Run them with ‘R’ having the KinGUI 2 packages and sourcefunctions installed
- Get the resulting reports and graphs with the KinGUII ResultViewer

The graphical user interface ‘KinGUII’ is so to say a specialized text editor for ‘R’-script files. With the intuitive ‘R’-script language you are also able to write the scripts with a normal text editor and run them form the DOS command line. Results can be viewed using the KinGUII ResultViewer.

2 Installation

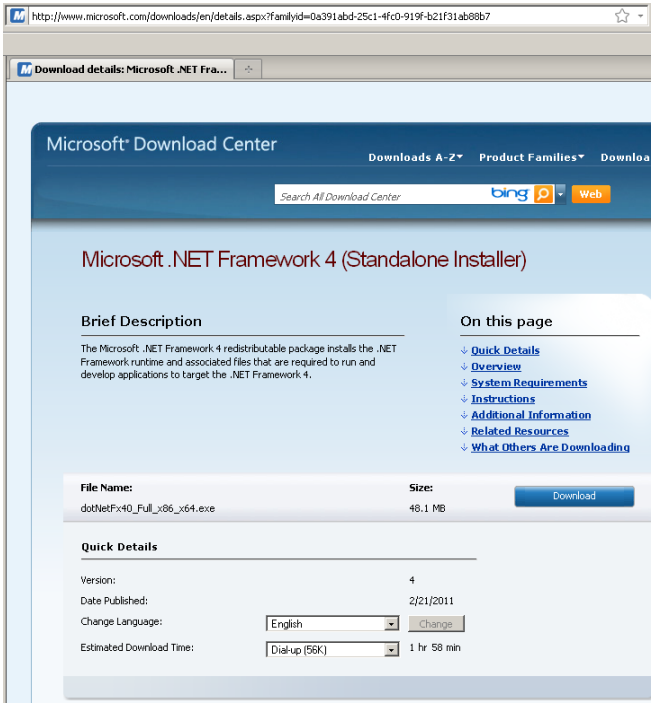
2.1 Workflow

No real installation process necessary!

- Check if .NET framework v 4.0 (or later) is installed
- Copy program files to your local hard drive
- Dblclick '..\KinGUII\GUI**KinGUII.exe**' to start the GUI'

2.2 Requirements

- .Net framework version 4.0 or later. Download here the version for your language settings (~ 48MB).



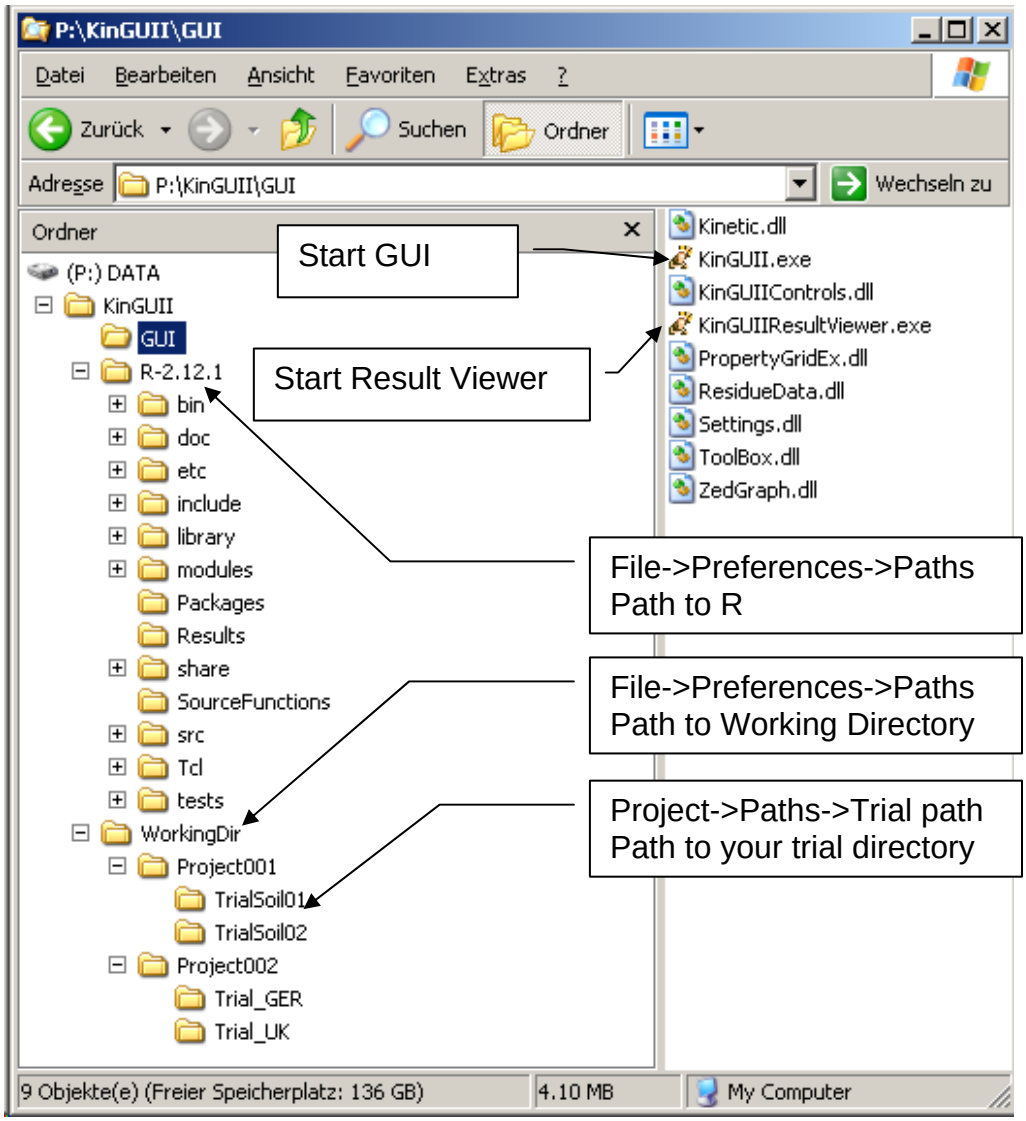
- ~ 140 MB harddisk space
- **No** installed version of 'R' necessary
- **No** Admin rights necessary!

2.3 Installation

Copy source (SourceDrive:\KinGUII) incl. subfolders to your local drive

- Do **not** use network drives!
- Do **not** use system paths like 'C:\Program Files' or 'C:\WINDOWS'
- Check access rights to target path

The resulting directory structure should look like this:



Dblclick '..\KinGUII\GUI**KinGUII.exe**' to start the GUI'

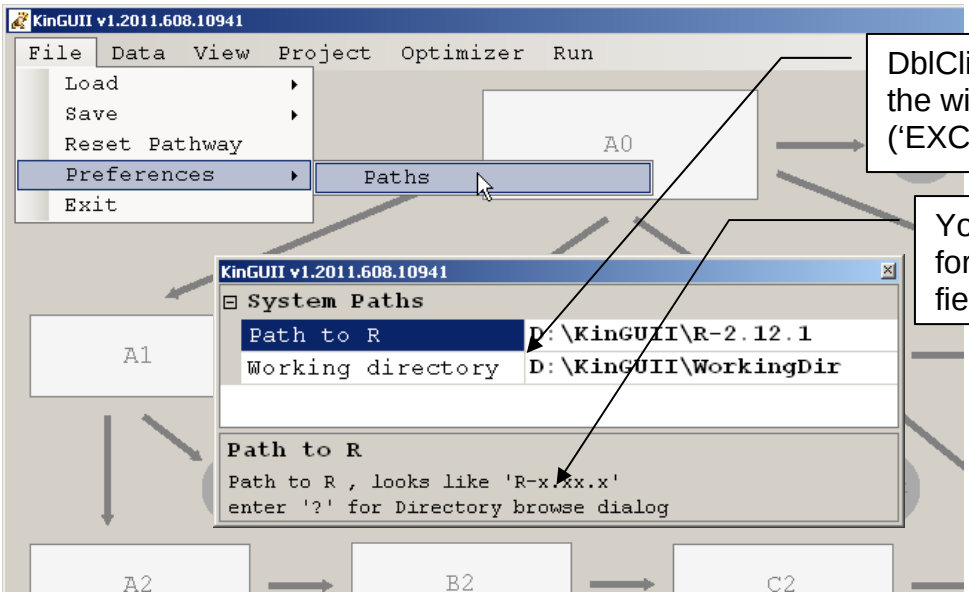
3 Getting started

3.1 Workflow

- Check preferences (paths to ‘R’ and ‘Working Directory’)
- Set Trial path and name

3.2 Set ‘R’ and ‘Working Directory’

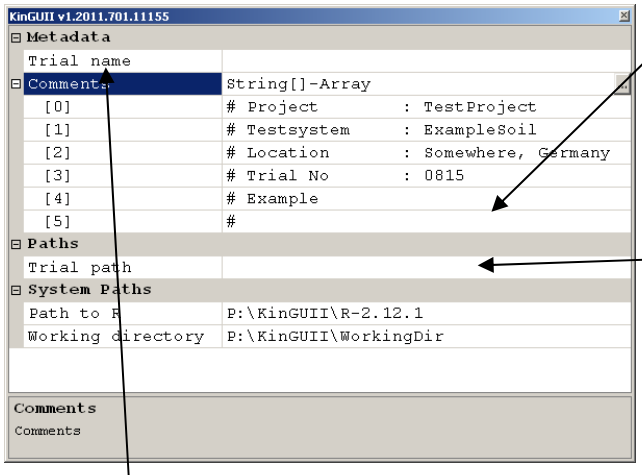
Check/set paths to the main ‘R’ directory and to the ‘Working Directory’, where your projects will be saved (normally these paths are already chosen by the program). You have to do this only once, your selections will be saved to program settings automatically.



DblClick here to auto adjust the width of the fields (‘EXCEL like’)

You can find a description for the value in the selected field here.

3.3 Set Trial - name and path



Comments taken from residue data file.
Can be extended at any time

Type ‚?’ to get a directory browse dialog.
Directory structure:
Working Directory
-> (opt.) Project path
->Trial path

Used to construct ‘R’-script file name:
‘TrialName’ ‘Optimizer’ ‘Kinetic model parent’ ‘parent compartment name’ .r
e.g.: ‘`TestTrial IRLS DFOP Parent.r`‘

4 Data management

4.1 Workflow

- Prepare ASCII text- file with residue data
- Load data to workplace
- Assign compartment residue data to pathway position
- Connect compartments

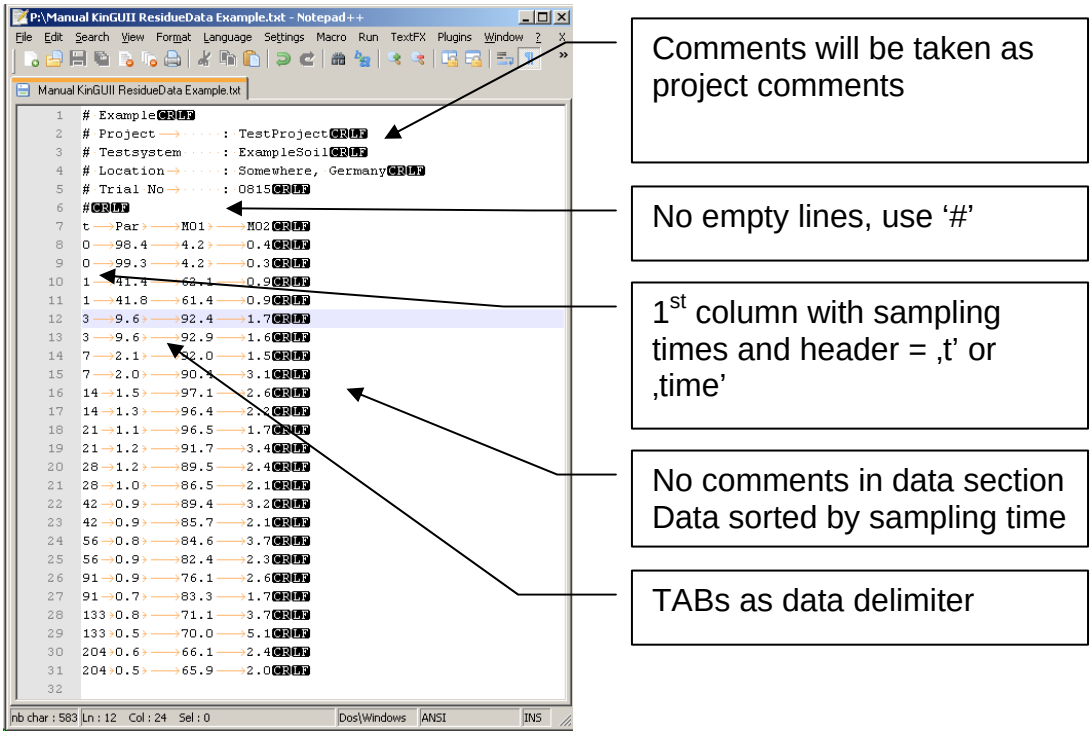
4.2 Preparation of residue input data

- Plain ASCII text-file
- Comment lines must contain "#", ":" or "/"
- You may have as many comment lines as you want
- No empty lines allowed!
- 1st data column must always contain the sampling times, header for this column must be 't' or 'time'
- No special chars for compartment names (e.g. space, "?", "\", "*" etc.)
- Data delimiter :TAB

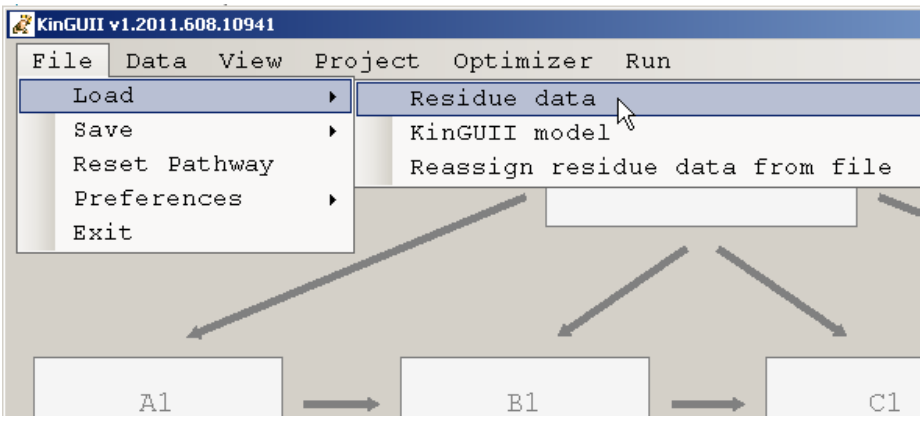
  delimiter between data colums,

  there may be more than one TAB between two values (for alignment reasons)
- No comments in data rows
- Residue data must be sorted by sampling times
- Missing data can be left blank or marked as ‘NaN’ (‘not a number’)
- No columns with weights for your data points (will be edited later, std. value = 1)

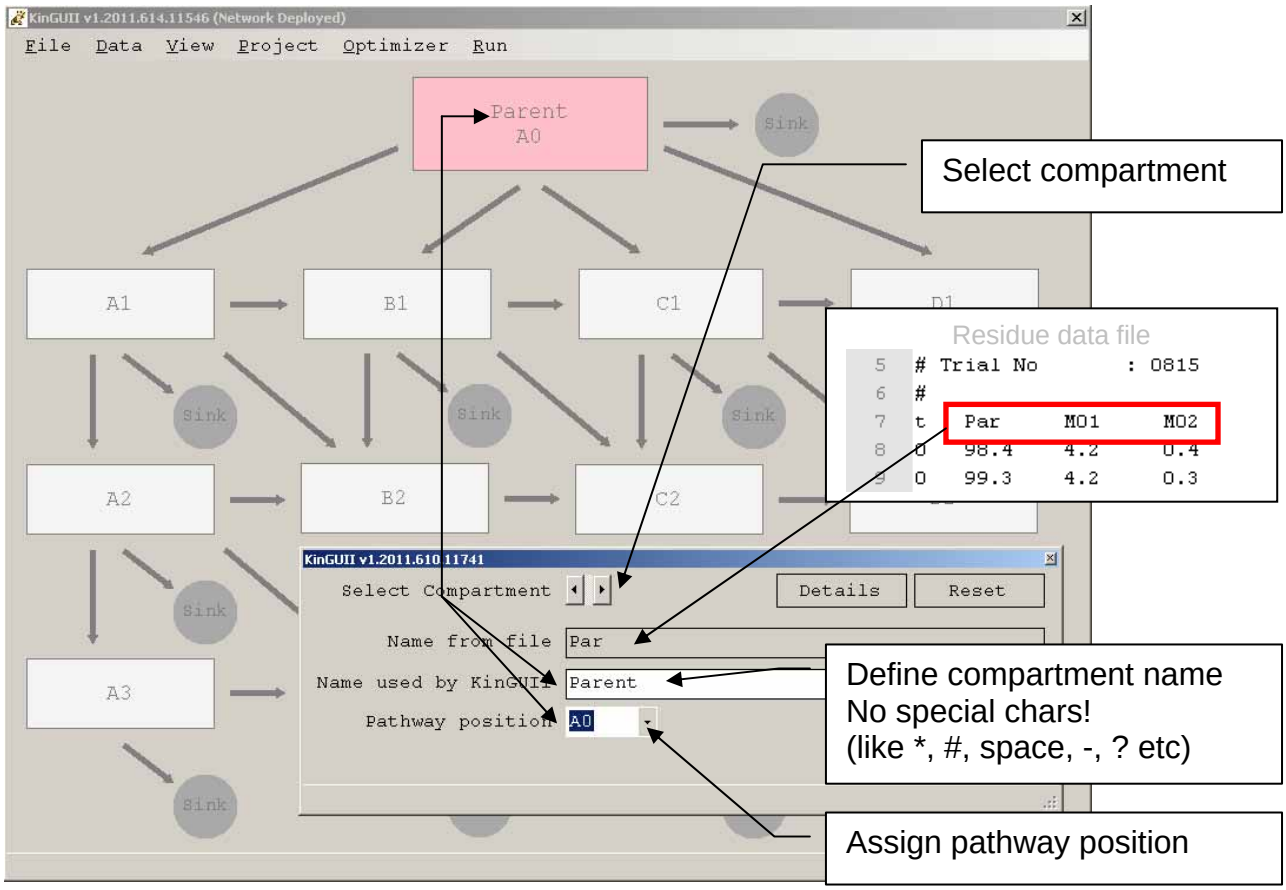
Example:



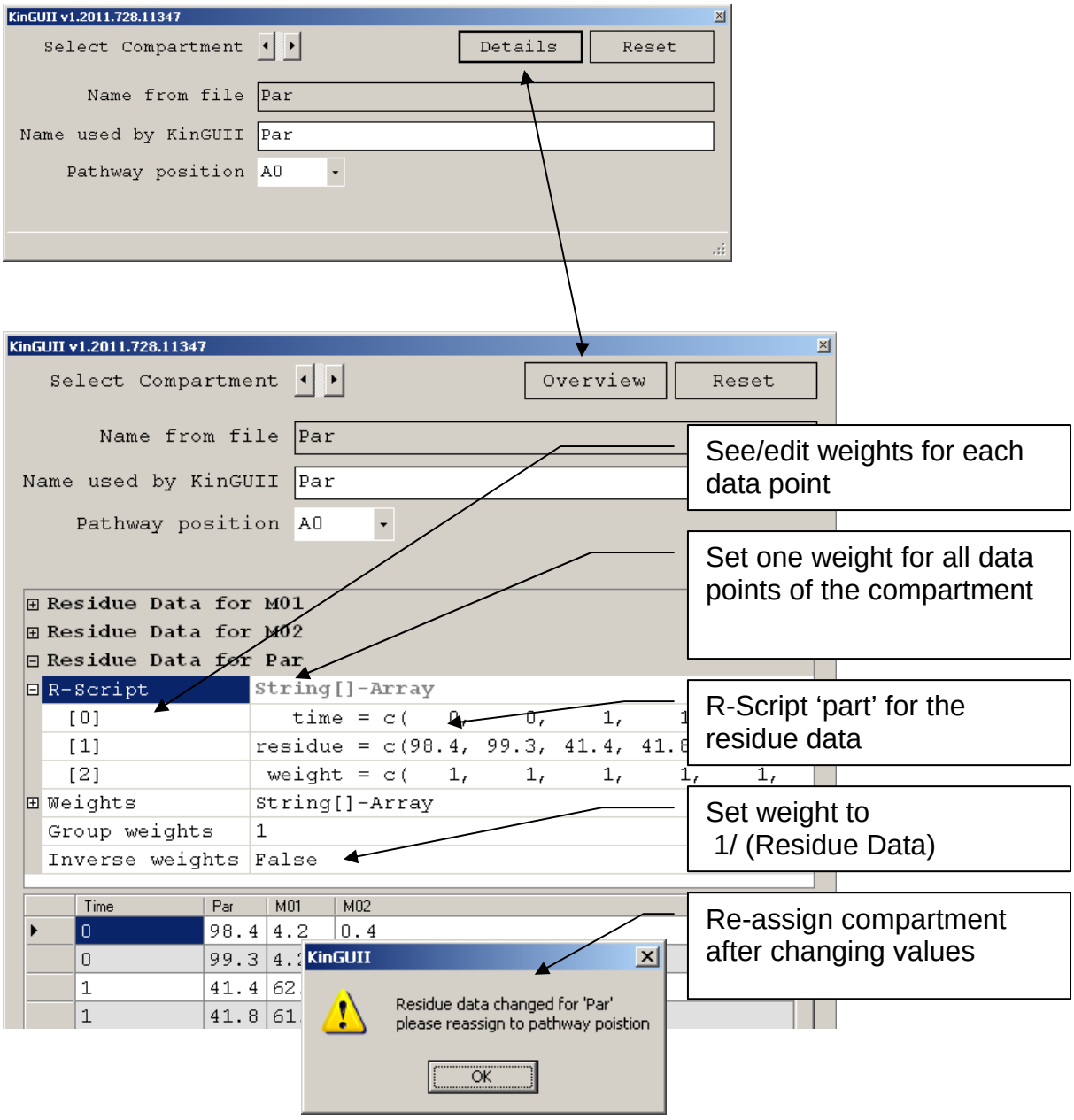
4.3 Load residue data



4.4 Assign residue data to pathway positions



4.5 Weights

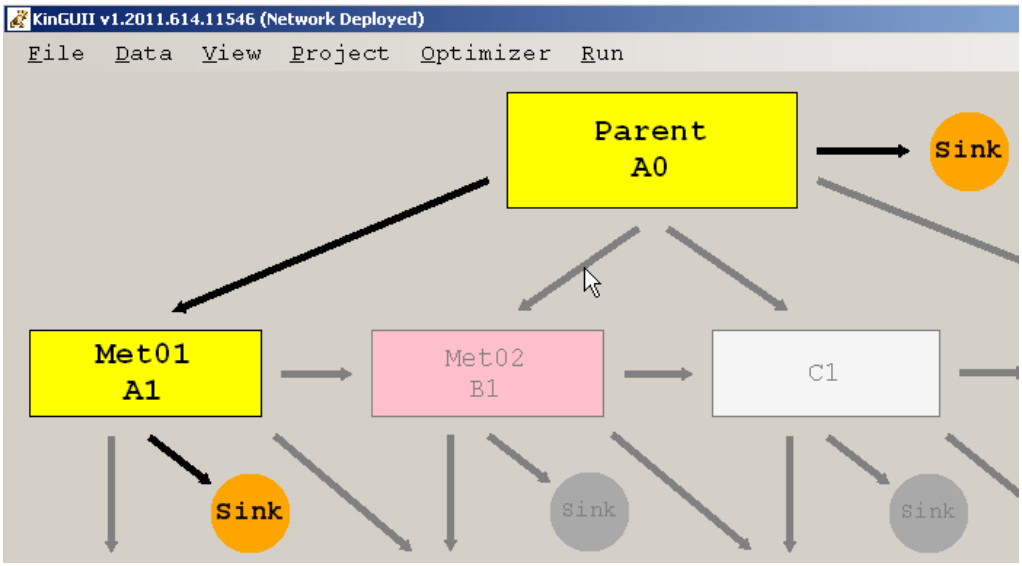


Important: If you change the weights always (re)assign the compartment to the desired pathway position to apply the changes!

4.6 Connect Compartments

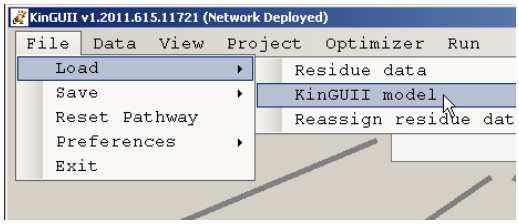
Just click on the gray arrows to change the compartment connection

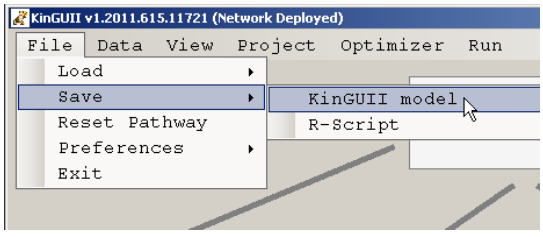
- 1st Click: Connect compartment (black arrow)
- 2nd Click: Change direction of the connection
- 3rd Click: Break connection (grey arrow)



4.7 Save/Load Workspace as XML-file

The complete workspace (model structure and data allocation but excluding project settings) can be saved or loaded at any time to/from an xml file.

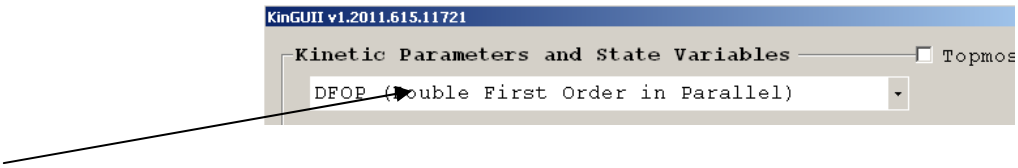




4.8 Reset Workspace

To start form scratch without closing and reopening the program click *File-> Reset Workspace*

5 Kinetic input



5.1 Important

Always click into this field before leaving this form, otherwise your changes will be lost!

If the form is not responding please close and reopen this dialog!

You can check the data input by leaving the entry screen and selecting “View-> R-Script” to see the script file that also echoes the input data.

5.2 Workflow

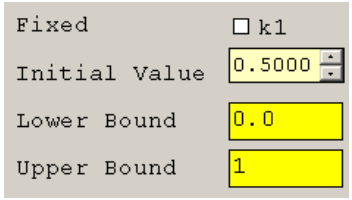
- Parent
  - Input:
    - kinetic model: SFO, DFOP, FOMC or HS
    - ‘M0’ (total amount of chemical present at time = 0 days)
    - formation fraction
- Metabolite
  - Only SFO is allowed
  - Keep M(0) of the metabolite fixed to zero (unless there is reason to do otherwise)
  - Choose formation fraction
- Define ‘Optimizer’-Settings
  - Optimizer std = ‘IRLS’ (Iteratively reweighted least square)
  - Method std = ‘solnp’
  - Submethod std = ‘Port’

5.3 Kinetic parameters

All kinetic parameters have the same data structure

Fixed 'TRUE' or 'FALSE'
std. value ='FALSE'
Select or unselect the "fixed" checkbox for each parameter
=> not fixed: parameter is optimised, starting with the initial value
=> fixed : parameter is not optimised, but kept at the initial value

Initial Value >= 0
Enter a (reasonable) initial value for each parameter
See what the graph would look like with the initial values you have chosen
Use Mouse Wheel or direct user input



Lower Bound >= 0
std. value = 0

Upper Bound >= 0, incl. 'Inf' for infinity
std. value = 'Inf'
For the formation fractions, the default upper boundary is 1

5.3.1 Input helper

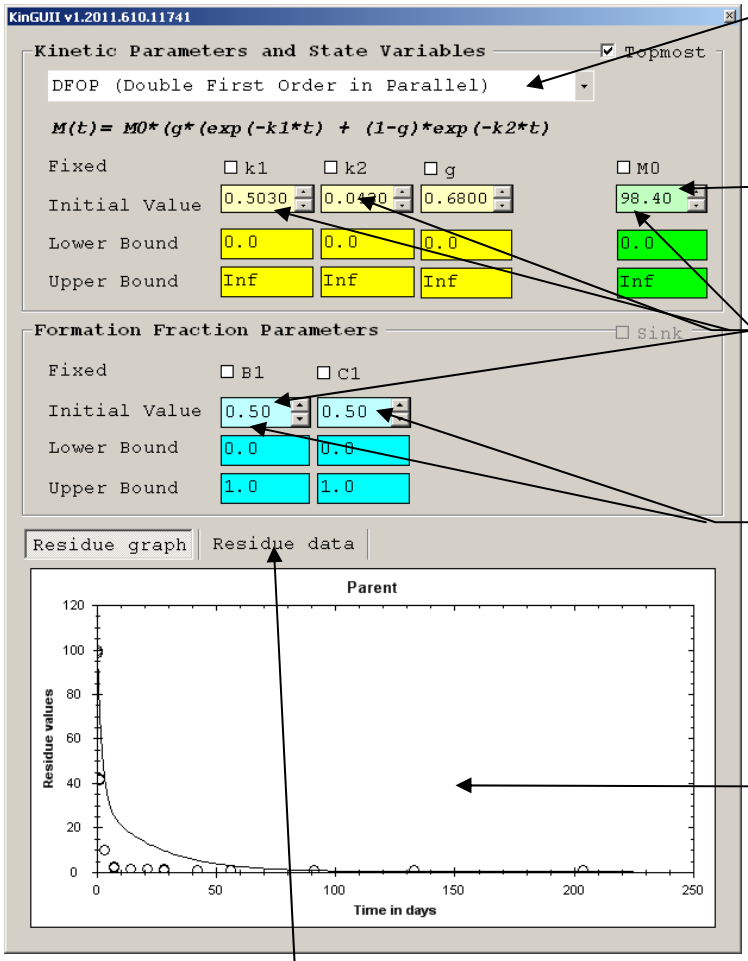
DblClick on

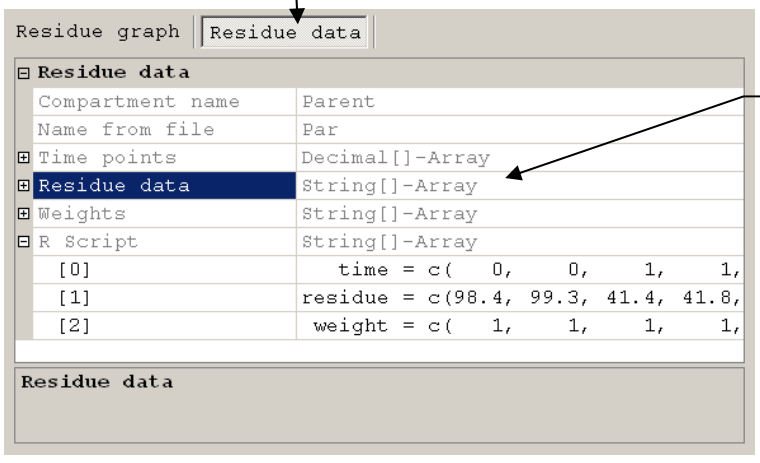
- 'M0' to set the total amount of chemical present at time = 0 days to the 1st residue data point (only for Parent)
- Any formation fraction (initial value input field) to distribute the formation equally between all metabolites (and sink, if defined)

Use mouse wheel or direct user input to change initial values for kinetic parameters

See what the graph would look like with the parameters you have chosen as initial values.

5.3.2 Parent





Select kinetic model.
Always click into this field before leaving this form.

DblClick to set M0 to 1st residue data value

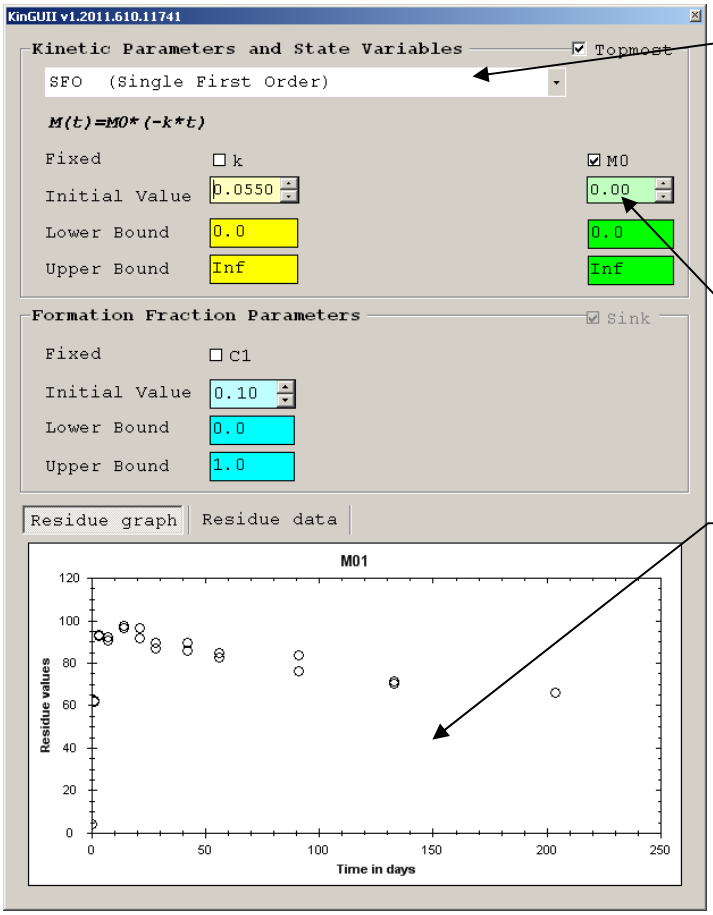
Use Mouse Wheel or direct user input to change initial values for kinetic parameters

DblClick on any ‚Initial Value' input field to distribute formation fraction equaly between the metabolites and sink (if defined)

Watch changes to the graph while changing the initial values for kinetic parameters

See residue data details for the compartment

5.3.3 Metabolite

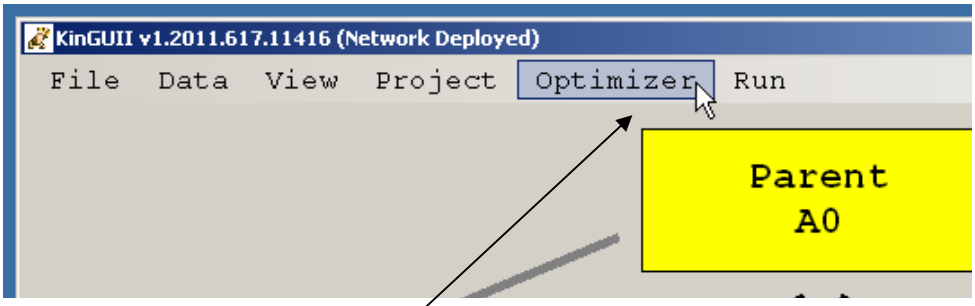


For metabolites only SFO is defined.
Always click into this field before leaving this form.

Keep M(0) of the metabolite fixed to zero (unless there is reason to do different).

Graph of residue data

5.3.4 Optimizer Settings



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Optimizer	
General	(...)
Used optimizer	IRLS
Used method	solnp
Used submethod	Port
Used solver	lsoda
Plot	True
Plot title	
Quiet	True
Error tolerance	1E-06
Max. no of iterations	100
NLLS	(...)
IRLS	(...)
Error tolerance	0.001
Max. no of iterations	10
MCMC	(...)
No of Iterations	10000
Output lenght	10000
Burn-in length	0
Fit start	True

IRLS
Iteratively reweighted least square settings

Optimizers

Three options are available:

- **NLLS:** Classical Nonlinear Least Squares method as implemented in KinGUI 1
- **IRLS:** Iteratively Reweighted Least Squares. Improved algorithm that more realistically estimates parameter confidence intervals (see. Gao et al., 2011, "Improving Uncertainty Analysis in Kinetic Evaluations Using Iteratively Reweighted Least Squares" submitted to Environmental Toxicology and Chemistry).
- **MCMC:** Markov Chain Monte Carlo method for determination of parameter distributions (see: Görlitz et al., 2011, "Statistical Analysis of Chemical Transformation Kinetics using Markov-Chain Monte-Carlo Methods", *Environ. Sci. Technol.*, 45 (10), pp 4429–4437). CAUTION: This method is very time consuming.

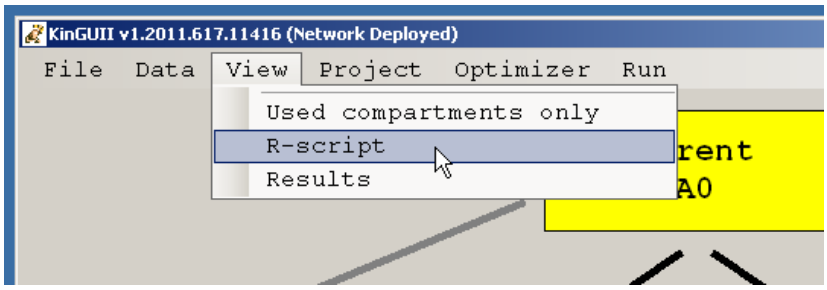
For all other setting the default values should be used in first instance. Changes should only be made if no successful optimization is achieved. Choosing other methods will usually result in significantly increased processing times.

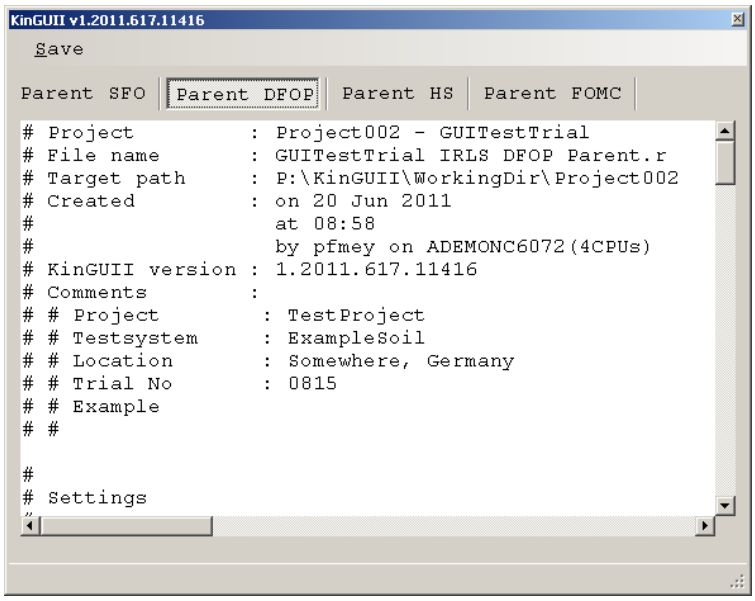
For the description of the different methods the user is referred to the descriptions of the respective R-packages.

6 'R'-Script

The R-Script contains all parameters and setting for running an optimization. It can be viewed by clicking "R-script" under the "View"-option.

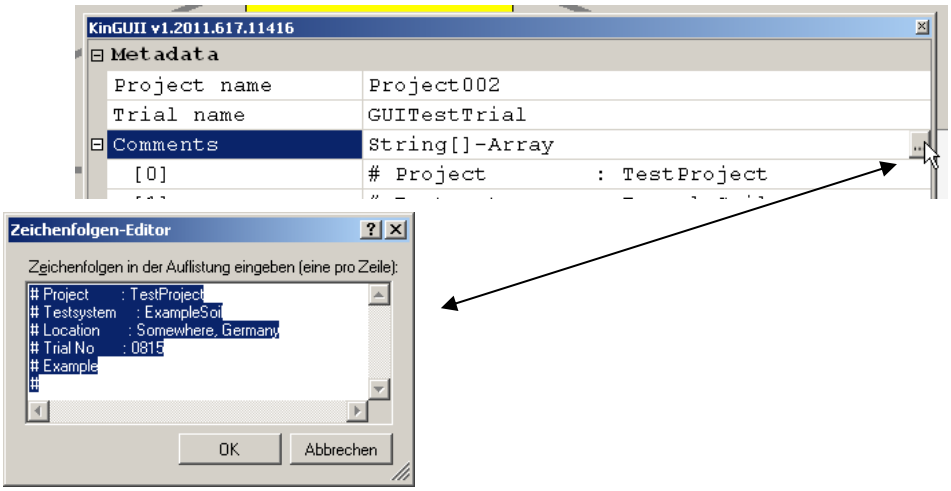
The following explains the structure of the R-Script and how it is compiled with KINGUII.



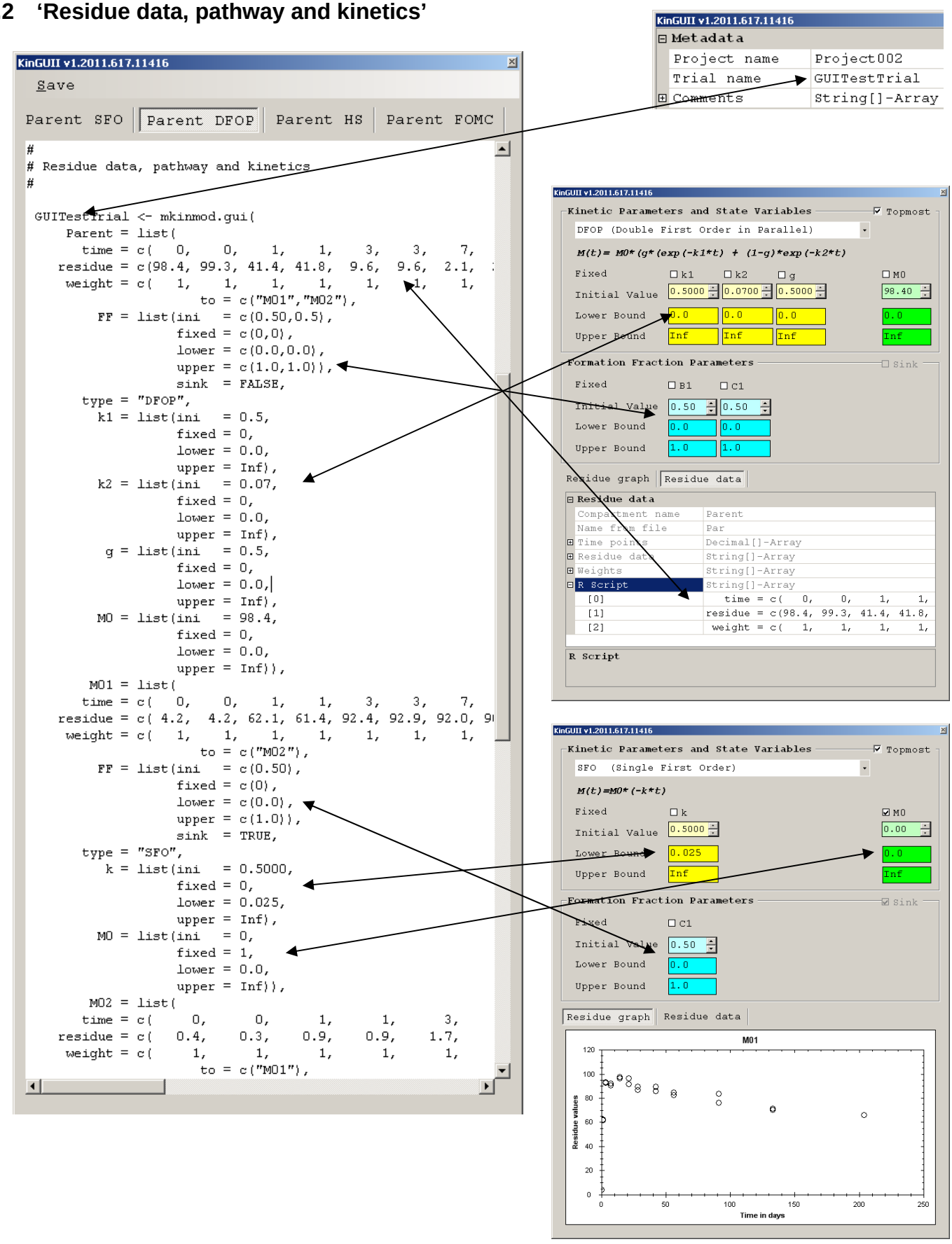


6.1 Metadata

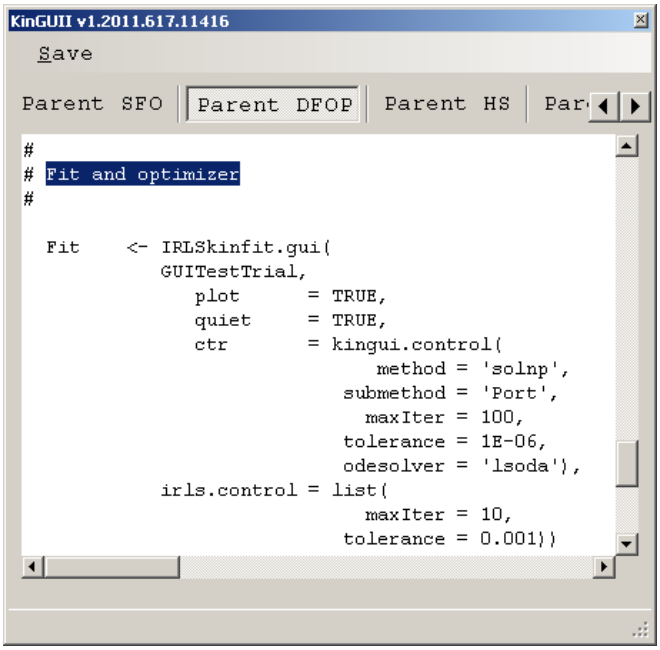
Comments are taken from your residue data file. You can add further comments *via Projects->Metadata->Comments.*

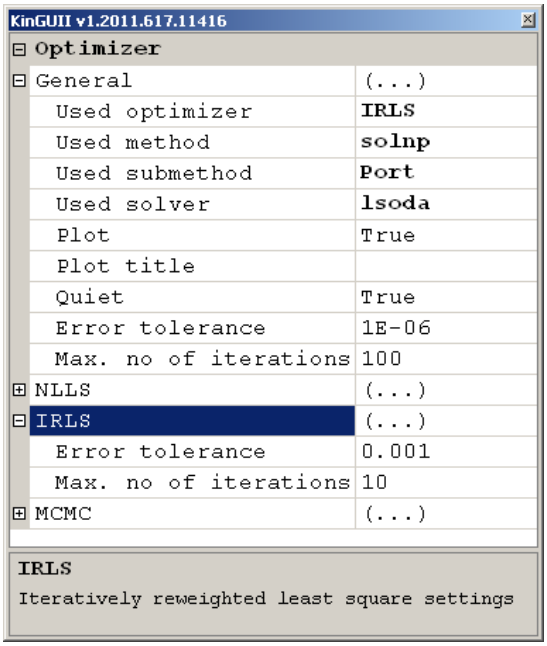


6.2 'Residue data, pathway and kinetics'

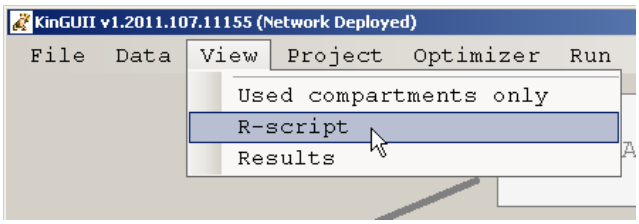


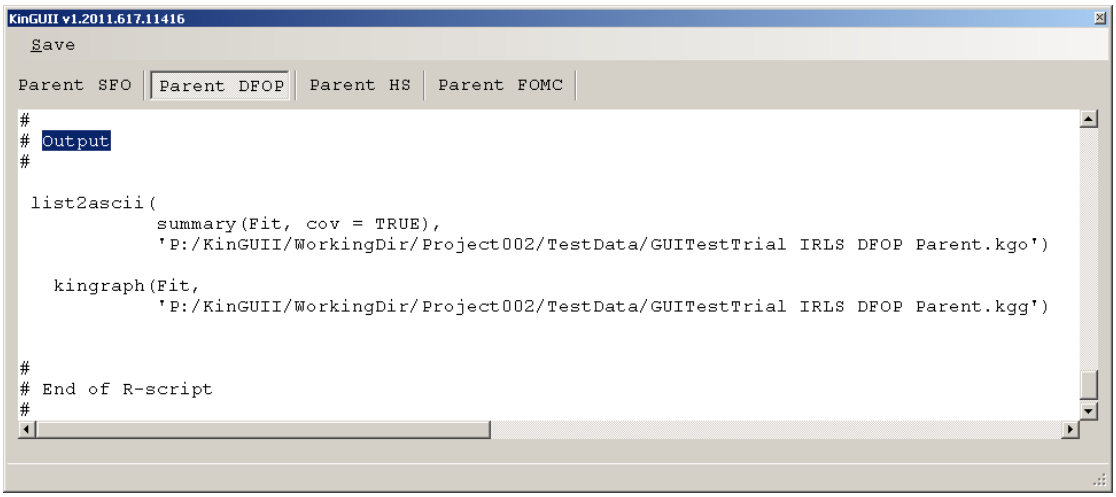
6.3 'Fit and optimizer'





6.4 'Output'

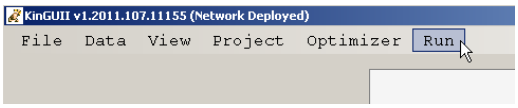


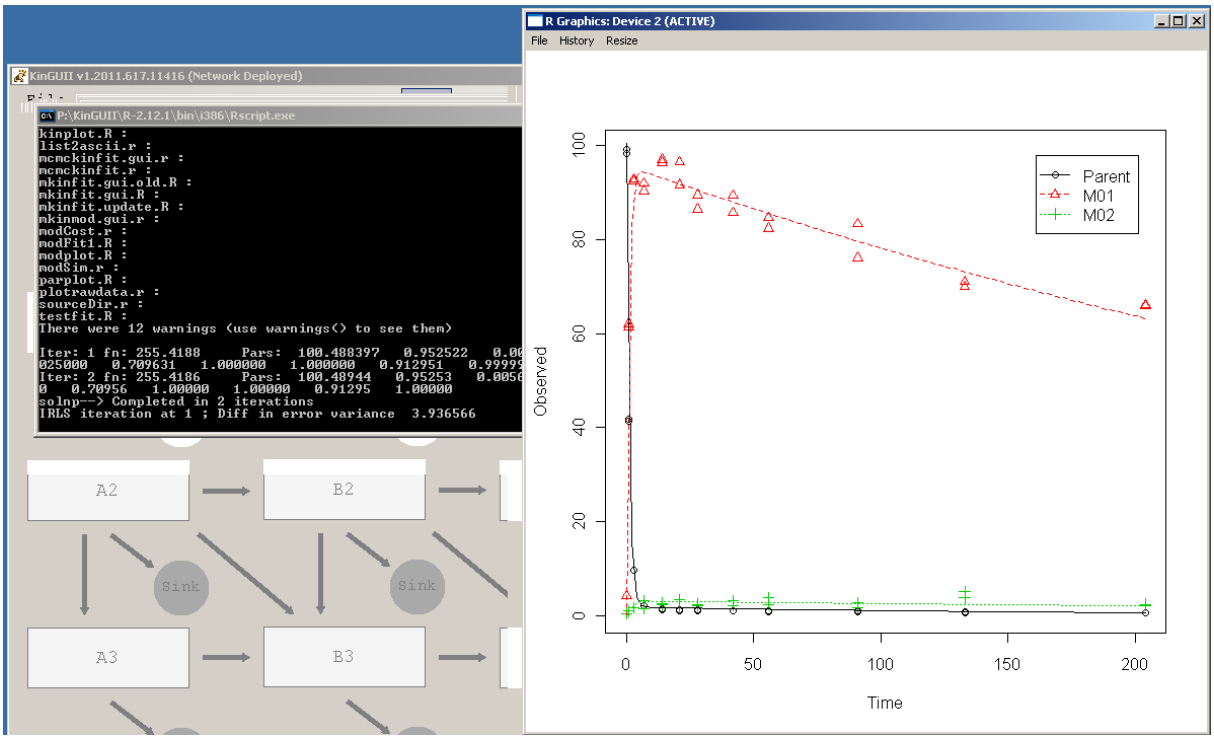


Result file names (kgo, kgg):
'TrialName Optimizer' 'Kinetic model parent' 'parent compartment name' .kgx
e.g.: `'TestTrial IRLS DFOP Parent.kgo'`

6.5 'Run'

For running an optimisation simply press "Run"



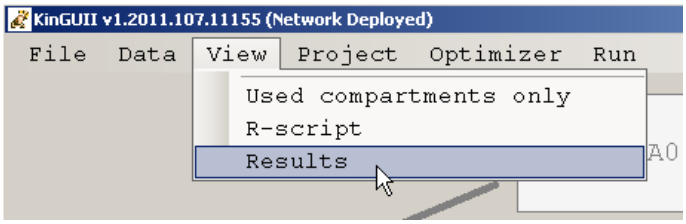


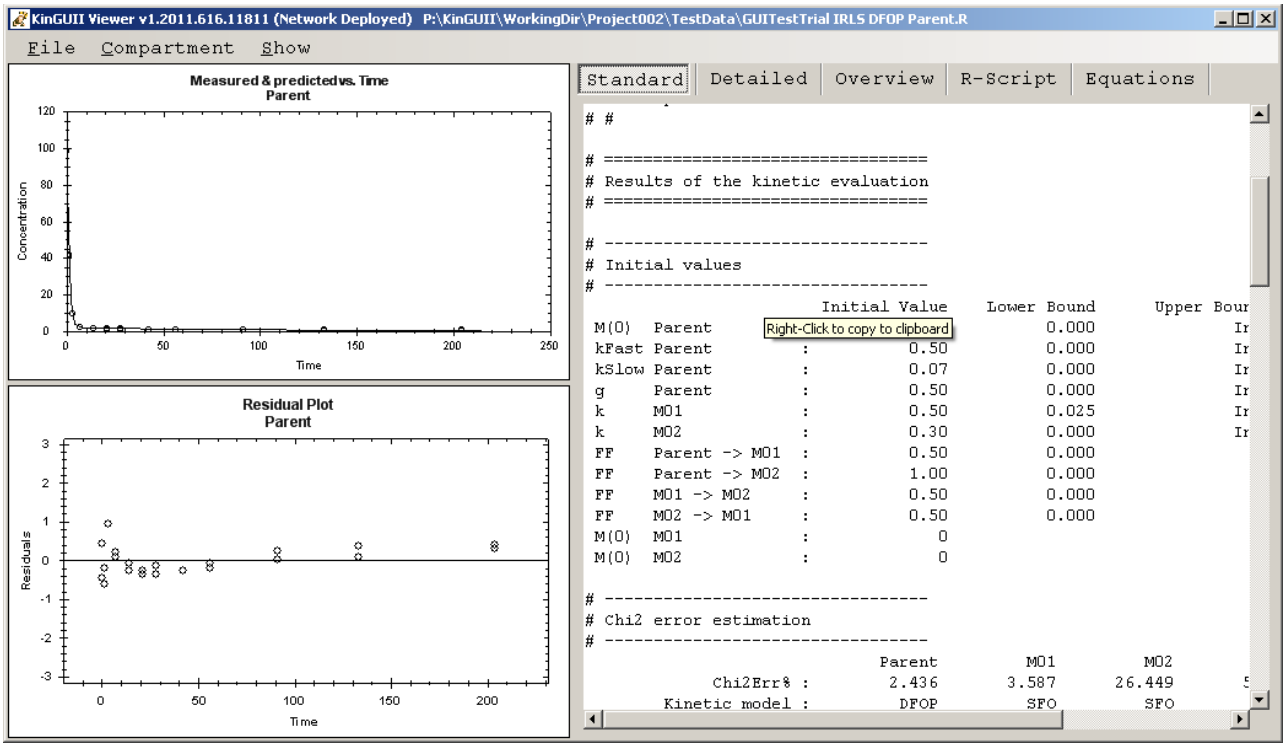
7 Results

The KINGUIIResultViewer is started by “View” -> “Results”.

The result viewer presents graphs of the observed and calculated data as well as the residuals separately for each compartment (choose under “Compartment”) and different views on the calculated results and the underlying R-script.

All data can be copied or saved after right click on the respective window panel.





Note: The result viewer can also be used independently by starting “KINGUIIResultViewer.exe” and loading the R-file of which the results shall be viewed.

7.1 MCMC

For runs with MCMC additionally a correlation and a density graph is available.