

Package ‘mixlow’

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R topics documented:

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| | |
|----------------|---|
| mixlow-package | <i>Calculate synergism/antagonism indices based on concentration- response curve parameters</i> |
|----------------|---|

Description

Uses a mixed-effects model to calculate parameters of concentration- response curves. These parameters are used in calculating Loewe interaction indices to quantify drug synergism/antagonism.

Details

Package: mixlow
 Type: Package
 Version: 1.0
 Date: 2008-06-27
 License: GPL-2

Functions are generally called in this order: readDataFile, prepareData, doNls, doNlme, and doLoewe. Plot functions are available to view results graphically, and values returned can be used to create custom plots.

Author(s)

John Boik (jcboik@stanford.edu)

References

- Boik J.C., Newman R.A., Boik R.J. (2008) Quantifying synergism/antagonism using nonlinear mixed-effects modeling: a simulation study. *Statistics in Medicine* 27(7), 1040-61
- Boik J.C. Narasimhan B. (2008, submitted) "Introducing the R Package mixlow for Assessment of Drug Synergism/Antagonism"

Examples

```
# trayData data object is obtained using the readDataFile function
data("trayData")
mixlowData <- prepareData(trayData)
trays <- getTrays(trayData)
parameterDefaults <- getNlsParameterDefaults(trays[1:9])
nlsData = doNls(mixlowData, parameterDefaults)
nlmeData = doNlme(mixlowData, nlsData)
loeweData = doLoewe(mixlowData, nlmeData)
```

doLoewe

*Estimate Loewe indices and confidence intervals***Description**

Uses parameter and covariance estimates produced by `doNlme` to estimate Loewe indices and confidence intervals at different fraction affected values.

Usage

```
doLoewe(mixlowData, nlmeData, verbose)
```

Arguments

| | |
|-------------------------|---|
| <code>mixlowData</code> | A list obtained from the output of <code>prepareData</code> |
| <code>nlmeData</code> | A list obtained from the output of <code>doNlme</code> |
| <code>verbose</code> | An optional logical value. If <code>TRUE</code> , information from intermediate steps in the Loewe analysis is printed. Default is <code>FALSE</code> . |

Details

Loewe indices are estimated based on parameter and covariance values generated by use of the `doNlme` function. In addition to returning interaction indices, the `doLoewe` function returns a vector indicating the degree of statistically significant synergism at each fraction affected value. The degree of statistically significant synergism at each fraction affected value is zero if the upper confidence limit is above 1.0, and is the difference between the upper confidence limit and 1.0 otherwise. A vector of statistically significant antagonism is calculated in an analogous manner. These vectors summarize the degree of synergism/antagonism occurring over a range of fraction affected values.

The width of the index confidence intervals is dependent in part on the critical value taken from the t-distribution, which in turn is dependent on the degrees of freedom. For multiple drug analysis with `doNlme`, the degrees of freedom is taken directly from the `nlme` results. For single drug analysis, the degrees of freedom is taken as the minimum degrees of freedom over all drugs.

Value

A list with the following named components:

| | |
|--------------------|--|
| <code>drugs</code> | The drugs analyzed |
| <code>mix</code> | The mixture analyzed |
| <code>ciL</code> | A data frame containing Loewe index estimates and confidence intervals based on the log of the index, for different fraction affected values |
| <code>covv</code> | Covariance matrix of the parameter estimates |
| <code>g0</code> | gamma, shape parameters |

p0 psi, IC50 parameters
 uu u parameter
 dat0 Data frame containing concentration-response values
 score.interval Interval of fraction affected values over which synergism/antagonism scores were computed
 syner Synergism scores for fraction affected values in interval
 syner.total Sum of synergism scores over interval
 antag Antagonism scores for fraction affected values in interval
 antag.total Sum of antagonism scores over interval

See `doNlme` for a description of `gamma`, `psi`, and `u` parameters.

Author(s)

John Boik (jcboik@stanford.edu)

References

The model is described in Boik J.C., Newman R.A., Boik R.J. (2008) Quantifying synergism/antagonism using nonlinear mixed-effects modeling: a simulation study. *Statistics in Medicine* 27(7), 1040-61

See Also

[doNlme](#), [plotLoeweData](#)

Examples

```

# mixlowData data object is obtained using the prepareData function
data(mixlowData)
# nlmeData data object is obtained using the doNlme function
data(nlmeData)
loeweData <- doLoewe(mixlowData, nlmeData)

```

doNlme *Conduct nonlinear mixed-effects analysis of sigmoidal concentration-response data*

Description

Organizes input and calls the `nlme` function to obtain parameter estimates for sigmoidal concentration-response curves. Starting values for the fixed effects are obtained from the output of the `doNls` function.

Usage

```

doNlme(mixlowData, nlsData, drugs=getDrugs(mixlowData), analysis="single",
       varFunction= 1, method="ML", verbose=FALSE)

```

Arguments

| | |
|--------------------------|--|
| <code>mixlowData</code> | A list obtained from the output of <code>prepareData</code> . It contains adjusted concentration-response data. |
| <code>nlsData</code> | A list obtained from the output of <code>doNls</code> . It contains parameter estimates for the concentration-effect curves, which are used as fixed-effects starting values by the <code>nlme</code> function. |
| <code>drugs</code> | A vector of drug names |
| <code>analysis</code> | An optional character string either “single” or “multiple” where “single” indicates that each drug is to be analyzed separately and “multiple” indicates that all drugs should be analyzed together. The default is “single”. |
| <code>varFunction</code> | An optional numerical vector or list of lists from the set (1,2,3,4) that specifies the variance function(s) to be used for each analysis. If <code>analysis</code> is “multiple”, <code>varFunction</code> can be a vector. If <code>analysis</code> is “single” it can also be a vector, in which case all drugs will use the same <code>varFunction</code> vector. Or, if <code>analysis</code> is “single”, a list can be supplied of length equal to the number of drugs. Each entry in the list should be a list with named component <code>varFunction</code> . This allows a different set of <code>varFunctions</code> to be used with each drug. The default is 1. |
| <code>method</code> | An optional character string. If “REML” the model is fit by maximizing the restricted log-likelihood. If “ML” the log-likelihood is maximized. Default is “ML”. |
| <code>verbose</code> | An optional logical value. If <code>TRUE</code> information from intermediate steps in the <code>doNlme</code> analysis is printed. The default is <code>FALSE</code> . |

Details

This function uses output from `doNls` as starting values for fixed effects. It organizes input and sets up calls to the `nlme` function in order to estimate parameters of sigmoidal concentration-response curves.

The variance functions for analysis of single drugs are:

- 1 `sigma`
- 2 `sigma * E[response]`
- 3 `sigma * E[response]^beta`
- 4 `sigma * (beta1 + E[response])`

The variance functions for analysis of multiple drugs are:

- 1 `sigma`
- 2 `sigma * alpha`, where `alpha` is drug-dependent
- 3 `sigma * E[response]`
- 4 `sigma * E[response]^beta`, where `beta` is drug-dependent

`E[response]` is used above to designate the expected response in a given well of a tray. For heteroscedastic errors, `varFunction=2` (for single) and `varFunction=3` (for multiple) analysis may

be appropriate in many cases. The simpler error functions could be tried if the `n1me` function does not converge.

See Boik et al., 2008 for details of the model. The parameters estimated by the model are:

g gamma, designates the steepness of the concentration-effect curve at the IC50

p psi, designates the IC50

u $E[\exp(u) + b_t]$, the expected value of all control wells across trays, where *b* is a tray-dependent random variable

lambda Optional. The non-zero asymptote of a “modified” sigmoidal concentration-response curve. The value of *lambda* represents the fraction of $E[\exp(u) + b_t]$ that is associated with the non-zero asymptote.

Parameters *u*, *g*, and *p* are in log scale.

Use of analysis=“multiple” for mixtures that contain more than two drugs can sometimes be problematic in that the estimation procedure may not converge or may take a long time to converge. If a mixture contains more than a few drugs, one alternative is to estimate concentration-response curve parameters for each drug/mixture separately (i.e., use analysis=“single”). The disadvantage with this approach is that for analysis of any given drug, control-well data from the trays of other drugs are not used. Control-well responses are then estimated based on only a few (replicate) trays.

Value

Returns a list of class `n1meData` for each analysis with the following components:

`n1meResults` A list of results from the `doN1me` analysis:

- nam** Name of the best model, chosen according to BIC score
- method** Method used to estimate the model
- drug** A string containing drug names
- setNum** The sequential number of the analysis
- cell** String indicating the cell line
- lik** Log likelihood
- bic** BIC score
- sig** sigma
- modelstruct** A list containing $\log(\text{stdev}(b_t)/\text{sigma})$ and other variance structures
- rc** Goodness-of-fit statistic
- r2** r^2 goodness-of-fit statistic
- se** Standard errors
- coeff** Fixed effects
- df** Degrees of freedom
- covv** Parameter covariance values

`n1meGraph` A list of data used for graphing `n1me` results:

- pred0** Predicted values
- dat1** Data values
- ord** A string containing drug names
- residu** Residuals from the best model
- best** A string denoting the name of the best model

Author(s)

John Boik (jcboik@stanford.edu)

References

The model is described in Boik J.C., Newman R.A., Boik R.J. (2008) Quantifying synergism/antagonism using nonlinear mixed-effects modeling: a simulation study. *Statistics in Medicine* 27(7), 1040-61

See Also

[doNls](#), [plotNlmeData](#)

Examples

```
# mixlowData data object is obtained using the prepareData function
data(mixlowData)
# nlsData data object is obtained using the doNls function
data(nlsData)
drugs = getDrugs(mixlowData)
nlmeData = doNlme(mixlowData, nlsData, drugs=drugs, varFunction= c(1,2))
```

doNls

Conduct nonlinear least-squares analysis of sigmoidal concentration-response data

Description

Organizes input and calls the `nls` function to estimate the parameters of sigmoidal concentration-response curves. Users can supply starting values for parameters or can use default values that are based on the data.

Usage

```
doNls(mixlowData, parameterDefaults, lambdaThreshold=0.05, numRandomTries=10,
      verbose=FALSE)
```

Arguments

`mixlowData` A list obtained from `prepareData`.

`parameterDefaults` A list obtained from `getNlsParameterDefaults`. The default values can be edited as desired before sending to the `doNls` function.

`lambdaThreshold` A scalar designating any lower boundary for `lambda`. If a model estimates a `lambda` value less than the threshold, that model will be discarded and a model that does not use a `lambda` parameter will be used instead.

| | |
|-----------------------------|---|
| <code>numRandomTries</code> | A scalar designating the number of attempts that should be made to reach convergence for each model. For each attempt, starting values are randomly selected from a normal distribution with mean equal to the given parameter starting value and a standard deviation equal to the given standard deviation. |
| <code>verbose</code> | An optional logical value. If <code>TRUE</code> , information from intermediate steps in the <code>doNls</code> analysis is printed. Default is <code>FALSE</code> . |

Details

See `doNlsme` for a description of the parameters estimated. See `getNlsParameterDefaults` for a description of default parameter values. Parameter values of `NaN` indicate the following default values will be used: `param.g=0`, `param.g.std=1`, `param.p` = the closest tested log concentration corresponding to 1/2 the mean response of control wells, and `param.p.std` = the absolute value of `param.p/2`. The default for `param.lambda` is `NaN`, which indicates that a lambda term will not be used. If a lambda term is used, its value should be between zero and 0.5.

Value

A list of type `nlsData` of length equal to the number of trays with the following components:

| | |
|---------------------------|--|
| <code>nlsEstimates</code> | Data frame containing parameter estimates |
| <code>nlsGraphing</code> | List used by <code>plotNlsData</code> for making graphs: |
| tray | String tray name |
| drug | String drug name |
| xx | Concentration values for graphing predictions |
| pred | Predicted values |
| y | Adjusted observed responses |
| x2 | Adjusted observed concentrations |

Adjusted responses take into account responses in optical control wells (see `prepareData`). In the adjusted concentrations, values of zero are replaced by concentrations of 1/1000th of the lowest nonzero concentration (for log-plot graphing purposes only).

Author(s)

John Boik (jcboik@stanford.edu)

References

Boik J.C., Newman R.A., Boik R.J. (2008) Quantifying synergism/antagonism using nonlinear mixed-effects modeling: a simulation study. *Statistics in Medicine* 27(7), 1040-61

See Also

[prepareData](#), [plotNlsData](#)

Examples

```
# mixlowData data object is obtained using the prepareData function
data(mixlowData)
trays <- getTrays(mixlowData)
parameterDefaults <- getNlsParameterDefaults(trays=trays[1:9])
nlsData <- doNls(mixlowData=mixlowData, parameterDefaults)
```

| | |
|--------------|---|
| getCellLines | <i>Retrieve a vector of cell line names from data</i> |
|--------------|---|

Description

Convenience function called on output from `prepareData` or `readDataFile` to obtain a vector of cell line names.

Usage

```
getCellLines(data, drugs=NULL, trays=NULL)
```

Arguments

| | |
|--------------------|--|
| <code>data</code> | A list obtained from <code>prepareData</code> or <code>readDataFile</code> functions |
| <code>drugs</code> | A vector of drug names. If <code>NULL</code> , cell lines will not be subset by drugs. |
| <code>trays</code> | A vector of tray names. If <code>NULL</code> , cell lines will not be subset by trays. |

Details

A data file may contain experimental results for multiple cell lines. If so, the `prepareData` function requires that one of these be specified for further analysis. Slices of the vector returned from `getCellLines` can be used as an argument to the `prepareData` function to subset the data.

Value

A vector of strings indicating which cell lines are contained in the input data object.

Author(s)

John Boik (jcboik@stanford.edu)

See Also

[getTrays](#), [getDrugs](#)

Examples

```
# mixlowData data object is obtained using the prepareData function
data("mixlowData")
cellLines <- getCellLines(mixlowData)
```

getDrugs

Retrieve a vector of drug names from data

Description

Convenience function called on output from `prepareData` or `readDataFile` to obtain a vector of drug names.

Usage

```
getDrugs(data, trays=NULL, cellLines=NULL)
```

Arguments

| | |
|------------------------|---|
| <code>data</code> | A list obtained from <code>prepareData</code> or <code>readDataFile</code> functions. |
| <code>trays</code> | A vector of tray names. If <code>NULL</code> , drugs will not be subset by trays. |
| <code>cellLines</code> | A vector of cell line names. If <code>NULL</code> , drugs will not be subset by cell lines. |

Details

A data file may contain experimental results for multiple drugs. If so, slices of the vector returned from `getDrugs` can be used as an argument to the `prepareData` function in order to select a subset of the data.

Value

A vector of strings indicating which drugs are contained in the input data object.

Author(s)

John Boik (jcboik@stanford.edu)

See Also

[getTrays](#), [getCellLines](#)

Examples

```
# mixlowData data object is obtained using the prepareData function
data("mixlowData")
drugs <- getDrugs(mixlowData)
```

```
getNlsParameterDefaults
```

Generate a data frame of default values for nonlinear least-squares analysis

Description

Convenience function to generate default values for input to the `doNls` function. Defaults are indicated by NaN values. Users can manually change these values once the data frame is generated.

Usage

```
getNlsParameterDefaults(trays)
```

Arguments

`trays` A vector of tray names that can be generated by the `getTrays` function.

Details

See `doNlme` for a description of the parameters. The data frame contains names:

param.g gamma

param.g.std Standard deviation of gamma

param.p psi

param.p.std Standard deviation of psi

param.lambda lambda

See help for functions `doNls` and `doNlme` for information on parameters. `getNlsParameterDefaults` sets all parameter values to NaN, instructing the `doNls` function to use default values. After generating the data frame, NaNs can be set to numerical values as desired. All parameter values except lambda should be in log scale.

Value

A data frame containing NaN values for all parameter estimates.

Author(s)

John Boik (jcboik@stanford.edu)

See Also

[doNls](#)

Examples

```
# mixlowData data object is obtained using the prepareData function
data(mixlowData)
trays <- getTrays(mixlowData)
parameterDefaults <- getNlsParameterDefaults(trays=trays[1:9])
parameterDefaults["t2d1", "param.lambda"] <- .05
```

getTrays

Retrieve a vector of tray names from data

Description

Convenience function called on output from `prepareData` or `readDataFile` to obtain a vector of tray names.

Usage

```
getTrays(data, drugs=NULL, cellLines=NULL)
```

Arguments

`data` A list obtained from `prepareData` or `readDataFile` functions.
`drugs` A vector of drug names. If `NULL`, trays will not be subset by drugs.
`cellLines` A vector of cell line names. If `NULL`, trays will not be subset by cell lines.

Details

A data file will contain experimental results for multiple trays, with one drug tested per tray. Slices of the vector returned from `getTrays` can be used as an argument to the `prepareData` function in order to select a subset of the data.

Value

A vector of strings indicating which trays are contained in the input data object.

Author(s)

John Boik (jcboik@stanford.edu)

See Also

[getCellLines](#), [getDrugs](#)

Examples

```
# mixlowData data object is obtained using the prepareData function
data("mixlowData")
trays <- getTrays(mixlowData)
```

`loeweData`*loeweData Dataset*

Description

Dataset obtained as a result of using function `doNls`, based on data in the text file “`mixlowExampleData.txt`”. This file contains made-up example data.

Usage

```
data(loeweData)
```

Format

See help file for function `doLoewe` for composition of `loeweData` dataset.

Details

The text file “`mixlowExampleData.txt`” provides example data for a cytotoxicity experiment in which two drugs and their mixture is tested. Each drug is tested in three replicate trays.

See Also

[doNls](#)

Examples

```
data(loeweData)
```

`mixlowData`*mixlowData Dataset*

Description

Dataset obtained as a result of using function `prepareData`, based on data in the text file “`mixlowExampleData.txt`”. This file contains made-up example data.

Usage

```
data(mixlowData)
```

Format

See help file for function `prepareData` for composition of `mixlowData` dataset.

Details

The text file “mixlowExampleData.txt” provides example data for a cytotoxicity experiment in which two drugs and their mixture is tested. Each drug is tested in three replicate trays.

See Also

[prepareData](#)

Examples

```
data(mixlowData)
```

nlmeData

nlmeData Dataset

Description

Dataset obtained as a result of using function `doNlme`, based on data in the text file “mixlowExampleData.txt”. This file contains made-up example data.

Usage

```
data(nlmeData)
```

Format

See help file for function `doNlme` for composition of `nlmeData` dataset.

Details

The text file “mixlowExampleData.txt” provides example data for a cytotoxicity experiment in which two drugs and their mixture is tested. Each drug is tested in three replicate trays.

Examples

```
data(nlmeData)
```

`NlmePrintVarFunctions`*Print variance function options for nonlinear mixed-effects analysis*

Description

Prints a table of variance function options that can be used in arguments to the `doNlme` function.

Usage

```
NlmePrintVarFunctions()
```

Arguments

None

Details

One argument to the `doNlme` function is specification of the variance functions to be used in `nlme` analysis. Eight different variance functions are allowed. The convenience function `NlmePrintVarFunctions` prints information on each of the eight possible choices. There are four choices for analysis type “single” and four for analysis type “multiple”.

Value

None

Author(s)

John Boik (jcboik@stanford.edu)

See Also

[doNlme](#)

Examples

```
NlmePrintVarFunctions()
```

nlsData

nlsData Dataset

Description

Dataset obtained as a result of using function `doNls`, based on data in the text file “mixlowExampleData.txt”. This file contains made-up example data.

Usage

```
data(nlsData)
```

Format

See help file for function `doNls` for composition of `nlsData` dataset.

Details

The text file “mixlowExampleData.txt” provides example data for a cytotoxicity experiment in which two drugs and their mixture is tested. Each drug is tested in three replicate trays.

See Also

[doNls](#)

Examples

```
data(nlsData)
```

plotLoeweData

Plot Loewe analysis results

Description

Plots results returned from the `doLoewe` function.

Usage

```
plotLoeweData(loeweData, ...)
```

Arguments

| | |
|------------------------|--|
| <code>loeweData</code> | A list returned from the <code>doLoewe</code> function. |
| <code>...</code> | Additional parameters, including <code>main</code> and <code>legend</code> to be passed to the plot function |

Details

Two figures are generated from the Loewe analysis. The first shows the estimated index and its confidence intervals, along with the reference index at 1.0. Values below this reference line are indicative of synergism and values above are indicative of antagonism. When the upper and lower confidence interval limits both fall below 1.0, then statistically significant synergism is occurring. When the upper and lower confidence interval limits both fall above 1.0, then statistically significant antagonism is occurring. The second figure shows the estimated concentration- response curves for each drug and the mixture. To save both figures to disk, sandwich the `plotLoeweData` command between `pdf` and `dev.off` commands, for example.

Value

None

Author(s)

John Boik (jcboik@stanford.edu)

Examples

```
# loeweData data object is obtained using the doLoewe function
data("loeweData")
plotLoeweData(loeweData, ask=TRUE)
```

plotMixlowData *Plot prepared data*

Description

Plots results obtained from the `prepareData` function.

Usage

```
plotMixlowData(mixlowData, trays=getTrays(mixlowData), ask,
  showBlanks= TRUE)
```

Arguments

| | |
|-------------------------|---|
| <code>mixlowData</code> | A list obtained from the <code>prepareData</code> function. |
| <code>trays</code> | A vector of strings indicating the trays for which data should be plotted. |
| <code>ask</code> | Logical. If TRUE (and the R session is interactive) the user is asked for input, before a new figure is drawn. |
| <code>showBlanks</code> | Logical. If TRUE, data from the optical control wells (“blanks”) in a tray are included in the graph. Default is TRUE |

Details

This function is used to plot prepared data. Adjusted concentration-response data are plotted, and mean responses over replicate wells receiving identical drug concentrations are connected by a line. The adjustments subtracted from the raw data (see `PrepareData` function) can be included in the plot by setting `showBlanks` equal to `TRUE`. For purposes of plotting on a log-scale plot, drug concentrations of zero are changed to 1/1000 of the lowest nonzero drug concentration. This adjustment only affects plotting, not analysis.

Value

A list of length equal to the number of trays with components:

| | |
|-------------------------|---|
| <code>drug</code> | Drug name |
| <code>cell</code> | Cell line name |
| <code>Units</code> | Units of measurement |
| <code>title</code> | Title for plot |
| <code>adjResp</code> | Adjusted response data |
| <code>adjConc</code> | Adjusted concentration data |
| <code>ylim</code> | y limits of plot |
| <code>meanLineY</code> | Response values for mean line between group replicates |
| <code>meanLineX</code> | Concentration values for mean line between group replicates |
| <code>blankY</code> | Responses from optical control wells |
| <code>blankX</code> | Concentrations for optical control wells |
| <code>blankLineY</code> | Responses for optical control data line |
| <code>blankLineX</code> | Concentrations for optical control data line |

Author(s)

John Boik (jcboik@stanford.edu)

See Also

[readDataFile](#), [prepareData](#)

Examples

```
# mixlowData data object is obtained using the prepareData function
data(mixlowData)
trays <- getTrays(mixlowData)
saved_mixlow_graphing_data <- plotMixlowData(mixlowData=mixlowData,
      trays= trays[1:9], ask=FALSE, showBlanks= TRUE)
```

plotNlmeData *Plot results obtained from nonlinear mixed-effects analysis*

Description

Plots results obtained from doNlme function

Usage

```
plotNlmeData(nlmeData, ask, ...)
```

Arguments

| | |
|----------|--|
| nlmeData | A list obtained from the do.NLME function |
| ask | Logical. If TRUE (and the R session is interactive) the user is asked for input, before a new figure is drawn. |
| ... | Additional parameters, including main and legend to be passed to the plot function |

Details

Two sets of figures are generated per nlme analysis. The first is concentration-response curves for all trays treated with a given drug, and the second is qqnorm plots of residuals for each drug.

Value

None

Author(s)

John Boik (jcboik@stanford.edu)

See Also

[doNlme](#)

Examples

```
# nlmeData data object is obtained using the doNlme function
data("nlmeData")
plotNlmeData(nlmeData=nlmeData, ask=FALSE)
```

plotNlsData

Plot results obtained from nonlinear least-squares analysis

Description

Plots results from the doNls function

Usage

```
plotNlsData(nlsData, mixlowData, trays=getTrays(mixlowData), ask,
            showBlanks=TRUE)
```

Arguments

| | |
|------------|---|
| nlsData | A list obtained from the doNls function |
| mixlowData | A list obtained from the prepareData function |
| trays | A vector of strings indicating the trays for which data should be plotted. |
| ask | Logical. If TRUE (and the R session is interactive) the user is asked for input, before a new figure is drawn. |
| showBlanks | Logical. If TRUE, data from the optical control wells (“blanks”) in a tray are included in the graph. Default is TRUE |

Details

Plots concentration-response curves for each tray and each drug. See plotMixlowData for more information about the plots of concentration-response data and optical control data.

Value

A list of length equal to the number of trays with components:

graphDataTray

A list of graph data per tray with components:

tray Tray name

drug Drug name

cell Cell line name

Units Units of measurement

title Title for plot

adjResp Adjusted response data

adjConc Adjusted concentration data

ylim y limits of plot

linesY Response values for mean line between group replicates

linesX Concentration values for mean line between group replicates

blankPointsY Responses from optical control wells

blankPointsX Concentrations for optical control wells
blankLineY Responses for optical control data line
blankLineX Concentrations for optical control data line
predLinesY Predicted responses
predLinesX Concentrations for predicted responses
graphDataDrug
A list of graph data per drug with components:
trays Tray names
Units Units of measurement
title Title for plot
drug Drug name
y Adjusted responses
x Adjusted concentrations
ylim y limits of plot
lineList List of x and y coordinates for each line of plot
legend Legend for plot

Author(s)

John Boik (jcboik@stanford.edu)

See Also

[doNls](#), [doNls](#)

Examples

```

# mixlowData data object is obtained using the prepareData function
data(mixlowData)
trays <- getTrays(mixlowData)
# nlsData data object is obtained using the doNls function
data(nlsData)
saved_nls_GraphingData <- plotNlsData(nlsData=nlsData, mixlowData=mixlowData,
  trays= trays[1:9], ask=FALSE, showBlanks= TRUE)

```

```
prepareData
```

Prepares raw data for use by other functions

Description

Prepares data for use by `doNls` and other functions.

Usage

```
prepareData(trayData, drugs, trays, cellLines)
```

Arguments

| | |
|-----------|---|
| trayData | A list returned from readDataFile |
| drugs | A vector of drug names used to subset data |
| trays | A vector of tray names used to subset data |
| cellLines | A vector of cell line names used to subset data |

Details

Data contained in a trayData object (produced by use of the readDataFile function) must be adjusted before it can be used by other functions of this package. The prepareData function adjusts observed responses based on responses in the optical control (“blank”) wells. The method used to adjust observed responses is stated in the data file (methods are either “bbt” or “bbc”). For method “bbc”, a fourth order polynomial is fit to the concentration-dependent optical control data. Predictions for each concentration are subtracted from the observed experimental responses. For type “bbt”, the average optical control response is subtracted from all observed responses.

To aid in forming the arguments drugs, trays, and cellLines, vectors of each can be obtained using the convenience functions getDrugs, getTrays, and getCellLines.

Value

A list of class mixlowData with the following components:

| | |
|-----------------------|--|
| concentrationResponse | A data frame containing adjusted concentration-response data |
| drugRatios | A data frame containing drug ratios |
| plottingData | A list used by plotMixlowData in plotting |

Author(s)

John Boik (jboik@stanford.edu)

See Also

[readDataFile](#), [plotMixlowData](#), [summarizeData](#)

Examples

```
# trayData data object is obtained using the readDataFile function
data(trayData)
trays <- getTrays(trayData)
cellLines <- getCellLines(trayData)
mixlowData <- prepareData(trayData=trayData, drugs="drug1", trays=trays[1:9],
  cellLines=cellLines[1])
```

| | |
|--------------|---|
| readDataFile | <i>Read a formatted file of concentration-response data</i> |
|--------------|---|

Description

Reads a formatted data file that contains concentration-response information.

Usage

```
readDataFile(filename, excludeWells)
```

Arguments

filename A string designating the data file to be read.

excludeWells An optional list that specifies rows and columns that should be skipped in the analysis. Paired components of the list are:

- row** row to skip
- col** column to skip

Details

The data file read by this function must be formatted according to a specific structure. See the example file `mixlowExampleData.txt` for use as a template. The data file is tab-delimited pure ASCII (without enclosing quotations) and the first entry on each line is a line label. The first eight lines contain general information about the experiments. Of these lines, only the entries `conc_units`, `rows`, and `cols` are required. The remainder of the data file is split into blocks, one block for each tray. For each block, the required entries are `tray_label`, `cell_line`, `drug_name_short`, `composition`, as well as the entries for `conc` (concentration), `label`, and `resp` (response) for each row and column of a tray. Even if the optional entries are left blank, the line labels must still be included (including the “space” labels).

The “ray” design should be used for each experiment. In this design, various dilutions of a drug or mixture are tested in the wells. If a mixture is being tested, a fixed ratio between component drugs occurs at every concentration tested. A tray should contain data for only a single drug or mixture. Replicate trays should be analyzed for each drug or mixture (for a given cell line). At least three replicate trays are recommended. However, if only one tray is available for a drug, `doNlme` will duplicate that tray (to make two replicates) so that analysis can be done in “experimental” mode. Tray labels can be alphanumeric, but avoid any characters other than digits and letters (the underscore can be used). The same is true for the abbreviated drug names that are required.

Each tray should contain wells used as treatment controls (i.e., those that receive cells but no drug). In addition, trays should contain wells used as optical controls (called “blanks” here). These can be of two types: 1) wells that contain only media, and 2) wells at each drug concentration that contain media and drug. The first type is referred to as “bbt”, or blanks-by-tray, and the second type is referred to as “bbc”, or blanks-by-concentration. The use of “bbc” is recommended when concentration-dependent responses can be induced by the drug alone (e.g., autofluorescence). For type “bbt”, raw responses are adjusted by subtracting the mean response of all “bbt” wells in a tray.

For type “bbc”, a 4th degree polynomial is fit to the “bbc” responses and predicted values for each concentration are subtracted from treatment well responses.

In many cases, a reasonable arrangement for a 96-well tray in a cytotoxicity experiment is to use the last two rows of every column as “bbc” blanks, use the first six rows of the first two columns as treatment controls, and use the first six rows of the third to twelfth columns as treatment wells, with each column receiving a different drug concentration.

When conducting large simulations, it is recommended that many small files be read from disk rather than one large file. The time required to read large files can be prohibitive.

Value

A list of class trayData with components:

```
concentrationResponse    Data frame containing concentration- response information
drugRatios               Data frame containing summary information for each tray
```

Author(s)

John Boik (jboik@stanford.edu)

See Also

[prepareData](#), [summarizeData](#)

Examples

```
dataFile = system.file(package="mixlow", "exdata/mixlowExampleData.txt")
excludeWells= list(row= c(1,2), col= c(1,1))
trayData <- readDataFile(filename=dataFile, excludeWells=excludeWells)
```

summarizeData *Print summary of data object*

Description

Prints a summary of a mixlowData or trayData data object.

Usage

```
summarizeData(object)
```

Arguments

object A list obtained from the prepareData or readDataFile functions.

Details

Prints a summary of information for data objects returned by the `prepareData` or `readDataFile` functions.

Value

None

Author(s)

John Boik (jcboik@stanford.edu)

See Also

[readDataFile](#), [prepareData](#)

Examples

```
# mixlowData data object is obtained using the prepareData function
data("mixlowData")
summarizeData(mixlowData)
```

trayData

trayData Dataset

Description

Dataset obtained as a result of using function `readDataFile`, based on data in the text file “mixlowExampleData.txt”. This file contains made-up example data.

Usage

```
data(trayData)
```

Format

See help file for function `readDataFile` for composition of `trayData` dataset.

Details

The text file “mixlowExampleData.txt” provides example data for a cytotoxicity experiment in which two drugs and their mixture is tested. Each drug is tested in three replicate trays.

See Also

[readDataFile](#)

Examples

```
data(trayData)
```

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