

Package ‘Xeva’

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Type Package

Title Analysis of patient-derived xenograft (PDX) data

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Description The Xeva package provides efficient and powerful functions for patient-derived xenograft (PDX) based pharmacogenomic data analysis.

This package contains a set of functions to perform analysis of patient-derived xenograft data. This package was developed by the BHKLab, for further information please see our documentation.

License GPL-3

Encoding UTF-8

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| | |
|-----|--|
| ABC | <i>area between curves Computes the area between two time-volume curves.</i> |
|-----|--|

Description

area between curves Computes the area between two time-volume curves.

Usage

```
ABC(  
  contr.time = NULL,  
  contr.volume = NULL,  
  treat.time = NULL,  
  treat.volume = NULL  
)
```

Arguments

| | |
|--------------|------------------------------|
| contr.time | Time vector for control. |
| contr.volume | Volume vector for control. |
| treat.time | Time vector for treatment. |
| treat.volume | Volume vector for treatment. |

Value

Returns batch response object.

Examples

```
contr.time <- treat.time <- c(0, 3, 7, 11, 18, 22, 26, 30, 32, 35)  
contr.volume<- contr.time * tan(60*pi/180)  
treat.volume<- treat.time * tan(15*pi/180)  
abc <- ABC(contr.time, contr.volume, treat.time, treat.volume)  
par(pty="s")  
xylimit <- range(c(contr.time, contr.volume, treat.time, treat.volume))  
plot(contr.time, contr.volume, type = "b", xlim = xylimit, ylim = xylimit)  
lines(treat.time, treat.volume, type = "b")  
polygon(c(treat.time, rev(treat.time)), c(contr.volume, rev(treat.volume)),  
  col = "#fa9fb5", border = NA)
```

addExperimentalDesign *Add a new experimental design*

Description

Add a new experimental design in the expDesign slot.

Usage

```
addExperimentalDesign(  
  object,  
  treatment = NULL,  
  control = NULL,  
  batch.id = NULL,
```

```

    replace = FALSE
  )

  ## S4 method for signature 'XevaSet'
  addExperimentalDesign(
    object,
    treatment = NULL,
    control = NULL,
    batch.id = NULL,
    replace = FALSE
  )

```

Arguments

| | |
|-----------|--|
| object | The Xeva dataset. |
| treatment | The model . id of treatment. |
| control | The model . id of control. |
| batch.id | The batch . id for a new batch. |
| replace | If TRUE, replace an old batch with new values. |

Value

Returns Xeva dataset with new experimental design added.

Examples

```

data(brca)
brca <- addExperimentalDesign(object=brca, treatment=c("X.6047.LL71"),
                             control=c("X.6047.uned"), batch.id="new.batch", replace=FALSE)

```

| | |
|-------|---|
| angle | <i>compute angle Computes the angle between two time-volume curves.</i> |
|-------|---|

Description

compute angle Computes the angle between two time-volume curves.

Usage

```

angle(
  contr.time = NULL,
  contr.volume = NULL,
  treat.time = NULL,
  treat.volume = NULL,
  degree = TRUE
)

```

Arguments

| | |
|---------------------------|---|
| <code>contr.time</code> | Time vector for control. |
| <code>contr.volume</code> | Volume vector for control. |
| <code>treat.time</code> | Time vector for treatment. |
| <code>treat.volume</code> | Volume vector for treatment. |
| <code>degree</code> | Default TRUE will give angle in degrees and FALSE will return in radians. |

Value

Returns batch response object.

Examples

```

contr.time <- treat.time <- c(0, 3, 7, 11, 18, 22, 26, 30, 32, 35)
contr.volume <- contr.time * tan(60*pi/180)
treat.volume <- treat.time * tan(15*pi/180)
ang <- angle(contr.time, contr.volume, treat.time, treat.volume)
print(ang)
par(pty="s")
xylim = range(c(contr.time, contr.volume, treat.time, treat.volume))
plot(contr.time, contr.volume, type = "b", xlim = xylim, ylim = xylim)
lines(treat.time, treat.volume, type = "b")
abline(lm(contr.volume~contr.time))
abline(lm(treat.volume~treat.time))

```

AUC

area under the curve AUC Returns area under the curve

Description

area under the curve AUC Returns area under the curve

Usage

```
AUC(time, volume)
```

Arguments

| | |
|---------------------|--|
| <code>time</code> | A vector of time points recorded for the experiment. |
| <code>volume</code> | First vector of volume. |

Value

Returns angle and slope object.

Examples

```

time <- c(0, 3, 7, 11, 18, 22, 26, 30, 32, 35)
volume1<- time * tan(30*pi/180)
volume2<- time * tan(45*pi/180)
auc1 <- AUC(time, volume1)
auc2 <- AUC(time, volume2)
par(pty="s")
xylim = range(c(time, volume1, volume2))
plot(time, volume1, type = "b", xlim = xylim, ylim = xylim)
lines(time, volume2, type = "b")
abline(lm(volume1~time))
abline(lm(volume2~time))

```

batchInfo

Get batch information

Description

Get batch information from a Xeva dataset.

Usage

```

batchInfo(
  object,
  batch = NULL,
  model.id = NULL,
  model.id.type = c("any", "control", "treatment")
)

```

```
## S4 method for signature 'XevaSet'
```

```

batchInfo(
  object,
  batch = NULL,
  model.id = NULL,
  model.id.type = c("any", "control", "treatment")
)

```

Arguments

| | |
|---------------|--|
| object | The Xeva object from which batch information is obtained. |
| batch | Name of the batch. Default NULL. |
| model.id | Model ID for which need to be searched in the batches. Default NULL. |
| model.id.type | Type of the model ID in a batch. See the Details section below. |

Details

By default this function will return the names of all the batches present in the dataset. If a batch specified, it will return the experiment design (control and treatment model IDs) of that particular batch. If `model.id` is specified, it will return the names of all the batches where this particular `model.id` is present. If both `batch` and `model.id` are specified, `batch` will take precedent.

For `model.id.type`, the default value 'any' will return all the batch IDs where the given model ID is present in any arm (ie. control or treatment) of the batch. It can also be restricted to look only for treatment (or control) arm by specifying the type.

Value

A Vector with batch names.

Examples

```
data(brca)
##to get all the batch names
batch.name <- batchInfo(brca)

##to get a specific batch
batch.design <- batchInfo(brca, batch=batch.name[1])

##to get all the batches where a model.id is present
batchInfo(brca, model.id="X.6047.uned")
```

brca

PDXE breast cancer dataset

Description

A Xeva object containing only breast cancer PDXs from the PDXE dataset For details about PDX-MI, see: Gao et al. High-throughput screening using patient-derived tumor xenografts to predict clinical trial drug response. Nature medicine, 21(11):1318, 2015.

Usage

```
data(brca)
```

Format

An object of class XevaSet of length 1.

Source

<https://www.nature.com/articles/nm.3954?draft=journal>

| | |
|---------------|----------------------------|
| createXevaSet | <i>XevaSet constructor</i> |
|---------------|----------------------------|

Description

A constructor to create XevaSet. Only objects returned by this constructor are expected to work with the XevaSet methods.

Usage

```
createXevaSet(
  name,
  model = data.frame(),
  drug = data.frame(),
  experiment = data.frame(),
  expDesign = list(),
  modelSensitivity = data.frame(),
  batchSensitivity = data.frame(),
  molecularProfiles = list(),
  modToBiobaseMap = data.frame()
)
```

Arguments

| | |
|-------------------|---|
| name | A character string detailing the name of the dataset. |
| model | A data.frame containing the annotations for all the models used in the experiment. |
| drug | A data.frame containing the annotations for all the drugs profiled in the dataset, across all data types. |
| experiment | A data.frame containing all experiment information. |
| expDesign | A list containing name of the batch, control and treatment model.id |
| modelSensitivity | A data.frame containing sensitivity for each model |
| batchSensitivity | A data.frame containing sensitivity for each batch |
| molecularProfiles | A list of ExpressionSet objects containing different molecular profiles. |
| modToBiobaseMap | A data.frame containing model.id corresponding Biobase object id and name of the molecularProfiles |

Details

This function creates a XevaSet object. It takes different model information and genomic data as input. For detailed discription of all varaibles please see Xeva vignette section "**Creating new Xeva object**"

Value

Returns Xeva object

Examples

```
## read raw data files containg PDX experiment information and genomic data
model = read.csv(system.file("extdata", "model.csv", package = "Xeva"))
drug = read.csv(system.file("extdata", "drug.csv", package = "Xeva"))
experiment= read.csv(system.file("extdata", "experiments.csv", package = "Xeva"))
expDesign=readRDS(system.file("extdata", "batch_list.rds", package = "Xeva"))
RNASeq=readRDS(system.file("extdata", "rnaseq.rds", package = "Xeva"))
modToBiobaseMap=read.csv(system.file("extdata", "modelToExpressionMap.csv", package = "Xeva"))

## create Xeva object
xeval.set = createXevaSet(name="example xeval.set", model=model, drug=drug,
                          experiment=experiment, expDesign=expDesign,
                          molecularProfiles=list(RNASeq = RNASeq),
                          modToBiobaseMap = modToBiobaseMap)

print(xeval.set)
```

dosePlot

plot dose data

Description

plot data for dose in model.id

Usage

```
dosePlot(
  object,
  model.id,
  max.time = NULL,
  treatment.only = FALSE,
  vol.normal = FALSE,
  concurrent.time = FALSE,
  point.shape = 21,
  point.size = 3,
  line.size = 4,
  point.color = "#878787",
  line.color = "#bababa",
  fill.col = c("#f5f5f5", "#E55100"),
  modify.x.axis = FALSE
)
```

Arguments

| | |
|------------------------------|--|
| <code>object</code> | Xeva object. |
| <code>model.id</code> | one or multiple model.id |
| <code>max.time</code> | Maximum time point of the plot. Default NULL will plot complete data |
| <code>treatment.only</code> | Default FALSE. Given full data <code>treatment.only=TRUE</code> will plot data only during treatment |
| <code>vol.normal</code> | Default FALSE. If TRUE, volume will be normalized |
| <code>concurrent.time</code> | Default FALSE. If TRUE, cut the batch data such that control and treatment will end at the same time point |
| <code>point.shape</code> | shape of the point |
| <code>point.size</code> | size of the point |
| <code>line.size</code> | size of the line |
| <code>point.color</code> | color for point |
| <code>line.color</code> | color for line |
| <code>fill.col</code> | a vector with color to fill |
| <code>modify.x.axis</code> | Default FALSE |

Value

A ggplot2 plot

Examples

```
data(brca)
dosePlot(brca, model.id=c("X.6047.LJ16", "X.6047.LJ16.trab"), fill.col=c("#f5f5f5", "#993404"))
```

downloadXevaSet

Download a XevaSet object or table of available XevaSet objects

Description

This function allows you to see the available XevaSet object and download them for use with this package. The XevaSet have been extensively curated and organised within a XevaSet class, enabling use with all the analysis tools provided in Xeva.

Usage

```
downloadXevaSet(
  name = NULL,
  saveDir = file.path(".", "XevaSet"),
  XevaSetFileName = NULL,
  verbose = TRUE
)
```

Arguments

| | |
|-----------------|--|
| name | Character string, the name of the XevaSet to download. |
| saveDir | Character string with the folder path where the XevaSet should be saved. Defaults to './XevaSet/'. Will create directory if it does not exist. |
| XevaSetFileName | character string, the file name to save the dataset under |
| verbose | bool Should status messages be printed during download. Defaults to TRUE. |

Value

A data.frame if name is NULL, showing all the available XevaSet objects. If name is specified, it will download the dataset from our server

| | |
|------------|--|
| drugInform | <i>Get drug information Get the drug information slot from a XevaSet object.</i> |
|------------|--|

Description

Get drug information Get the drug information slot from a XevaSet object.

Usage

```
drugInform(object)

## S4 method for signature 'XevaSet'
drugInform(object)
```

Arguments

object The XevaSet to retrieve drug information from.

Value

A data.frame with the drug annotations.

Examples

```
data(brca)
head(drugInform(brca))
```

drugSensitivitySig *get drug sensitivity values*

Description

Given a Xeva object and drug name, this function will return sensitivity values for all the genes/features.

Usage

```
drugSensitivitySig(
  object,
  drug,
  mDataType = NULL,
  molData = NULL,
  features = NULL,
  model.ids = NULL,
  model2bidMap = NULL,
  sensitivity.measure = "slope",
  fit = c("lm", "CI", "pearson", "spearman", NA),
  standardize = c("SD", "rescale", "none"),
  nthread = 1,
  tissue = NULL,
  verbose = TRUE
)
```

Arguments

| | |
|---------------------|--|
| object | The Xeva dataset. |
| drug | Name of the drug. |
| mDataType | Molecular data type. |
| molData | External data matrix. Rows as features and columns as samples. |
| features | Set which molecular data features to use. Default NULL will use all features. |
| model.ids | Set which model.id to use from the dataset. Default NULL will use all model.ids. |
| model2bidMap | A data.frame with model.id and biobase.id. Default NULL will use internal mapping. |
| sensitivity.measure | Name of the sensitivity measure. |
| fit | Association method to use, can be 'lm', 'CI', 'pearson' or 'spearman'. If 'NA' only the data will be return. Default lm. |
| standardize | Default SD. Name of the method to use for data standardization before fitting. |
| nthread | number of threads |
| tissue | tissue type. Default NULL uses 'tissue' from object. |
| verbose | Default TRUE will show information |

Details

Method to compute association can be specified by `fit`. It can be one of the:

- "lm" for linear models
- "CI" for concordance index
- "pearson" for Pearson correlation
- "spearman" for Spearman correlation

If `fit` is set to NA, processed data (an ExpressionSet) will be returned.

A matrix of values can be directly passed to `molData`. In case where a `model.id` maps to multiple `biobase.ids`, the first `biobase.id` in the `data.frame` will be used.

Value

A `data.frame` with features and values.

Examples

```
data(brca)
senSig <- drugSensitivitySig(object=brca, drug="tamoxifen",
                           mDataType="RNASeq", features=c(1,2,3,4,5),
                           sensitivity.measure="slope", fit = "lm")

## example to compute the Pearson correlation between gene expression and PDX response
senSig <- drugSensitivitySig(object=brca, drug="tamoxifen",
                           mDataType="RNASeq", features=c(1,2,3,4,5),
                           sensitivity.measure="slope", fit = "pearson")
```

getExperiment

Get PDX experiment data

Description

For a given `model.id`, `getExperiment` will

Usage

```
getExperiment(
  object,
  model.id = NULL,
  batch = NULL,
  patient.id = NULL,
  drug = NULL,
  control.name = NULL,
  treatment.only = FALSE,
  max.time = NULL,
```

```

    vol.normal = FALSE,
    log.volume = FALSE,
    return.list = FALSE,
    impute.value = FALSE,
    concurrent.time = FALSE
  )

## S4 method for signature 'XevaSet'
getExperiment(
  object,
  model.id = NULL,
  batch = NULL,
  patient.id = NULL,
  drug = NULL,
  control.name = NULL,
  treatment.only = FALSE,
  max.time = NULL,
  vol.normal = FALSE,
  log.volume = FALSE,
  return.list = FALSE,
  impute.value = FALSE,
  concurrent.time = FALSE
)

```

Arguments

| | |
|------------------------------|---|
| <code>object</code> | The XevaSet object. |
| <code>model.id</code> | The model . id for which data is required, multiple IDs are allowed. |
| <code>batch</code> | Batch name from the XevaSet or experiment design. |
| <code>patient.id</code> | Patient id from the XevaSet. Default NULL. |
| <code>drug</code> | Name of the drug. |
| <code>control.name</code> | Name of drug used as control. Default NULL. |
| <code>treatment.only</code> | Default FALSE. If TRUE, give data for non-zero dose periods only (if dose data are available). |
| <code>max.time</code> | Maximum time for data. |
| <code>vol.normal</code> | If TRUE it will normalize the volume. Default FALSE. |
| <code>log.volume</code> | If TRUE log of the volume will be used. Default FALSE. |
| <code>return.list</code> | Default FALSE will return a data . frame. |
| <code>impute.value</code> | Default FALSE. If TRUE, impute the missing values. |
| <code>concurrent.time</code> | Default FALSE. If TRUE, cut the batch data such that control and treatment will end at same time point. |

Value

a data . fram will all the the values stored in experiment slot

Examples

```
data(brca)

getExperiment(brca, model.id="X.6047.uned", treatment.only=TRUE)

getExperiment(brca, model.id=c("X.6047.uned", "X.6047.pael"), treatment.only=TRUE)

getExperiment(brca, batch="X-6047.paclitaxel", treatment.only=TRUE)

ed <- list(batch.name="myBatch", treatment=c("X.6047.LJ16","X.6047.LJ16.trab"),
          control=c("X.6047.uned"))

getExperiment(brca, batch=ed)
```

getMolecularProfiles *Get molecular profiles from a XevaSet object*

Description

This function serves to get molecular profiles from a XevaSet object.

Usage

```
getMolecularProfiles(object, data.type)
```

Arguments

| | |
|-----------|---|
| object | The XevaSet. |
| data.type | character, where one of the molecular data types is needed. |

Value

An ExpressionSet where sample names are the biobase.id of the model.

Examples

```
data(brca)
brca.RNA <- getMolecularProfiles(brca, data.type="RNASeq")
```

lmm *linear mixed model*

Description

Comput the linear mixed model (lmm) statistics for a PDX batch

Usage

```
lmm(data)
```

Arguments

data a data.frame containg a batch data

Details

The input data.frame (data) must contain these columns: model.id, volume, time, exp.type

Value

Returns a fit object

Examples

```
data(repdx)
data <- getExperiment(repdx, batch = "P1")$model
lmm(data)
```

modelInfo *modelInfo Generic Generic for modelInfo method*

Description

modelInfo Generic Generic for modelInfo method

Usage

```
modelInfo(object, mDataType = NULL)
```

```
## S4 method for signature 'XevaSet'
modelInfo(object, mDataType = NULL)
```


Arguments

object Xeva object
mDataType Molecular data type.

Value

A data.frame with the model annotations.

Examples

```
data(brca)
mid <- modelInfo(brca)
head(mid)
```

mRECIST

Computes the mRECIST

Description

mRECIST Returns the mRECIST for given volume response.

Usage

```
mRECIST(time, volume, min.time = 10, return.detail = FALSE)
```

Arguments

time Value of best response.
volume Value of best average response.
min.time Minimum time after which tumor volume will be considered.
return.detail Default FALSE. If TRUE, return all intermediate values.

Value

Returns the mRECIST.

Examples

```
time <- c(0, 3, 7, 11, 18, 22, 26, 30, 32, 35)
volume<- c(250.8, 320.4, 402.3, 382.6, 384, 445.9, 460.2, 546.8, 554.3, 617.9)
mRECIST(time, volume, min.time=10, return.detail=FALSE)
```

PDXMI

PDX-MI data

Description

A dataset containing PDX models minimal information (PDX-MI) standard and corresponding Xeva variable.

Usage

```
data(PDXMI)
```

Format

An object of class `data.frame` with 45 rows and 4 columns.

Details

For details about PDX-MI, see:

Meehan, Terrence F, et al. "PDX-MI: minimal information for patient-derived tumor xenograft models." *Cancer research* 77.21 (2017): e62-e66.

Source

<http://cancerres.aacrjournals.org/lookup/doi/10.1158/0008-5472.CAN-17-0582>

plotmRECIST

To plot mRECIST values

Description

plotmRECIST plots the mRECIST matrix obtained from `summarizeResponse`.

Usage

```
plotmRECIST(  
  mat,  
  control.name = NA,  
  control.col = "#238b45",  
  drug.col = "black",  
  colPalette = NULL,  
  name = "Drug & Models",  
  sort = TRUE,  
  row_fontsize = 12,  
  col_fontsize = 12,  
  draw_plot = TRUE  
)
```

Arguments

| | |
|--------------|---|
| mat | The mRECIST matrix where rows are drugs and columns are patients. |
| control.name | Name of the control. |
| control.col | Color of the control. |
| drug.col | Color of the drug names. |
| colPalette | Color palette for mRECIST values. |
| name | Title of the plot. |
| sort | If matrix should be sorted before plotting. |
| row_fontsize | Size of the row name font. |
| col_fontsize | Size of the column name font. |
| draw_plot | Default TRUE will plot the figure. If FALSE, return an object. |

Value

mRECIST plot.

Examples

```
data(brca)
brca.mr <- summarizeResponse(brca, response.measure = "mRECIST", group.by="patient.id")
plotmRECIST(as.matrix(brca.mr), control.name = "untreated")
```

plotPDX

Plot batch data

Description

Plot data for a batch.id, experiment design or model.id

Usage

```
plotPDX(
  object,
  batch = NULL,
  patient.id = NULL,
  drug = NULL,
  model.id = NULL,
  model.color = NULL,
  control.name = NULL,
  max.time = NULL,
  treatment.only = FALSE,
  vol.normal = FALSE,
  impute.value = TRUE,
  concurrent.time = FALSE,
```

```

control.col = "#e41a1c",
treatment.col = "#377eb8",
title = "",
xlab = "Time",
ylab = "Volume",
log.y = FALSE,
SE.plot = c("all", "none", "errorbar", "ribbon"),
aspect.ratio = c(1, NULL),
minor.line.size = 0.5,
major.line.size = 0.7
)

plotBatch(
  object,
  batch = NULL,
  patient.id = NULL,
  drug = NULL,
  control.name = NULL,
  max.time = NULL,
  treatment.only = FALSE,
  vol.normal = FALSE,
  impute.value = TRUE,
  concurrent.time = FALSE,
  control.col = "#6baed6",
  treatment.col = "#fc8d59",
  title = "",
  xlab = "Time",
  ylab = "Volume",
  log.y = FALSE,
  SE.plot = c("all", "none", "errorbar", "ribbon"),
  aspect.ratio = c(1, NULL),
  minor.line.size = 0.5,
  major.line.size = 0.7
)

```

Arguments

| | |
|-----------------------------|---|
| <code>object</code> | Xeva object. |
| <code>batch</code> | Batch name or experiment design list. |
| <code>patient.id</code> | Patient id from the XevaSet. Default NULL. |
| <code>drug</code> | Name of the drug. Default NULL. |
| <code>model.id</code> | One or multiple model.id. Default NULL. |
| <code>model.color</code> | Color for model.id. Default NULL. |
| <code>control.name</code> | Name of the control sample. |
| <code>max.time</code> | Maximum time point of the plot. Default NULL will plot complete data. |
| <code>treatment.only</code> | Default FALSE. Given full data <code>treatment.only=TRUE</code> will plot data only during treatment. |

| | |
|-----------------|---|
| vol.normal | Default FALSE. If TRUE, volume will be normalized. |
| impute.value | Default TRUE will impute values if missing. |
| concurrent.time | Default FALSE. If TRUE, cut the batch data such that control and treatment will end at the same time point. |
| control.col | Color for control plots. |
| treatment.col | Color for treatment plots. |
| title | Title of the plot. |
| xlab | Title of the x-axis. |
| ylab | Title of the y-axis. |
| log.y | Default FALSE. If TRUE, y-axis will be log-transformed. |
| SE.plot | Plot type. Default "all" will plot all plots and average curves. Possible values are "all", "none", "errorbar", and "ribbon". |
| aspect.ratio | Default 1 will create a plot of equal width and height. |
| minor.line.size | Line size for minor lines. Default 0.5. |
| major.line.size | Line size for major lines. Default 0.7. |

Value

A ggplot2 plot with control and treatment batch data.

Examples

```
data(brca)
plotPDX(brca, model.id=c("X.6047.LJ16", "X.6047.LJ16.trab"))

plotPDX(brca, batch="X-1004.BGJ398", vol.normal=TRUE)
expDesign <- list(batch.name="myBatch", treatment=c("X.6047.LJ16", "X.6047.LJ16.trab"),
                 control=c("X.6047.uned"))
plotBatch(brca, batch=expDesign, vol.normal=TRUE)
plotBatch(brca, batch=expDesign, vol.normal=FALSE, SE.plot = "errorbar")
```

```
print.batchResponse Print the batch response
```

Description

Print the batch response

Usage

```
## S3 method for class 'batchResponse'
print(x, ...)
```

Arguments

x batchResponse object
... Other arguments

Value

prints the batchResponse

print.modelResponse *Print the model response*

Description

Print the model response

Usage

```
## S3 method for class 'modelResponse'  
print(x, ...)
```

Arguments

x modelResponse object
... Other arguments

Value

prints the modelResponse

print.pdxBatch *Print the pdx batch*

Description

Print the pdx batch

Usage

```
## S3 method for class 'pdxBatch'  
print(x, ...)
```

Arguments

x pdxBatch object
... Other arguments

Value

prints pdxBatch

repx

Example PDX dataset

Description

A Xeva object containing anonymous PDX data with replicates. Each batch has 5 replicates.

Usage

data(repx)

Format

An object of class XevaSet of length 1.

response

compute PDX response

Description

response Computes the drug response of an individual PDX model or batch.

Usage

```
response(
  object,
  model.id = NULL,
  batch = NULL,
  res.measure = c("mRECIST", "slope", "AUC", "angle", "abc", "TGI", "lmm"),
  treatment.only = FALSE,
  max.time = NULL,
  impute.value = TRUE,
  min.time = 10,
  concurrent.time = TRUE,
  vol.normal = FALSE,
  log.volume = FALSE,
  verbose = TRUE
)
```

Arguments

| | |
|------------------------------|---|
| <code>object</code> | Xeva object. |
| <code>model.id</code> | <code>model.id</code> for which the drug response is to be computed. |
| <code>batch</code> | <code>batch.id</code> or experiment design for which the drug response is to be computed. |
| <code>res.measure</code> | Drug response measure. See Details below |
| <code>treatment.only</code> | Default FALSE. If TRUE, give data for non-zero dose periods only (if dose data are available). |
| <code>max.time</code> | Maximum time for data. |
| <code>impute.value</code> | Default FALSE. If TRUE, impute the missing values. |
| <code>min.time</code> | Default 10 days. Used for <i>mRECIST</i> computation. |
| <code>concurrent.time</code> | Default FALSE. If TRUE, cut the batch data such that control and treatment will end at same time point. |
| <code>vol.normal</code> | If TRUE it will normalize the volume. Default FALSE. |
| <code>log.volume</code> | If TRUE log of the volume will be used for response calculation. Default FALSE |
| <code>verbose</code> | Default TRUE will print information. |

Details

At present the following response measures are implemented

- *mRECIST* Computes *mRECIST* for individual PDX models
- *slope* Computes slope of the fitted individual PDX curves
- *AUC* Computes area under a PDX curve for individual PDX models
- *angle* Computes angle between treatment and control PDX curves
- *abc* Computes area between the treatment and control PDX curves
- *TGI* Computes tumor growth inhibition using treatment and control PDX curves
- *Imm* Computes linear mixed model (*Imm*) statistics for a PDX batch

Value

Returns model or batch drug response object.

Examples

```
data(brca)
response(brca, model.id="X.1004.BG98", res.measure="mRECIST")

response(brca, batch="X-6047.paclitaxel", res.measure="angle")

ed <- list(batch.name="myBatch", treatment=c("X.6047.LJ16", "X.6047.LJ16.trab"),
           control=c("X.6047.uned"))
response(brca, batch=ed, res.measure="angle")
```

| | |
|----------------|---|
| selectModelIds | <i>To select model IDs based on drug name and/or tissue type.</i> |
|----------------|---|

Description

To select model IDs based on drug name and/or tissue type.

Usage

```
selectModelIds(object, drug = NULL, drug.match.exact = TRUE, tissue = NULL)
```

```
## S4 method for signature 'XevaSet'
```

```
selectModelIds(object, drug = NULL, drug.match.exact = TRUE, tissue = NULL)
```

Arguments

| | |
|------------------|---------------------------|
| object | The XevaSet. |
| drug | Name of the drug. |
| drug.match.exact | Default TRUE. |
| tissue | Tumor type. Default NULL. |

Value

A vector with the matched model . ids.

Examples

```
data(brca)
df = selectModelIds(brca, drug="trastuzumab", drug.match.exact=TRUE, tissue="BRCA")
head(df)
df2 = selectModelIds(brca, drug="trastuzumab", drug.match.exact=FALSE)
head(df2)
```

| | |
|-------------|---|
| sensitivity | <i>Get sensitivity for an Xeva object</i> |
|-------------|---|

Description

Given a Xeva object, it will return a data . frame detailing sensitivity information.

Usage

```
sensitivity(object, type = c("model", "batch"), sensitivity.measure = NULL)
```

Arguments

| | |
|---------------------|---|
| object | The Xeva dataset. |
| type | Sensitivity type (either model or batch). |
| sensitivity.measure | Name of the sensitivity.measure. Default NULL will return all sensitivity measures. |

Value

A data.frame with model or batch ID and sensitivity values.

Examples

```
data(brca)
head(sensitivity(brca, type="batch"))
head(sensitivity(brca, type="model"))
```

| | |
|-------------|-------------------------|
| setResponse | <i>set PDX response</i> |
|-------------|-------------------------|

Description

setResponse sets response of all PDXs in an Xeva object.

Usage

```
setResponse(
  object,
  res.measure = c("mRECIST", "slope", "AUC", "angle", "abc", "TGI", "Imm"),
  min.time = 10,
  treatment.only = FALSE,
  max.time = NULL,
  vol.normal = FALSE,
  impute.value = TRUE,
  concurrent.time = TRUE,
  log.volume = FALSE,
  verbose = TRUE
)
```

Arguments

| | |
|----------------|--|
| object | Xeva object. |
| res.measure | Response measure, multiple measures are allowed. See Details below |
| min.time | Minimum number of days for <i>mRECIST</i> computation. Default 10 days. |
| treatment.only | Default FALSE. If TRUE, give data for non-zero dose periods only (if dose data are available). |

| | |
|------------------------------|--|
| <code>max.time</code> | Maximum number of days to consider for analysis. Data beyond this will be discarded. Default NULL takes full data. |
| <code>vol.normal</code> | If TRUE it will will normalize the volume. Default FALSE |
| <code>impute.value</code> | Default FALSE. If TRUE, impute the missing volume values. |
| <code>concurrent.time</code> | Default FALSE. If TRUE, cut the batch data such that control and treatment will end at same time point. |
| <code>log.volume</code> | If TRUE log of the volume will be used for response calculation. Default FALSE |
| <code>verbose</code> | Default TRUE will print information. |

Details

At present following response measure are implemented

- `mRECIST` Computes mRECIST for indivial PDX model
- `slope` Computes slope of the fitted indivial PDX curve
- `AUC` Computes area under a PDX curve for indivial PDX model
- `angle` Computes angle between treatment and control PDX curves
- `abc` Computes area between the treatment and control PDX curves
- `TGI` Computes tumor growth inhibition using treatment and control PDX curves
- `lmm` Computes linear mixed model (lmm) statistics for a PDX batch

Value

Returns updated Xeva object.

Examples

```
data(brca)
brca <- setResponse(brca, res.measure = c("mRECIST"), verbose=FALSE)
```

| | |
|--------------------|-----------------------|
| <code>slope</code> | <i>Computes slope</i> |
|--------------------|-----------------------|

Description

`slope` returns the slope for given time and volume data.

Usage

```
slope(time, volume, degree = TRUE)
```

Arguments

| | |
|--------|---|
| time | A vector of time. |
| volume | A vector of volume. |
| degree | Default TRUE will give angle in degrees and FALSE will return in radians. |

Value

Returns the slope and a fit object.

Examples

```
time <- c(0, 3, 7, 11, 18, 22, 26, 30, 32, 35)
volume<- c(250.8, 320.4, 402.3, 382.6, 384, 445.9, 460.2, 546.8, 554.3, 617.9)
sl <- slope(time, volume)
par(pty="s")
xylim <- range(c(time, volume))
plot(time, volume, type = "b", xlim = xylim, ylim = xylim)
abline(lm(volume~time))
```

| | |
|------------|----------------------------|
| subsetXeva | <i>Subset Xeva object.</i> |
|------------|----------------------------|

Description

Subset Xeva object.

Usage

```
subsetXeva(object, ids, id.name, keep.batch = TRUE)
```

Arguments

| | |
|------------|---|
| object | The XevaSet object. |
| ids | IDs to be selected for. |
| id.name | Names of the IDs. |
| keep.batch | Default TRUE. If FALSE, remove all other model.ids from the experient design that do not belong to selection. |

Value

New Xeva object.

Examples

```
data(brca)
print(brca)
df <- subsetXeva(brca, ids = c("X-1004", "X-1008", "X-1286"), id.name="patient.id", keep.batch=TRUE)
print(df)
```

`summarizeMolecularProfiles`*Summarize molecular profiles*

Description

This function serves to get molecular profiles from a XevaSet object.

Usage

```
summarizeMolecularProfiles(  
  object,  
  drug,  
  mDataType,  
  tissue = NULL,  
  sensitivity.measure = NULL,  
  unique.model = TRUE,  
  batch = NULL  
)
```

Arguments

| | |
|----------------------------------|---|
| <code>object</code> | The XevaSet. |
| <code>drug</code> | Name of the drug. |
| <code>mDataType</code> | character, where one of the molecular data types is needed. |
| <code>tissue</code> | Default NULL will return all tissue types. |
| <code>sensitivity.measure</code> | Default NULL will return all sensitivity measures. |
| <code>unique.model</code> | Default TRUE will return only one sequencing ID, in the case where one model ID maps to several sequencing IDs. |
| <code>batch</code> | Name of the batch. Default NULL. |

Details

- If a sequencing sample belongs to multiple models, `summarizeMolecularProfiles` will create a separate column for each model.
- All models without molecular data will be removed from the output ExpressionSet.

Value

An ExpressionSet where sample names are `model.id` and sensitivity measures will be presented in `pData`.

Examples

```
data(brca)
pacRNA <- summarizeMolecularProfiles(brca, drug="paclitaxel", mDataType="RNASeq",
                                     tissue= "BRCA", sensitivity.measure="mRECIST")
print(pacRNA)
```

summarizeResponse *Summarize Response of PDXs*

Description

This function summarizes the drug response information of PDXs.

Usage

```
summarizeResponse(
  object,
  response.measure = "mRECIST",
  model.id = NULL,
  batch.id = NULL,
  group.by = "patient.id",
  summary.stat = c(";", "mean", "median"),
  tissue = NULL
)
```

Arguments

| | |
|------------------|---|
| object | The XevaSet object. |
| response.measure | character indicating which response measure to use. Use the responseMeasures function to find out what measures are available for each XevaSet. |
| model.id | The model.id for which data is required. |
| batch.id | A vector of batch names. Default NULL will return all batches. |
| group.by | Default patient.id. Dictates how the models should be grouped together. See details below. |
| summary.stat | Dictates which summary method to use if multiple IDs are found. |
| tissue | Name of the tissue. Default NULL |

Details

There can be two types of drug response measure.

- Per model response: One response value for each Model, eg. mRECIST_recomputed for each model.
- Per batch response: One response value for each Batch, eg. angle between treatment and control groups.

For the per model response output, columns will be model.id (or group.by). For the per batch response output, the group.by value can be "batch.name".

Value

A matrix with rows as drug names, column as group.by. Each cell contains response.measure for the pair.

Examples

```
data(brca)
brca.mR <- summarizeResponse(brca, response.measure = "mRECIST", group.by="patient.id")
```

| | |
|-----|--|
| TGI | <i>tumor growth inhibition (TGI) Computes the tumor growth inhibition (TGI) between two time-volume curves</i> |
|-----|--|

Description

tumor growth inhibition (TGI) Computes the tumor growth inhibition (TGI) between two time-volume curves

Usage

```
TGI(contr.volume, treat.volume)
```

Arguments

| | |
|--------------|-----------------------------|
| contr.volume | Volume vector for control |
| treat.volume | Volume vector for treatment |

Value

Returns batch response object

Examples

```
contr.volume <- c(1.35, 6.57, 13.94, 20.39, 32.2, 39.26, 46.9, 53.91)
treat.volume <- c(0.4, 1.26, 2.59, 3.62, 5.77, 6.67, 7.47, 8.98, 9.29, 9.44)
TGI(contr.volume, treat.volume)
```

| | |
|-----------|--|
| waterfall | <i>waterfall plot</i> Creates waterfall plot for a given drug. |
|-----------|--|

Description

waterfall plot Creates waterfall plot for a given drug.

Usage

```
waterfall(
  object,
  res.measure,
  drug = NULL,
  group.by = NULL,
  summary.stat = c(";", "mean", "median"),
  tissue = NULL,
  model.id = NULL,
  model.type = NULL,
  type.color = "#cc4c02",
  legend.name = NULL,
  yname = NULL,
  title = NULL,
  sort = TRUE
)
```

Arguments

| | |
|--------------|---|
| object | The XevaSet object |
| res.measure | PDX model drug response measure |
| drug | Name of the drug |
| group.by | Group drug response data |
| summary.stat | How to summarize multiple values |
| tissue | Tissue type |
| model.id | Indicates which model.id to plot. Default NULL will plot all models |
| model.type | Type of model, such as mutated or wild type |
| type.color | A list with colors used for each type in the legend |
| legend.name | Name of the legend |
| yname | Name for the y-axis |
| title | Title of the plot |
| sort | Default TRUE will sort the data |

Value

waterfall plot in ggplot2

Examples

```
data(brca)
waterfall(brca, drug="binimetinib", res.measure="best.avg.response_published")
## example with model.type where we color the models by TP53 mutation type
mut <- summarizeMolecularProfiles(brca, drug = "binimetinib", mDataType="mutation")
model.type <- Biobase::exprs(mut)["TP53", ]
waterfall(brca, drug="binimetinib", res.measure="best.avg.response_published",
          tissue="BRCA", model.id=names(model.type), model.type= model.type)
```

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