

# 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

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

---

### 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

|              |                                                                           |
|--------------|---------------------------------------------------------------------------|
| contr.time   | Time vector for control.                                                  |
| contr.volume | Volume vector for control.                                                |
| treat.time   | Time vector for treatment.                                                |
| treat.volume | Volume vector for treatment.                                              |
| degree       | 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")
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")
abline(lm(contr.volume~contr.time))
abline(lm(treat.volume~treat.time))
```

---

|     |                                                              |
|-----|--------------------------------------------------------------|
| AUC | <i>area under the curve</i> AUC Returns area under the curve |
|-----|--------------------------------------------------------------|

---

**Description**

area under the curve AUC Returns area under the curve

**Usage**

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

**Arguments**

|        |                                                      |
|--------|------------------------------------------------------|
| time   | A vector of time points recorded for the experiment. |
| volume | 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")
xylimit <- range(c(time, volume1, volume2))
plot(time, volume1, type = "b", xlim = xylimit, ylim = xylimit)
lines(time, volume2, type = "b")
abline(lm(volume1~time))
abline(lm(volume2~time))
```

---

|           |                              |
|-----------|------------------------------|
| batchInfo | <i>Get batch information</i> |
|-----------|------------------------------|

---

## 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

|                            |                                                                      |
|----------------------------|----------------------------------------------------------------------|
| <code>object</code>        | The Xeva object from which batch information is obtained.            |
| <code>batch</code>         | Name of the batch. Default NULL.                                     |
| <code>model.id</code>      | Model ID for which need to be searched in the batches. Default NULL. |
| <code>model.id.type</code> | 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

*XevaSet constructor*

---

### 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 description of all variables please see Xeva vignette section "**Creating new Xeva object**"

**Value**

Returns Xeva object

**Examples**

```
## read raw data files containing 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**

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

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


---

**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 | <i>get drug sensitivity values</i> |
|--------------------|------------------------------------|

---

**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 <code>model.id</code> 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.                                             |

`concurrent.time`

Default FALSE. If TRUE, cut the batch data such that control and treatment will end at same time point.

### Value

a data.frame with all 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.pae1"), 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

|                        |                                                             |
|------------------------|-------------------------------------------------------------|
| <code>object</code>    | The XevaSet.                                                |
| <code>data.type</code> | 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 | <i>linear mixed model</i> |
|-----|---------------------------|

---

**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 | <i>modelInfo Generic Generic for modelInfo method</i> |
|-----------|-------------------------------------------------------|

---

**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 | <i>Computes the mRECIST</i> |
|---------|-----------------------------|

---

**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**

|                           |                                                                   |
|---------------------------|-------------------------------------------------------------------|
| <code>mat</code>          | The mRECIST matrix where rows are drugs and columns are patients. |
| <code>control.name</code> | Name of the control.                                              |
| <code>control.col</code>  | Color of the control.                                             |
| <code>drug.col</code>     | Color of the drug names.                                          |
| <code>colPalette</code>   | Color palette for mRECIST values.                                 |
| <code>name</code>         | Title of the plot.                                                |
| <code>sort</code>         | If matrix should be sorted before plotting.                       |
| <code>row_fontsize</code> | Size of the row name font.                                        |
| <code>col_fontsize</code> | Size of the column name font.                                     |
| <code>draw_plot</code>    | 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.       |
| <code>vol.normal</code>      | Default FALSE. If TRUE, volume will be normalized.                                                          |
| <code>impute.value</code>    | Default TRUE will impute values if missing.                                                                 |
| <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>control.col</code>     | 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 | <i>Print the batch response</i> |
|---------------------|---------------------------------|

---

**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 | <i>Print the model response</i> |
|---------------------|---------------------------------|

---

**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 | <i>Print the pdx batch</i> |
|----------------|----------------------------|

---

**Description**

Print the pdx batch

**Usage**

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

**Arguments**

|     |                 |
|-----|-----------------|
| x   | pdxBatch object |
| ... | Other arguments |

**Value**

prints pdxBatch

---

|       |                            |
|-------|----------------------------|
| repdx | <i>Example PDX dataset</i> |
|-------|----------------------------|

---

### Description

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

### Usage

```
data(repdx)
```

### Format

An object of class XevaSet of length 1.

---

|          |                             |
|----------|-----------------------------|
| response | <i>compute PDX response</i> |
|----------|-----------------------------|

---

### 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

|                |                                                                                                |
|----------------|------------------------------------------------------------------------------------------------|
| object         | Xeva object.                                                                                   |
| model.id       | model.id for which the durg response is to be computed.                                        |
| batch          | batch.id or experiment design for which the drug response is to be computed.                   |
| res.measure    | Drug response measure. See Details below                                                       |
| treatment.only | Default FALSE. If TRUE, give data for non-zero dose periods only (if dose data are available). |
| max.time       | Maximum time for data.                                                                         |

|                 |                                                                                                         |
|-----------------|---------------------------------------------------------------------------------------------------------|
| impute.value    | Default FALSE. If TRUE, impute the missing values.                                                      |
| min.time        | Default <b>10</b> days. Used for <i>mRECIST</i> computation.                                            |
| concurrent.time | Default FALSE. If TRUE, cut the batch data such that control and treatment will end at same time point. |
| vol.normal      | If TRUE it will normalize the volume. Default FALSE.                                                    |
| log.volume      | If TRUE log of the volume will be used for response calculation. Default FALSE                          |
| verbose         | 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

*Get sensitivity for an Xeva object*


---

**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", "lmm"),
  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 <b>10</b> days.                                     |
| treatment.only  | Default FALSE. If TRUE, give data for non-zero dose periods only (if dose data are available).                     |
| max.time        | Maximum number of days to consider for analysis. Data beyond this will be discarded. Default NULL takes full data. |
| vol.normal      | If TRUE it will will normalize the volume. Default FALSE                                                           |
| impute.value    | Default FALSE. If TRUE, impute the missing volume values.                                                          |
| concurrent.time | Default FALSE. If TRUE, cut the batch data such that control and treatment will end at same time point.            |
| log.volume      | If TRUE log of the volume will be used for response calculation. Default FALSE                                     |
| verbose         | Default TRUE will print information.                                                                               |

## Details

At present following response measure are implemented

- mRECIST Computes mRECIST for individual PDX model
- slope Computes slope of the fitted individual PDX curve
- AUC Computes area under a PDX curve for individual 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)
```

---

|       |                       |
|-------|-----------------------|
| slope | <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 experimnt 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 | <i>Summarize molecular profiles</i> |
|----------------------------|-------------------------------------|

---

**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**

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

---

**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

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

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

---

## Description

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

## Usage

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

**Arguments**

|                           |                             |
|---------------------------|-----------------------------|
| <code>contr.volume</code> | Volume vector for control   |
| <code>treat.volume</code> | 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)
```

---

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

---

**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**

|                           |                                                                                  |
|---------------------------|----------------------------------------------------------------------------------|
| <code>object</code>       | The XevaSet object                                                               |
| <code>res.measure</code>  | PDX model drug response measure                                                  |
| <code>drug</code>         | Name of the drug                                                                 |
| <code>group.by</code>     | Group drug response data                                                         |
| <code>summary.stat</code> | How to summarize multiple values                                                 |
| <code>tissue</code>       | Tissue type                                                                      |
| <code>model.id</code>     | Indicates which <code>model.id</code> to plot. Default NULL will plot all models |

|                          |                                                     |
|--------------------------|-----------------------------------------------------|
| <code>model.type</code>  | Type of model, such as mutated or wild type         |
| <code>type.color</code>  | A list with colors used for each type in the legend |
| <code>legend.name</code> | Name of the legend                                  |
| <code>yname</code>       | Name for the y-axis                                 |
| <code>title</code>       | Title of the plot                                   |
| <code>sort</code>        | 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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