Package 'SuperCurve'

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Title SuperCurve Package
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Maintainer P. Roebuck <pre></pre>
Description A package to analyze reverse phase protein lysate arrays.
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SuperCurve-package Reverse phase protein lysate array analysis

Description

A package for analyzing reverse phase protein lysate arrays (RPPA).

Details

```
For a complete list of functions, use library (help="SuperCurve"). For a high-level summary of the changes for each revision, use file.show(system.file("NEWS", package="SuperCurve"))
```

Author(s)

Kevin R. Coombes (kcoombes@mdanderson.org), P. Roebuck (plroebuck@mdanderson.org)

```
CobsFitClass-class Class "CobsFitClass"
```

Description

The CobsFitClass class represents models that were fit with the nonparametric model.

Usage

```
## S4 method for signature 'CobsFitClass':
fitted(object, conc, ...)
```

Arguments

object of class CobsFitClass

conc numeric vector containing estimates of the log concentration for each dilution series

... extra arguments for generic routines

Value

The coef and coefficients methods return NULL.

The fitted method returns a numeric vector.

Methods

fitted(object, conc, ...) Extracts fitted values of the model

Objects from the Class

Objects are created internally by calls to the methods fitSlide or RPPAFit.

Directory-class 3

Slots

model: object of class cobs summarizing nonparametric fit

lambda: numeric

Extends

```
Class FitClass, directly.
```

Author(s)

P. Roebuck (plroebuck@mdanderson.org)

References

KRC

See Also

FitClass

Directory-class Class "Directory"

Description

The Directory class represents a file system directory.

Usage

```
Directory(path)
is.Directory(x)
```

Arguments

path character string specifying a directory
x object of class Directory

Value

The ${\tt Directory}$ generator returns an object of class ${\tt Directory}.$

The is . Directory method returns ${\tt TRUE}$ if its argument is an object of class ${\tt Directory}.$

Objects from the Class

Although objects of the class can be created by a direct call to new, the preferred method is to use the Directory generator function.

Slots

path: character string specifying a directory

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Author(s)

P. Roebuck (plroebuck@mdanderson.org)

Examples

```
txtdir <- Directory(system.file("rppaTumorData", package="SuperCurve"))
txtdir.path <- as(txtdir, "character")</pre>
```

FitClass-class

Class "FitClass"

Description

The FitClass class represents the model that was fit in the RPPAFit routine. Functions for use with the FitClass are only to be used internally.

Usage

Arguments

X	object of (sub)class FitClass	
object	object of (sub)class FitClass	
diln	numeric vector of dilutions for series to be fit	
intensity	numeric vector of observed intensities for series to be fit	
est.conc	numeric estimated concentration for dilution = 0	
method	character string specifying regression method to use fit the series	
silent	logical scalar. If ${\tt TRUE},$ report of error messages will not be suppressed in ${\tt try}(nlsmeth())$	
trace	logical scalar. Used in nls method.	
conc	numeric vector containing current estimates of concentration for each series	
design	object of class RPPADesign describing the layout of the array	
trimLevel	numeric scalar multiplied to MAD	
	extra arguments for generic routines	

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Value

The is. FitClass method returns TRUE if its argument is an object of subclass of class FitClass.

Methods

coef(object,...) Extracts model coefficients from objects returned by modeling functions. Returns NULL if subclass does not override.

coefficients(object,...) An alias for coef.

fitSeries(object, diln, intensity, est.conc, method="nls", silent=TRUE, trace=FALSE, ...) Finds the concentration for an individual dilution series given the curve fit for the slide.

fitSlide(object, conc, intensity, ...) Uses the concentration and intensity series for an entire slide to fit a curve for the slide of intensity = f(conc).

trimConc(object, conc, intensity, design, trimLevel, ...) Returns concentration and intensity cutoffs for the model.

Author(s)

P. Roebuck (plroebuck@mdanderson.org)

References

KRC

getConfidenceInterval

Compute Confidence Intervals for a Model Fit to Dilution Series

Description

This function computes confidence intervals for the estimated concentrations in a four-parameter logistic model fit to a set of dilution series in a reverse-phase protein array experiment.

Usage

```
getConfidenceInterval(result, alpha=0.1, nSim=50)
```

Arguments

result	object of class ${\tt RPPAFit}$ representing the result of fitting a four-parameter logistic model
alpha	numeric scalar specifying desired significance of the confidence interval; the width of the resulting interval is 1 - alpha.
nSim	numeric scalar specifying number of times to resample the data in order to estimate the confidence intervals.

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Details

In order to compute the confidence intervals, the function assumes that the errors in the observed Y intensities are independent normal values, with mean centered on the estimated curve and standard deviation that varies smoothly as a function of the (log) concentration. The smooth function is estimated using loess. The residuals are resampled from this estimate and the model is refit; the confidence intervals are computed empirically as symmetrically defined quantiles of the refit parameter sets.

Value

An object of class RPPAFit, containing updated values for the slots lower, upper, and conf. width that describe the confidence interval.

Author(s)

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References

KRC

See Also

```
RPPAFit-class, RPPAFit
```

Examples

LoessFitClass-class

Class "LoessFitClass"

Description

The LoessFitClass class represents models that were fit with the nonparametric model.

Usage

```
## S4 method for signature 'LoessFitClass':
fitted(object, conc, ...)
```

LogisticFitClass-class 7

Arguments

object of class LoessFitClass

conc numeric vector containing estimates of the log concentration for each dilution

series

... extra arguments for generic routines

Value

The coef and coefficients methods return NULL.

The fitted method returns a numeric vector.

Methods

fitted(object, conc, ...) Extracts fitted values of the model

Objects from the Class

Objects are created internally by calls to the methods fitSlide or RPPAFit.

Slots

model: object of class loess summarizing loess fit

Extends

Class FitClass, directly.

Author(s)

P. Roebuck (plroebuck@mdanderson.org)

References

KRC

See Also

FitClass

LogisticFitClass-class

Class "LogisticFitClass"

Description

The LogisticFitClass class represents models that were fit with the logistic model.

Usage

```
## S4 method for signature 'LogisticFitClass':
coef(object, ...)
## S4 method for signature 'LogisticFitClass':
coefficients(object, ...)
## S4 method for signature 'LogisticFitClass':
fitted(object, conc, ...)
```

Arguments

object of class LogisticFitClass

conc numeric vector containing estimates of the log concentration for each dilution series

... extra arguments for generic routines

Value

The coef and coefficients methods return a named vector of length three with logistic curve coefficients.

The fitted method returns a numeric vector.

Methods

```
coef(object,...) Extracts model coefficients
coefficients(object,...) An alias for coef.
fitted(object, conc,...) Extracts fitted values of the model
```

Objects from the Class

Objects are created internally by calls to the methods fitSlide or RPPAFit.

Slots

```
coefficients: numeric vector of length 3, representing alpha, beta, and gamma respectively.
```

Extends

```
Class FitClass, directly.
```

Author(s)

P. Roebuck (plroebuck@mdanderson.org)

References

KRC

See Also

FitClass

registerModel 9

registerModel Model Registration Methods

Description

These routines represent the high-level access for model registration, which enables data-driven access by other routines. This represents the initial implementation and may change in the future.

Usage

```
getRegisteredModel(key)
getRegisteredModelLabel(key)
getRegisteredModelKeys()
registerModel(key, classname, ui.label=names(key))
```

Arguments

key character string representing a registered model
classname character string specifying Model class name to register
ui.label character string specifying label to display by UI

Value

```
getRegisteredModel returns the classname associated with key.

getRegisteredModelLabel returns the ui.label associated with key.

getRegisteredModelKeys returns vector of keys for all registered models.

registerModel is invoked for its side effect, which is registering classname and ui.label by association to key.
```

Author(s)

P. Roebuck (plroebuck@mdanderson.org)

See Also

```
getRegisteredObject, getRegisteredObjectKeys, registerClassname
```

Examples

registerNormalizationMethod

Normalization Method Registration Methods

Description

These routines represent the high-level access for normalization method registration, which enables data-driven access by other routines. This represents the initial implementation and may change in the future.

Usage

```
getRegisteredNormalizationMethod(key)
getRegisteredNormalizationMethodLabel(key)
getRegisteredNormalizationMethodKeys()
registerNormalizationMethod(key, method, ui.label=names(key))
```

Arguments

key character string representing a registered normalization method

method function to invoke for normalization

ui.label character string specifying label to display by UI

Value

getRegisteredNormalizationMethod returns the method associated with key.
getRegisteredNormalizationMethodLabel returns the ui.label associated with key.

getRegisteredNormalizationMethodKeys returns vector of keys for all registered normalization methods.

registerNormalizationMethod is invoked for its side effect, which is registering method and ui.label by association to key.

Author(s)

P. Roebuck (plroebuck@mdanderson.org)

See Also

getRegisteredObject, getRegisteredObjectKeys, registerMethod

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Examples

```
## Not run:
## Create new normalization method
normalize.foo <- function(concs, bar) {
    return(normconcs <- concs - bar)
}

## Register normalization method to enable its use by package
registerNormalizationMethod("foo", normalize.foo, "Foo is as foo does")

## Use it...
concs <- matrix(runif(500), nrow=10)
    # :TBD: Remove package prefix when released to public...
SuperCurve:::normalize(concs, method="foo", bar=0.005)
    ## End(Not run)</pre>
```

RPPA-class

Class "RPPA"

Description

The RPPA class represents the raw quantification data from a reverse-phase protein array experiment.

Usage

Arguments

file	character string or connection specifying text file containing quantifications of a reverse-phase protein array experiment
path	character string specifying the path from the current directory to the file. The default value assumes the file is contained in the current directory. If file is a connection, this argument is ignored.
antibody	character string specifying antibody name. If missing, default value is filename (referenced by file argument) without extension.
software	character string specifying the software used to generate the quantification file (see section 'Details' below)
object	object of class RPPA
Х	object of class RPPA

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measure	character string containing the name of the measurement column in data that should be displayed by the image method
main	character string used to title the image plot
colorbar	logical scalar that determines whether to include a color bar in the plot. If TRUE, the image cannot be used as one panel in a window with multiple plots. Default is FALSE.
col	graphics parameter used by image. It is included here to change the default color scheme to use terrain.colors.
	extra arguments for generic or plotting routines

Details

The data frame slot (data) in a valid RPPA object constructed from a quantification file using the RPPA generator function is guaranteed to contain at least 6 columns of information:

Main.Row	logical location of spot on the array
Main.Col	logical location of spot on the array
Sub.Row	logical location of spot on the array
Sub.Col	logical location of spot on the array
Sample	unique identifier of sample spotted at location
Mean.Net	measurement representing background-corrected mean intensity of the spot

The first four components (taken together) give the logical location of a spot on an array. Additional columns may be included or may be added later.

Other methods can be specified to read the quantification files. The software argument is used in the selection of the actual method to perform this function. For example, if the argument value is "foo", the code will attempt to invoke method read.foo to read the file. The method will be passed a connection object to the file and should return a data frame containing the file's data. The method will be searched for in the global namespace, then within the package itself. The default value selects method read.microvigene, which this package provides to read *MicroVigene* quantification files in text format.

Value

The RPPA generator returns an object of class RPPA.

The is.RPPA method returns TRUE if its argument is an object of class RPPA.

The dim method returns a numeric vector of length 4.

The image method invisibly returns the RPPA object on which it was invoked.

The summary method returns a summary of the underlying data frame.

Objects from the Class

Although objects of the class can be created by a direct call to new, the preferred method is to use the RPPA generator function.

Slots

data: data.frame containing the contents of a quantification file

file: character string specifying the name of the file that the data was loaded from

antibody: character string specifying name of antibody

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Methods

dim(x) Returns the dimensions of the slide layout.

image(x, measure="Mean.Net", main=measure, colorbar=FALSE, col=terrain.colors(256), ...)

Produces a "geographic" image of the measurement column named by the measure argument. The colors in the image represent the intensity of the measurement at each spot on the array, and the display locations match the row and column locations of the spot. Any measurement column can be displayed using this function. An optional color bar can be added; this will be placed at the right edge.

summary(object,...) Prints a summary of the underlying data frame.

Author(s)

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References

KRC

See Also

```
RPPAFit, RPPADesign
```

Examples

```
path <- system.file("rppaTumorData", package="SuperCurve")
erk2 <- RPPA("ERK2.txt", path=path)
dim(erk2)
summary(erk2)
image(erk2)
image(erk2, colorbar=TRUE)
image(erk2, "Vol.Bkg", main="Background Estimates", colorbar=TRUE)</pre>
```

rppaCell-data

AKT, ERK2, and CTNNB1 expression in cell lines

Description

This data set contains the expression levels of three proteins: AKT, ERK2, and beta catenin (CTNNB1) in 40 cell lines, measured in duplicate dilution series using reverse-phase protein arrays.

The data set also contains a description of the design of the reverse-phase protein array used in a set of experiments to measure protein levels in 40 different cell lines. Cell lysates were spotted on the array in duplicate in eight-step dilution series. The layout of the array consisted of a grid of 4x4 subgrids. Each subgrid contained the duplicate dilution series for a single sample. Each of the identical top two rows of a subgrid contained the four most concentrated dilution steps (in decreasing concentrations from left to right), and the identical bottom two rows contained the four least concentrated dilution steps.

Usage

```
data(rppaCell)
```

Format

The objects akt, c.erk2, and ctnnb1 are objects of class RPPA. The object design40 is an object of class RPPADesign.

Source

Bryan Hennessey and Gordon Mills

References

KRC

```
RPPADesign-class Class "RPPADesign" and Class "RPPADesignParams"
```

Description

The RPPADesign class represents the information that describes how a particular set of RPPA slides was designed. The RPPADesignParams class is used to bundle the parameter set together for easier re-use.

Usage

```
RPPADesign (raw,
           steps=rep(0, 1),
           series=factor(rep(0, 1)),
           grouping=c("byRow", "byCol", "bySample", "blockSample"),
           ordering=c("decreasing", "increasing"),
           alias=NULL,
           center=FALSE,
           controls=NULL,
           aliasfile=NULL,
           designfile=NULL,
           path=".")
RPPADesignParams(steps=rep(0,1),
                 series=factor(rep(0,1)),
                 grouping=c("byRow", "byCol", "bySample", "blockSample"),
                 ordering=c("decreasing", "increasing"),
                 alias=NULL,
                 center=FALSE,
                 controls=NULL,
                 aliasfile=NULL,
                 designfile=NULL,
                 path=".")
RPPADesignFromParams(raw, designparams)
getSteps(design)
is.RPPADesign(x)
is.RPPADesignParams(x)
```

seriesNames(design)

path

center

```
## S4 method for signature 'RPPADesign':
    dim(x)
    ## S4 method for signature 'RPPADesign':
    image(x, ...)
    ## S4 method for signature 'RPPADesign':
    names(x)
    ## S4 method for signature 'RPPADesignParams':
    paramString(object, ...)
    ## S4 method for signature 'RPPA, RPPADesign':
    plot(x, y, ...)
    ## S4 method for signature 'RPPADesign':
    summary(object, ...)
Arguments
                     data frame, matrix, or object of class RPPA.
    raw
    designparams object of class RPPADesignParams.
                     numeric vector listing the dilution step associated with each spot, on a logarith-
    steps
                     mic scale.
                     character vector or factor identifying the dilution series to which each spot cor-
    series
                     responds.
                     character string specifying the orientation of the dilution series on the array.
    grouping
                     Valid values are:
          "byRow"
                             each row of a subgrid is its own dilution series
          "byColumn"
                             each column of a subgrid is its own dilution series
          "bySample"
                             each unique sample id is its own dilution series
          "blockSample"
                             all occurrences of sample id in subgrid refer to same series
                     character string specifying arrangement of dilution series. Valid values are:
    ordering
                                  arranged in order of decreasing concentrations
                "decreasing"
                "increasing"
                                  arranged in order of increasing concentrations
                     optional list or data frame for attaching sample labels or biologically relevant
    alias
                     descriptors to the dilution series with the following required named components:
                                           TBD description
                                 Alias
                                           TBD description
                                 Sample
                     optional character string specifying filename. Data would be read by read.delim
    aliasfile
                     and expected format is as described above for alias argument.
    designfile
                     optional character string specifying filename. Data would be read by read.delim
                     and expected format is that produced as output by the SlideDesignerGUI pack-
```

optional character string specifying directory path to prepend when either aliasfile

or designfile argument refer to relative filename; ignored when filename is

logical scalar. If TRUE, then dilution steps are centered around 0.

optional list containing the character strings that identify control spots on the array. RPPADesignParams will also coerce a character vector appropriately.

x object of class RPPADesign (or RPPA in plot method)

y object of class RPPADesign

object of class RPPADesign (or RPPADesignParams in paramString method)

design object of class RPPADesign

... extra arguments for generic or plotting routines.

Details

From their inception, reverse-phase protein array experiments have spotted samples on the array in dilution series. Thus, a critical aspect of the design and analysis is to understand how the dilution series are placed on the array.

The optional grouping and ordering arguments allows the user to specify several standard layouts without having to go into great detail. The most common layout is byRow, which indicates that each row of a subgrid on the array should be considered as a separate dilution series. Although considerably less common (for reasons related to the robotics of how arrays are printed), the byCol layout indicates that each column of a subgrid is its own dilution series. The bySample layout means that each unique sample name indicates its own dilution series. Finally, the blockSample layout indicates that all occurrences of a sample name within a subgrid (or block) refer to the same dilution series. The blockSample layout can be used, for example, when a dilution series is long enough to extend over more than one row of a subgrid. One layout we have seen used seven dilution steps followed by a control spot, contained in two successive rows of a design with 4x4 subgrids, leading to the pattern:

7654

321C

If the design of an RPPA experiment does not follow one of the built-in patterns, you can create an object by supplying vectors of dilution series names (in the series argument) and corresponding dilution steps (in the steps argument) that explicitly provide the mapping for each spot.

The arguments alias and aliasfile are mutually exclusive; they specify the exact same thing. The arguments controls and designfile are also mutually exclusive. The *Sample-Type* column of the slide design datafile is used to automatically populate the controls slot of RPPADesign class.

Value

The RPPADesign generator returns an object of class RPPADesign.

The RPPADesignParams generator returns an object of class RPPADesignParams.

The is.RPPADesign method returns TRUE if its argument is an object of class RPPADesign.

The is.RPPADesignParams method returns TRUE if its argument is an object of class RPPADesignParams.

The dim method returns a numeric vector of length 4.

The image method invisibly returns the displayed matrix of dilution steps.

The names method returns a character vector.

The paramString method returns a character vector, possibly empty but never NULL.

The summary method returns the summary object of the layout data frame.

The getSteps function returns a numeric vector containing, for each non-control spot, the step represented by that spot in its dilution series.

The seriesNames function returns a character vector containing the names of the unique (non-control) dilution series on the array.

Objects from the Class

Although objects of these classes can be created by a direct call to new, the preferred method is to start with the RPPADesignParams generator, followed by the RPPADesignFromParams function to construct the final object (the RPPADesign generator is directly implemented in this way).

Slots

For RPPADesign class:

call: object of class call specifying the function call that was used during construction

layout: data frame

alias: list

sampleMap: character vector

controls: list containing character strings that identify control spots on the array. Controls are not included as part of any dilution series.

For RPPADesignParams class:

steps: see corresponding argument above series: see corresponding argument above grouping: see corresponding argument above ordering: see corresponding argument above

center: see corresponding argument above

controls: list or NULL. see corresponding argument above alias: list or NULL. see corresponding argument above

aliasfile: character specifying absolute pathname of file containing alias information, or NULL

designfile: character specifying absolute pathname of file containing slide design information, or NULL

Methods

dim(**x**) Returns the dimensions of the slide layout.

image(x,...) Produces a two-dimensional graphical display of the layout design. Colors are used to represent different dilution steps, and laid out in the same pattern as the rows and columns of the array. This provides a visual check that the design has been specified correctly.

paramString(object) Returns string representation of object.

plot(x, y, ...) Plots an object of class RPPA by showing its dilution series with respect to the corresponding object of class RPPADesign.

summary(object,...) Lists the names of the control spots on the array and prints a summary of the data frame describing the layout.

Warning

The paramString method should not be called by user except for informational purposes. The content and format of the returned string may vary between different versions of this package.

Author(s)

Kevin R. Coombes (kcoombes@mdanderson.org), P. Roebuck (plroebuck@mdanderson.org)

References

KRC

See Also

RPPA

Examples

```
path <- system.file("rppaTumorData", package="SuperCurve")</pre>
erk2 <- RPPA("ERK2.txt", path=path)</pre>
design <- RPPADesign(erk2, grouping="blockSample", center=TRUE)</pre>
dim(design)
image(design)
summary (design)
designparams <- RPPADesignParams(grouping="blockSample",</pre>
                                   controls=list("neg con", "pos con"))
design <- RPPADesignFromParams(erk2, designparams)</pre>
image (design)
summary (design)
plot(erk2, design)
path <- system.file("rppaCellData", package="SuperCurve")</pre>
akt <- RPPA("Akt.txt", path=path)</pre>
\#\# Uses duplicate 8-step dilution series within 4x4 subgrids.
## They are interleaved, with top two identical rows containing the first
## 4 steps and the bottom two identical rows containing the last 4 steps.
steps \leftarrow rep(c(rep(8:5, 2), rep(4:1, 2)), 40) - 4.5
rep.temp <- factor(paste('Rep', rep(rep(1:2, each=4), 80), sep=""))
series <- factor(paste(as.character(akt@data$Sample),</pre>
                        as.character(rep.temp),
                         sep="."))
design40 <- RPPADesign(akt, steps=steps, series=series)</pre>
dim(design40)
image(design40)
summary(design40)
```

Description

Objects of the RPPAFit class represent the results of fitting a statistical model of response to the dilution series in a reverse-phase protein array experiment.

Usage

```
## S4 method for signature 'RPPAFit':
coef(object, ...)
## S4 method for signature 'RPPAFit':
coefficients (object, ...)
## S4 method for signature 'RPPAFit':
fitted(object, type=c("Y", "y", "X", "x"), ...)
## S4 method for signature 'RPPAFit':
hist(x, type=c("Residuals", "StdRes", "ResidualsR2"),
  xlab=NULL, main=NULL, ...)
## S4 method for signature 'RPPAFit':
image(x, measure=c("Residuals", "ResidualsR2", "StdRes", "X", "Y"), ...)
## S4 method for signature 'RPPAFit, missing':
plot(x, y, type=c("cloud", "series", "individual"),
  xlab="Log Concentration", ylab="Intensity", colors=NULL, ...)
## S4 method for signature 'RPPAFit':
resid(object, type=c("raw", "standardized", "r2"),
## S4 method for signature 'RPPAFit':
residuals(object, type=c("raw", "standardized", "r2"),
  . . . )
## S4 method for signature 'RPPAFit':
summary(object, ...)
```

Arguments

object	object of class RPPAFit
X	object of class RPPAFit
type	character string describing the type of fitted values, residuals, images, histograms, or plots
measure	character string specifying measure to compute from fit
xlab	graphics parameter specifying how the x-axis should be labeled
ylab	graphics parameter specifying how the y-axis should be labeled
main	character string specifying title for the plot
У	not used
colors	graphics parameter, used only if type='series', to color the lines connecting different dilution series. Eight default colors are used if the argument is NULL.
	extra arguments for generic or plotting routines

Details

The RPPAFit class holds the results of fitting a response model to all the dilution series on a reverse-phase protein array. For details on how the model is fit, see the RPPAFit function. By fitting a joint model, we assume that the response curve is the same for all dilution series on the

array. The real point of the model, however, is to be able to draw inferences on the δ_i , which represent the (log) concentration of the protein present in different dilution series.

Value

The coef and coefficients methods return the numeric model coefficients from objects returned by modeling functions.

The fitted method returns a numeric vector.

The hist method returns an object of class histogram.

The image method invisibly returns the object x on which it was invoked.

The plot method invisibly returns the object x on which it was invoked.

The resid and residuals methods return a numeric vector.

The summary method invisibly returns NULL.

Objects from the Class

Objects should be constructed using the RPPAFit function.

Slots

call: object of class call specifying the function call that was used to generate this model fit

rppa: object of class RPPA containing the raw data that was fit

design: object of class RPPADesign describing the layout of the array

measure: character string containing the name of the measurement column in the raw data that was fit by the model

method: character string containing the name of the method that was used to estimate the upper and lower limit parameters in the model

trimset: numeric vector of length 5 containing the low and high intensities, the low and high concentrations that mark the trimming boundaries, and the trim level used

model: object of class FitClass unique to the model that was fit

concentrations: numeric vector of estimates of the relative log concentration of protein present in each sample

lower: numeric vector containing the lower bounds on the confidence interval of the log concentration estimates

upper: numeric vector containing the upper bounds on the confidence interval of the log concentration estimates

conf.width: numeric scalar specifying width of the confidence interval

intensities: numeric vector containing the predicted observed intensity at the estimated concentrations for each dilution series

ss.ratio: numeric vector containing statistic measuring the \mathbb{R}^2 for each individual dilution series

warn: character vector containing any warnings that arose when trying to fit the model to individual dilution series

version: character string containing the version of SuperCurve that produced the fit

Methods

coef(object,...) Extracts model coefficients from objects returned by modeling functions. **coefficients(object,...)** An alias for coef.

- **fitted(object, type=c("Y", "y", "X", "x"),...)** Extracts the fitted values of the model. This process is more complicated than it may seem at first, since we are estimating values on both the X and Y axes. By default, the fitted values are assumed to be the intensities, Y, which are obtained using either an uppercase or lowercase 'y' as the type argument. The fitted log concentrations are returned when type is set to either uppercase or lowercase 'x'. In the notation used above to describe the model, these fitted values are given by $X_i = X \delta_i$.
- hist(x, type=c("Residuals", "StdRes", "ResidualsR2"), xlab=NULL, main=NULL,...) Produces a histogram of the residuals. The exact form of the residuals being displayed depends on the value of the type argument.
- image(x, measure=c("Residuals", "StdRes", "X", "Y"),...) Produces a 'geographic' plot of
 either the residuals or the fitted values, depending on the value of the measure argument.
 The implementation reuses code from the image method for an RPPA object.
- plot(x, y, type=c("cloud", "series", "individual", "steps", "resid"), xlab="Log Concentration", ylab="Intensity"
 Produces a diagnostic plot of the model fit. The default type, 'cloud', simply plots the fitted
 X values against the observed Y values as a cloud of points around the jointly estimated sigmoid curve. The 'series' plot uses different colored lines to join points belonging to the same dilution series. The 'individual' plot produces separate graphs for each dilution series, laying each one alongside the jointly fitted sigmoid curve.
- resid(object, type=c("raw", "standardized", "r2"), ...) An alias for residuals.
- residuals(object, type=c("raw", "standardized", "r2"),...) Reports the residual errors. The 'raw' residuals are defined as the difference between the observed intensities and the fitted intensities, as computed by the fitted function. The 'standardized' residuals are obtained by standardizing the raw residuals.
- **summary(object,...)** Prints a summary of the RPPAFit object. At present, this reports the function call used to fit the model and important fitting parameters.

Author(s)

Kevin R. Coombes (kcoombes@mdanderson.org), P. Roebuck (plroebuck@mdanderson.org)

References

KRC

See Also

```
RPPA, RPPADesign, RPPAFit, hist
```

Examples

```
image(fit.nls)
image(fit.nls, measure="Residuals")
plot(fit.nls, type="cloud")

## :TBD: Why recreate exact same fit as above?
fit.q <- RPPAFit(erk2, design, "Mean.Net")
hist(fit.q, type="StdRes")
plot(fit.q, type="series")

coef(fit.nls)
coef(fit.nls)
plot(fitted(fit.q), resid(fit.q))</pre>
```

RPPAFitParams-class

Fitting Dilution Curves to Protein Lysate Arrays with Class "RPPAFit-Params"

Description

The RPPAFit function fits an intensity response model to the dilution series in a reverse-phase protein array experiment. Individual sample concentrations are estimated by matching individual sample dilution series to the overall logistic response for the slide. The RPPAFitParams class is a convenient place to wrap the parameters that control the model fit into a reusable object.

Usage

```
RPPAFit (rppa,
        design,
        measure,
        model="logistic",
        xform=NULL,
        method=c("nls", "nlrob", "nlrq"),
        trim=2,
        ci=FALSE,
        ignoreNegative=TRUE,
        trace=FALSE,
        verbose=FALSE,
        veryVerbose=FALSE,
        warnLevel=0)
RPPAFitParams (measure,
              model="logistic",
              xform=NULL,
              method=c("nls", "nlrob", "nlrq"),
               trim=2,
               ci=FALSE,
               ignoreNegative=TRUE,
               trace=FALSE,
               verbose=FALSE,
```

```
veryVerbose=FALSE,
                       warnLevel=0)
    RPPAFitFromParams (rppa,
                             design,
                             fitparams)
    is.RPPAFit(x)
    is.RPPAFitParams(x)
    ## S4 method for signature 'RPPAFitParams':
    paramString(object, ...)
Arguments
                      object of class RPPA containing the raw data to be fit
    rppa
                      object of class RPPADesign describing the layout of the array
    design
                      object of the class RPPAFitParams, bundling together the following argu-
    fitparams
                      ments.
                      character string identifying the column of the raw RPPA data that should be used
    measure
                      to fit to the model.
                      character string specifying the model for the response curve fitted for the slide.
    model
                      Valid values are:
 "logistic"
                  assumes a logistic shape for the curve
 "loess"
                  fits a loess curve to the response
 "cobs"
                  fits a b-spline curve to the slide with the constraint that curve be strictly increasing
                      optional function that takes a single input vector and returns a single output
    xform
                      vector of the same length. The measure column is transformed using this
                      function before fitting the model.
                      character string specifying the method for matching the individual dilution series
    method
                      to the response curve fitted for the slide. Valid values are:
         "nls"
                     uses the optimal fit based on nonlinear least squares
                     uses nlrob which is robust nls from robustbase package
         "nlrob"
         "nlrq"
                     uses nlrq which is robust median regression from quantreg package
                      numeric or logical scalar specifying trim level for concentrations. If positive,
    trim
                      concentrations will be trimmed to reflect min and max concentrations we can
                      estimate given the background noise. If TRUE, the trim level defaults to 2,
                      which was originally the hardcoded value; otherwise, raw concentrations are
                      returned without trimming.
                      logical scalar. If TRUE, compute 90% confidence intervals on the concentration
    ci
                      estimates.
    ignoreNegative
                      logical scalar. If TRUE, convert negative values to NA before fitting the model.
                      logical scalar passed to nls in the method portion of the routine
    trace
                      logical scalar. If TRUE, print updates while fitting the data
    verbose
                      logical scalar. If TRUE, print voluminous updates as each individual dilution
    veryVerbose
                      series is fitted
```

warnLevel integer scalar used to set the warn option before calling method. Since this is wrapped in a try function, it won't cause failure but will give us a chance

to figure out which dilution series are failing. Setting warnLevel to two or

greater may change the values returned.

object of class RPPAFitParams

x object of class RPPAFit (or RPPAFitParams)

... extra arguments for generic routines.

Details

The basic mathematical model is given by

$$Y = f(X - \delta_i),$$

where Y is the observed intensity, X is the designed dilution step and f is the model for the protein response curve. By fitting a joint model, we assume that the response curve is the same for all dilution series on the array. The real point of the model, however, is to be able to draw inferences on the δ_i , which represent the (log) concentration of the protein present in different dilution series.

As the first step in fitting the model, we compute crude estimates of the individual δ_i assuming a rough logistic shape for the protein response curve.

Next, we fit an overall response curve for the slide f using the estimated concentrations and observed intensities $Y = f(\delta_i)$. The model for f is specified in the model parameter.

Next, we update the estimates of the individual δ_i using our improved fitted model f for the overall slide response curve. These individual series are matched to the overall slide response curve using the algorithm specified in method. The default method is nls, a least squares matchup, but we also offer robust alternatives which can do better.

Finally, we re-estimate f using the improved estimates for δ_i . We continue to iterate between f and δ_i . We do this twice since that seems to give reasonable convergence.

If the ci argument is TRUE, then the function also computes confidence intervals around the estimates of the log concentration. Since this step can be time-consuming, it is not performed by default. Moreover, confidence intervals can be computed after the main model is fit and evaluated, using the getConfidenceInterval function.

Value

The RPPAFit generator and RPPAFitFromParams function return an object of class RPPAFit.

The RPPAFitParams generator returns an object of class RPPAFitParams.

The is. RPPAFit method returns TRUE if its argument is an object of class RPPAFit.

The is. RPPAFitParams method returns TRUE if its argument is an object of class RPPAFitParams.

The paramString method returns a character vector, possibly empty but never NULL.

Objects from the Class

Although objects of the class can be created by a direct call to new, the preferred method is to use the RPPAFitParams function.

Slots

measure: character; see arguments above

xform: function or NULL; see arguments above

method: character; see arguments above

ci: logical; see arguments above

ignoreNegative: logical; see arguments above

trace: logical; see arguments above

verbose: logical; see arguments above

veryVerbose: logical; see arguments above

warnLevel: numeric; see arguments above

trim: numeric; see arguments above

model: character; see arguments above

Methods

paramString(object) Returns string representation of object.

Warning

The paramString method should not be called by user except for informational purposes. The content and format of the returned string may vary between different versions of this package.

Author(s)

P. Roebuck (plroebuck@mdanderson.org), Kevin R. Coombes (kcoombes@mdanderson.org)

References

KRC

See Also

```
RPPAFit RPPAFit-class, RPPA, RPPADesign
```

Examples

26 RPPASet-class

RPPASet-class Class "RPPASet"

Description

The RPPASet class fits supercurves to an entire directory of reverse-phase protein array experiments.

Usage

Arguments

path	character string specifying the path from the current directory to the directory containing the files to be processed
designparams	$\begin{tabular}{ll} \textbf{object of class} \ \texttt{RPPADesignParams} \ \textbf{describing features common to all quantification files} \\ \end{tabular}$
fitparams	object of class ${\tt RPPAFitParams}$ containing parameters used to fit the supercurve model
antibodyfile	character string specifying filename cantaining mapping from quantification files to antibodies
software	character string specifying the software used to generate the quantification file (see section 'Details' of \mathtt{RPPA})
object	object of class RPPASet
prefix	character string used as a prefix on files generated by the summary method.
graphs	logical scalar specifying if standard graphs should be produced
tiffdir	character string specifying path to the directory containing the original TIFF files
X	object of class RPPASet
	extra arguments for generic or plotting routines

Details

Quantify all the slides in a directory using RPPASet generator. This returns an object containing slide data and fits for each slide. Typically this is followed by a call to summary or write.summary to write the resulting quantifications and diagnostic plots to a directory.

Value

The RPPASet generator returns an object of class RPPASet.

The $\verb"is.RPPAS"$ et method returns TRUE if its argument is an object of class RPPASet.

The summary method returns a summary of the underlying data frame.

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Objects from the Class

Although objects of the class can (in theory) be created by a direct call to new, the only realistic method is to use the RPPASet generator function.

Slots

call: object of class call specifying the function call that was used during construction
version: character string containing the version of this package used to construct the object
design: object of class RPPADesign, common to all the slides
rppas: array of objects of class RPPA
fitparams: object of class RPPAFitParams that was used to construct the model fits
fits: array of fitted objects of class RPPAFit

Methods

summary(object, path, prefix, graphs, tiffdir,...) Creates a record of the entire RPPASet, including fitted values, residuals, and images of the processed slides. See the documentation of write.summary for details.

Author(s)

Kevin R. Coombes (kcoombes@mdanderson.org), P. Roebuck (plroebuck@mdanderson.org)

References

KRC

See Also

```
RPPA, RPPADesign, RPPAFit
```

Examples

```
## Not run:
parentdir <- file.path("C:", "MyData")</pre>
txtdir <- file.path(parentdir, "txt")  # quantification files
imgdir <- file.path(parentdir, "tif")  # and corresponding image files</pre>
outdir <- file.path(parentdir, "results") # output files</pre>
designparams <- RPPADesignParams(grouping="blockSample",</pre>
                                        center=FALSE,
                                        aliasfile="layoutInfo.tsv",
                                        designfile="slidedesign.tsv")
fitparams <- RPPAFitParams (measure="Mean.Net",</pre>
                                method="nlrob",
                                 model="cobs",
                                 ignoreNegative=FALSE,
                                warnLevel=-1,
                                 verbose=FALSE)
fitset <- RPPASet(txtdir,</pre>
                      designparams,
                      fitparams)
```

28 rppaTriple-data

rppaTriple-data

ACTB, CAS3, FAK, and ODC1 expression in 14 fed/starved cell lines

Description

This data set contains the expression levels of four proteins: beta-Actin (ACTB), Caspase 3 (CAS3), Focal adhesion kinase (FAK), and Ornithine decarboxylase (ODC1) from a study that was done to compare protein levels in 14 cell lines from both a "fed" and a dQuotestarved state. There are two files included for beta-Actin, one that was scanned in color (actb) and the other in 16-bit grayscale (actb.gray); all other proteins were scanned in color.

This data set also contains a description of the design used for the reverse-phase protein arrays from this study. Cell lysates were spotted on the array in six-step dilution series. The layout of the array consists of a grid of 6x6 subgrids. The first three rows of a subgrid contain 3 replicates of a cell line. The last three rows contain 3 replicates of another cell line. Each subgrid is replicated on the array 3 times, so that there are a total of 9 replicates per cell line per state. The top part of the array contains the fed cell lines and the bottom part of the array contains the starved cell lines. There is one subgrid on the array that contains only buffer material and another subgrid that did not have anything printed (blank). There are a total of 18 spots each of buffer and blank material.

Usage

```
data(rppaTriple)
```

Format

The objects actb, actb.gray, cas3, fak, and odc1 are objects of class RPPA. The object tripledesign is an object of class RPPADesign.

Source

Victor Levin

References

KRC

rppaTumor-data 29

rppaTumor-data

ERK2, GSK3, and JNK expression in tumor samples

Description

This data set contains the expression levels of three proteins: ERK2, GSK3, and JNK in 96 breast tumor samples and controls, measured in dilution series using reverse-phase protein arrays.

This data set also contains a description of the design of the reverse-phase protein array used in a set of experiments to measure protein levels. Cell lysates were spotted on the array in seven-step dilution series with eith a positive or negative control at the end of the series. The layout of the array consisted of a grid of 4x4 subgrids. The first two rows of a subgrid contained a single dilution series and a negative control spot. The last two rows of the subgrid contained another dilution series and a positive control spot.

Usage

```
data(rppaTumor)
```

Format

The objects erk2, gsk3, and jnk are objects of class RPPA. The object tDesign is an object of class RPPADesign.

Source

Doris Swank and Gordon Mills

References

KRC

```
spatialCorrection Spatial Correction
```

Description

This function estimates a smoothed surface from positive control spots on an RPPA slide. The surface is used to perform spatial corrections (i.e., because of uneven hybridization) on the array. It is used before RPPAFit, one slide at a time.

Usage

30 spatialCorrection

Arguments

rppa object of class RPPA

design object of class RPPADesign

measure character string specifying fit measure to smooth

cutoff numeric scalar used to identify the background cutoff with value in range [0..1]

k numeric scalar used as smoothing model argument.

gamma numeric scalar used as model parameter with value in range [0..2]

plotSurface logical scalar specifying whether to plot surfaces

Details

The observed spot intensities are assumed to be a combination of true signal, background noise, and hybridization effects according to the following model:

$$Y_r c = Y * H_r c + B_r c$$

where Y_rc is the observed intensity, Y is the true signal, H_rc is the effect of hybridization, and B_rc is the background noise. The subscripts "r" and "c" refer to the physical row and column of the spot on the array. Background noise is estimated locally by the array software. The hybridization effect is estimated fitting a generalized additive model (GAM) to positive control spots printed uniformly across the array.

The estimated surface is used to scale the intensities on the array. Each intensity is adjusted by the amount that is needed to make the positive control surface flat at the value of the median of the surface. This is done by dividing each spot by the estimated surface value and then multiplying by the median of the surface.

Positive control spots that are expressed below the cutoff for the noise region are excluded from the computation of the surface.

Sometimes, positive control spots are printed in a dilution series to avoid saturation problems with these spots. When this happens, the observed intensities are adjusted by the positive control surface that has the most similar expression level.

The design argument must have already been augmented with slide design information.

The cutoff argument passed to quantile is percentile of the background estimates used to define the noise region of slide.

The k argument passed to s sets upper limit on degrees of freedom associated with smoothing.

The gamma argument passed to gam provides a constant multiplier used to inflate model degrees of freedom in the GCV or UBRE/AIC score.

Value

Returns modified rppa with an additional measurement column named Spatial.Adj.

Note

This code may not yet work with slides containing more than one positive control series. Currently untested.

Author(s)

P. Roebuck (plroebuck@mdanderson.org), E. Shannon Neeley (sneeley@stat.byu.edu)

References

"Spatial Corrections for Reverse Phase Protein Arrays" (in progress).

See Also

```
quantile, gam, s, choose.k
```

Examples

```
SuperCurveSettings-class
```

Class "SuperCurveSettings"

Description

The SuperCurveSettings class represents the arguments needed to perform curve fitting.

Usage

Arguments

txtdir	character string specifying the directory containing quantification files in text format
imgdir	character string specifying the directory containing TIFF image files associated with each of the aforementioned quantification files
outdir	character string specifying the directory where output from analysis should be stored. Must be writable.

designparams object of class RPPADesignParams

fitparams object of class RPPAFitParams

object object of class SuperCurveSettings settings object of class SuperCurveSettings object of class SuperCurveSettings х

extra arguments for generic routines. . . .

Value

The SuperCurveSettings generator returns an object of class SuperCurveSettings.

The is.SuperCurveSettings method returns TRUE if its argument is an object of class SuperCurveSettings.

The paramString method returns a character vector, possibly empty but never NULL.

Objects from the Class

Although objects of the class can be created by a direct call to new, the preferred method is to use the SuperCurveSettings generator function.

Slots

txtdir: object of class Directory specifying the directory containing quantification files in text format

imgdir: object of class Directory specifying the directory containing TIFF image files

outdir: object of class Directory specifying the directory where analysis results should be stored

designparams: object of class RPPADesignParams specifying the parameters that describe how a particular set of RPPA slides was designed

fitparams: object of class RPPAFitParams specifying the parameters that control model fit version: character string containing the version of this package used to construct the object

Methods

paramString(object) Returns string representation of object.

Warning

The paramString method should not be called by user except for informational purposes. The content and format of the returned string may vary between different versions of this package.

Author(s)

P. Roebuck (plroebuck@mdanderson.org)

See Also

Directory, RPPAFitParams, RPPADesignParams

write.summary 33

Examples

```
## Not run:
designparams <- RPPADesignParams(center=FALSE,</pre>
                                  controls=list("neg con", "pos con"),
                                  grouping="blockSample")
fitparams <- RPPAFitParams(ignoreNegative=FALSE,</pre>
                            measure="Mean.Total",
                            method="nlrob",
                            model="loess",
                            warnLevel=-1)
fitparams <- RPPAFitParams(grouping="blockSample")</pre>
settings <- SuperCurveSettings(txtdir=system.file("rppaTumorData",</pre>
                                                    package="SuperCurve"),
                                 imgdir=file.path("", "path", "to", "images"),
                                 outdir=tempdir(),
                                 designparams=designparams,
                                 fitparams=fitparams)
fitCurveAndSummarizeFromSettings(settings)
## End(Not run)
```

write.summary

TBD

Description

This function produces a graphical summary for each array in an RPPASet and summarizes the quantification results into various files.

Usage

Arguments

rppaset	object of class RPPASet
path	character string specifying directory where output should be stored
prefix	character string providing a filename prefix to be applied when creating result files
graphs	logical scalar specifying whether to save fit graphs
tiffdir	character string specifying directory containing TIFF images corresponding to the TEXT quantification files

34 write.summary

Details

Generates three CSV files: one for the raw concentrations, one for the R^2 statistics, and one for the polished concentrations. If tiffdir is NULL, the directory is assumed to be a sibling directory to path named "tif". If graphs is TRUE, two PNG files containing output graphs are created per antibody. The ImageMagick 'convert' binary is then used to merge these output graphs with the source TIFF files, generating an additional JPEG file per antibody.

Author(s)

P. Roebuck (plroebuck@mdanderson.org)

References

KRC

See Also

RPPASet

Examples

```
## Not run:
parentdir <- file.path("lysate")</pre>
txtdir <- file.path(parentdir, "txt")</pre>
                                             # quantification files
imgdir <- file.path(parentdir, "tif")  # and corresponding image files</pre>
outdir <- file.path(parentdir, "results") # output files</pre>
designparams <- RPPADesignParams(grouping="blockSample",</pre>
                                   center=FALSE,
                                   controls=list("control",
                                                   "pos con",
                                                   "neg con"))
fitparams <- RPPAFitParams (measure="Mean.Net",</pre>
                            method="nlrob",
                             model="logistic",
                             ignoreNegative=FALSE,
                             warnLevel=-1,
                             verbose=FALSE)
fitset <- RPPASet(txtdir,
                   designparams,
                   fitparams,
                   antibodyfile="proteinAssay.tsv")
write.summary(fitset,
               outdir,
               graphs=TRUE,
               tiffdir=imgdir)
  ## End(Not run)
```

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