

Package ‘simulatorZ’

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Type Package

Title Simulator for Collections of Independent Genomic Data Sets

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Description simulatorZ is a package intended primarily to simulate collections of independent genomic data sets, as well as performing training and validation with predicting algorithms. It supports ExpressionSet and RangedSummarizedExperiment objects.

License Artistic-2.0

Depends R (>= 3.1), methods, BiocGenerics, Biobase, SummarizedExperiment, survival, CoxBoost

Imports graphics, stats, gbm, Hmisc, S4Vectors, IRanges, GenomicRanges

Suggests RUnit, BiocStyle, curatedOvarianData, parathyroidSE, superpc

URL <https://github.com/zhangyuqing/simulatorZ>

BugReports <https://github.com/zhangyuqing/simulatorZ>

biocViews Survival

NeedsCompilation yes

R topics documented:

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simulatorZ-package	<i>Simulator for Collections of Independent Genomic Data Sets</i>
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Description

simulatorZ is a package intended primarily to simulate collections of independent genomic data sets, as well as performing training and validation with predicting algorithms. It supports ExpressionSets and SummarizedExperiment objects.

Details

Package:	simulatorZ
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Author:	Yuqing Zhang, Christoph Bernau, Levi Waldron
Maintainer:	Yuqing Zhang <zhangyuqing.pkusms@gmail.com>
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Suggests:	BiocStyle, curatedOvarianData, parathyroidSE, superpc
URL:	https://github.com/zhangyuqing/simulatorZ
BugReports:	https://github.com/zhangyuqing/simulatorZ
biocViews:	Survival

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

cvSubsets	<i>cvSubsets</i>
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Description

To generate a list of subsets(indices of observations) from one set

Usage

```
cvSubsets(obj, fold)
```

Arguments

obj	a ExpressionSet, matrix or RangedSummarizedExperiment object. If it is a matrix, columns represent samples
fold	the number of folds in cross validation. Number of observations in the set does not need to be a multiple of fold

Value

returns the list of indices of subsets

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

Examples

```
library(curatedOvarianData)
```

```
data(E.MTAB.386_eset)
```

```
set.seed(8)
```

```
id <- cvSubsets(E.MTAB.386_eset, 3)
```

```
subset1 <- E.MTAB.386_eset[, id[[1]]]
```

```
subset2 <- E.MTAB.386_eset[, id[[2]]]
```

```
subset3 <- E.MTAB.386_eset[, id[[3]]]
```

```
## Number of observations in the set does not need to be a multiple of
```

```
## the fold parameter
```

```
id2 <- cvSubsets(E.MTAB.386_eset, 5)
```

```
subsets <- list()

subsets[[1]] <- E.MTAB.386_eset[, id2[[1]]]

subsets[[2]] <- E.MTAB.386_eset[, id2[[2]]]

subsets[[3]] <- E.MTAB.386_eset[, id2[[3]]]

subsets[[4]] <- E.MTAB.386_eset[, id2[[4]]]

subsets[[5]] <- E.MTAB.386_eset[, id2[[5]]]
```

funCV

funCV

Description

Cross validation function

Usage

```
funCV(obj, fold, y.var, trainFun = masomenos, funCvSubset = cvSubsets)
```

Arguments

obj	a ExpressionSet, matrix or RangedSummarizedExperiment object. If it is a matrix, columns represent samples
fold	the number of folds in cross validation
y.var	response variable, matrix, data.frame(with 2 columns) or Surv object
trainFun	training function, which takes gene expression matrix X and response variable y as input, the coefficients as output
funCvSubset	function to divide one Expression Set into subsets for cross validation

Value

returns the c statistics of cross validation(CV)

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

Examples

```
library(curatedOvarianData)

library(GenomicRanges)

set.seed(8)

data( E.MTAB.386_eset )

eset <- E.MTAB.386_eset[1:100, 1:30]

time <- eset$days_to_death

cens.chr <- eset$vital_status

cens <- c()

for(i in seq_along(cens.chr)){

  if(cens.chr=="living") cens[i] <- 1

  else cens[i] <- 0

}

y <- Surv(time, cens)

y1 <- cbind(time, cens)

nrows <- 200; ncols <- 6

counts <- matrix(runif(nrows * ncols, 1, 1e4), nrows)

rowRanges <- GRanges(rep(c("chr1", "chr2"), c(50, 150)),
```

```
IRanges(floor(runif(200, 1e5, 1e6)), width=100),

strand=sample(c("+", "-"), 200, TRUE))

colData <- DataFrame(Treatment=rep(c("ChIP", "Input"), 3),

row.names=LETTERS[1:6])

sset <- SummarizedExperiment(assays=SimpleList(counts=counts),

rowRanges=rowRanges, colData=colData)

time <- sample(4500:4700, 6, replace=TRUE)

cens <- sample(0:1, 6, replace=TRUE)

y.vars <- Surv(time, cens)

funCV(eset, 3, y)

funCV(eset, 3, y1, trainFun=plusMinus)

funCV(exprs(eset), 3, y)

funCV(sset, 3, y.vars)

## any training function will do as long as it takes the gene expression matrix X

## and response variable y(matrix, data.frame or Surv object) as parameters, and

## return the coefficients as its value
```

`geneFilter`*geneFilter*

Description

the function to filter genes by Integrative Correlation

Usage

```
geneFilter(obj, cor.cutoff = 0.5)
```

Arguments

<code>obj</code>	a list of ExpressionSet, matrix or RangedSummarizedExperiment objects. If its elements are matrices, columns represent samples, rows represent genes
<code>cor.cutoff</code>	the cutoff threshold for filtering genes. Only when the integrative correlation between every pair of sets is larger than the cutoff value, will the gene be selected.

Value

returns a list of ExpressionSets matrix or RangedSummarizedExperiment objects with genes filtered

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

References

Garrett-Mayer, E., Parmigiani, G., Zhong, X., Cope, L., Gabrielson, E., Cross-study validation and combined analysis of gene expression microarray data. *Biostatistics*. 2008 Apr;9(2):333-354.

Examples

```
set.seed(8)
```

```
library(curatedOvarianData)
```

```
library(GenomicRanges)
```

```
data(GSE17260_eset)
```

```
data(E.MTAB.386_eset)
```

```
data(GSE14764_eset)

esets <- list(GSE17260=GSE17260_eset, E.MTAB.386=E.MTAB.386_eset, GSE14764=GSE14764_eset)

esets.list <- lapply(esets, function(eset){

  return(eset[1:1500, 1:10])

})

result.set <- geneFilter(esets.list, 0)

result.set

### as we cannot calculate correlation with one set, this function just

### delivers the same set if esets has length 1

result.oneset <- geneFilter(esets.list[1])

result.oneset

## Support matrices

X.list <- lapply(esets.list, function(eset){

  return(exprs(eset)) ## Columns represent samples!

})

result.set <- geneFilter(X.list, 0)

dim(result.set[[1]])
```



```
## Support RangedSummarizedExperiment

nrows <- 200; ncols <- 6

counts <- matrix(runif(nrows * ncols, 1, 1e4), nrows)

rowRanges <- GRanges(rep(c("chr1", "chr2"), c(50, 150)),

                      IRanges(floor(runif(200, 1e5, 1e6)), width=100),

                      strand=sample(c("+", "-"), 200, TRUE))

colData <- DataFrame(Treatment=rep(c("ChIP", "Input"), 3),

                    row.names=LETTERS[1:6])

sset <- SummarizedExperiment(assays=SimpleList(counts=counts),

                             rowRanges=rowRanges, colData=colData)

s.list <- list(sset, sset)

result.set <- geneFilter(s.list, 0.9)

## the same set should resemble each other, no genes filtered

dim(assay(result.set[[1]]))
```

`getTrueModel`

getTrueModel

Description

The parametric bootstrap simulation depends on the true model of original sets.

This function is to generate useful values from the true models for further analysis.

We fit CoxBoost to the original sets and use the coefficients to simulate

the survival and censoring time. `grid`, `survH`, `censH`, which are useful for this purpose.

`grid`=grid corresponding to hazard estimations `censH` and `survH`

`survH`=cumulative hazard for survival times distribution

`censH`=cumulative hazard for censoring times distribution

Usage

```
getTrueModel(obj, y.vars, parstep)
```

Arguments

<code>obj</code>	a list of ExpressionSets, matrix or RangedSummarizedExperiment
<code>y.vars</code>	a list of response variables, Surv, matrix or data.frame object
<code>parstep</code>	number of steps in CoxBoost

Value

returns a list of values:

`beta`: True coefficients obtained by fitting CoxBoost to the original ExpressionSets

`grid`: timeline grid corresponding to hazard estimations `censH` and `survH`

`survH`: cumulative hazard for survival times distribution

`censH`: cumulative hazard for censoring times distribution

`lp`: true linear predictors

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

Examples

```
library(curatedOvarianData)
```

```
data(GSE17260_eset)
```

```
data(E.MTAB.386_eset)
```

```
data(GSE14764_eset)
```

```
esets <- list(GSE17260=GSE17260_eset, E.MTAB.386=E.MTAB.386_eset, GSE14764=GSE14764_eset)
```

```
esets.list <- lapply(esets, function(eset){
```

```
    return(eset[1:500, 1:20])

  })

  ## simulate on multiple ExpressionSets

  set.seed(8)

  y.list <- lapply(esets.list, function(eset){

    time <- eset$days_to_death

    cens.chr <- eset$vital_status

    cens <- c()

    for(i in seq_along(cens.chr)){

      if(cens.chr[i] == "living") cens[i] <- 1

      else cens[i] <- 0

    }

    y <- Surv(time, cens)

    return(y)

  })

  res1 <- getTrueModel(esets.list, y.list, 100)
```

```
## Get true model from one set

res2 <- getTrueModel(esets.list[1], y.list[1], 100)

names(res2)

res2$lp

## note that y.list[1] cannot be replaced by y.list[[1]]
```

masomenos

masomenos

Description

function for Mas-o-menos algorithm

Usage

```
masomenos(X, y, option = "fast", ...)
```

Arguments

X	matrix with rows corresponding to subjects and columns to features resp
y	response variable, a data.frame, matrix, or Surv object: c(time, event)
option	whether to use C or R code to fit the marginal Cox models
...	other arguments

Value

return the coefficients

Author(s)

Tim Triche, Jr.

References

Zhao, S., Huttenhower, G. P. C., and Waldron, L. (2013). Mas-o-menos: a simple sign averaging method for discrimination in genomic data analysis. <http://biostats.bepress.com/harvardbiostat/paper158/>. Accessed: 2013-10-24.

Examples

```
set.seed(8)

library(curatedOvarianData)

data( E.MTAB.386_eset )

eset <- E.MTAB.386_eset[1:100, 1:30]

X <- t(exprs(eset))

time <- eset$days_to_death

cens <- sample(0:1, 30, replace=TRUE)

y <- Surv(time, cens)

beta <- masomenos(X, y)

beta
```

plusMinus

plusMinus

Description

function for plusMinus algorithm

Usage

```
plusMinus(X, y, lambda = NULL, tuningpar = "nfeatures", standardize = FALSE,
```

```
directionality = "posneg", ties.method = "average", votingthresholdquantile = 0.5,  
  
modeltype = "plusminus")
```

Arguments

X	gene expression matrix
y	response variables
lambda	lambda
tuningpar	tuning parameter
standardize	standardize or not
directionality	directionality
ties.method	ties.method
votingthresholdquantile	votingthresholdquantile
modeltype	modeltype

Value

returns regression coefficients

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

Examples

```
set.seed(8)  
  
library(curatedOvarianData)  
  
data( E.MTAB.386_eset )  
  
eset <- E.MTAB.386_eset[1:100, 1:30]  
  
X <- t(exprs(eset))  
  
time <- eset$days_to_death
```

```
cens <- sample(0:1, 30, replace=TRUE)
```

```
y <- Surv(time, cens)
```

```
beta <- plusMinus(X, y)
```

```
beta
```

rowCoxTests

rowCoxTests

Description

method for performing Cox regression

Usage

```
rowCoxTests(X, y, option = c("fast", "slow"), ...)
```

Arguments

<i>X</i>	Gene expression data. The following formats are available: matrix Rows correspond to observations, columns to variables. data.frame Rows correspond to observations, columns to variables. ExpressionSet rowCoxTests will extract the expressions using exprs().
<i>y</i>	Survival Response, an object of class: Surv if <i>X</i> is of type data.frame or matrix character if <i>X</i> is of type ExpressionSet. In this case <i>y</i> is the name of the survival response in the phenoData of <i>X</i> . If survival time and indicator are stored separately in the phenoData one can specify a two-element character vector the first element representing the survival time variable.
option	"fast" loops over rows in C, "slow" calls coxph directly in R. The latter method may be used if something goes wrong with the "fast" method.
...	currently unused

Value

dataframe with two columns: coef = Cox regression coefficients, p.value = Wald Test p-values. Rows correspond to the rows of X.

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

Examples

```
#test

##regressor-matrix (gene expressions)

X<-matrix(rnorm(1e6),nrow=10000)

#seed

set.seed(123)

#times

time<-rnorm(n=ncol(X),mean=100)

#censoring(1->death)

status<-rbinom(n=ncol(X),size=1, prob=0.8)

##survival object

y<-Surv(time,status)

## Do 10,000 Cox regressions:
```



```
system.time(output <- rowCoxTests(X=X,y=y, option="fast"))
```

simBootstrap	<i>simBootstrap</i>
--------------	---------------------

Description

the driver function to perform three-step bootstrap resampling
to get independent genomic data sets

Usage

```
simBootstrap(obj, y.vars, n.samples, parstep, type = "two-steps",
            balance.variables = NULL, funSimData = simData, funTrueModel = getTrueModel,
            funSurvTime = simTime)
```

Arguments

obj	a list of ExpressionSet, matrix or RangedSummarizedExperiment
y.vars	a list of reponse variables, elements can be class Surv, matrix or data.frame
n.samples	number of samples to resample in each set
parstep	step number to fit CoxBoost
type	whether to include resampling set labels
balance.variables	covariate names to balance in the simulated sets
funSimData	function to perform non-parametric bootstrap
funTrueModel	function to construct true models in original sets
funSurvTime	function to perform parametric bootstrap

Value

a list of values including:

obj.list = a list of simulated objects the same type as input

indices.list = a list of indices indicating which sample the simulated sample is in the original set

setsID = a vector to indicate the original ID of simulated sets, if type=="original", setsID should be 1,2,3,...

lp.list = a list of true linear predictor of each original data sets

beta.list = a list of true coefficients used for simulating observations

survH.list = list of cumulative survival hazard

censH.list = list of cumulative censoring hazard

grid.list = list of timeline grid corresponding to survH and censH respectively

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

Examples

```
library(curatedOvarianData)

library(GenomicRanges)

data(GSE17260_eset)

data(E.MTAB.386_eset)

data(GSE14764_eset)

esets <- list(GSE17260=GSE17260_eset, E.MTAB.386=E.MTAB.386_eset, GSE14764=GSE14764_eset)

esets.list <- lapply(esets, function(eset){

  return(eset[1:500, 1:20])

})

## simulate on multiple ExpressionSets

set.seed(8)

y.list <- lapply(esets.list, function(eset){

  time <- eset$days_to_death

  cens.chr <- eset$vital_status

  cens <- c()
```

```
for(i in seq_along(cens.chr)){

  if(cens.chr[i] == "living") cens[i] <- 1

  else cens[i] <- 0

}

y <- Surv(time, cens)

return(y)

})

simmodels <- simBootstrap(obj=esets.list, y.vars=y.list, 10, 100)

simmodels$obj.list[[1]]

# balance covariates

simmodels <- simBootstrap(obj=esets.list, y.vars=y.list, 10, 100,

                           balance.variables="tumorstage")

## Support RangedSummarizedExperiment

nrows <- 200; ncols <- 10

counts <- matrix(runif(nrows * ncols, 1, 1e4), nrows)

rowRanges <- GRanges(rep(c("chr1", "chr2"), c(50, 150)),
```

```
IRanges(floor(runif(200, 1e5, 1e6)), width=100),

strand=sample(c("+", "-"), 200, TRUE))

colData <- DataFrame(Treatment=rep(c("ChIP", "Input"), 5),

row.names=LETTERS[1:10])

sset <- SummarizedExperiment(assays=SimpleList(counts=counts),

rowRanges=rowRanges, colData=colData)

s.list <- list(sset[,1:5], sset[,6:10])

time <- c(540, 527, 668, 587, 620, 540, 527, 668, 587, 620)

cens <- c(1, 0, 0, 1, 0, 1, 0, 0, 1, 0)

y.vars <- Surv(time, cens)

y.vars <- list(y.vars[1:5,],y.vars[6:10,])

simmodels <- simBootstrap(obj=s.list, y.vars=y.vars, 100, 100)
```

simData

simData

Description

simData is a function to perform non-parametric bootstrap resampling on a list of (original) data sets, both on set level and patient level, in order to simulate independent genomic sets.

Usage

```
simData(obj, n.samples, y.vars = list(), type = "two-steps",  
  
        balance.variables = NULL)
```

Arguments

`obj` a list of ExpressionSets, matrices or RangedSummarizedExperiments. If elements are matrices, columns represent samples

`n.samples` an integer indicating how many samples should be resampled from each set

`y.vars` a list of response variables, can be Surv object, or matrix or data.frame with two columns

`type` string "one-step" or "two-steps". If type="one-step", the function will skip resampling the datasets, and directly resample from the original list of obj

`balance.variables` balance.variables will be a vector of covariate names that should be balanced in the simulation. After balancing, the prevalence of covariate in each result set should be the same as the overall distribution across all original data sets. Default is set as NULL, when it will not balance over any covariate. if isn't NULL, esets parameter should only be of class ExpressionSet

Value

returns a list of simulated ExpressionSets, with names indicating its original set, and indices of the original patients.

`prob.desired` and `prob.real` are only useful when `balance.variables` is set.

`prob.desired` shows overall distribution of the specified covariate. `prob.list`

shows the sampling probability in each set after balancing

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

Examples

```
library(curatedOvarianData)
```

```
library(GenomicRanges)
```

```
data(GSE17260_eset)
```

```
data(E.MTAB.386_eset)

data(GSE14764_eset)

esets <- list(GSE17260=GSE17260_eset, E.MTAB.386=E.MTAB.386_eset, GSE14764=GSE14764_eset)

esets.list <- lapply(esets, function(eset){

  return(eset[1:1000, 1:10])

})

## simulate on multiple ExpressionSets

set.seed(8)

# one-step bootstrap: skip resampling set labels

simmodels <- simData(esets.list, 20, type="one-step")

# two-step-non-parametric bootstrap

simmodels <- simData(esets.list, 10, type="two-steps")

## simulate one set

simmodels <- simData(list(esets.list[[1]]), 10, type="two-steps")

## balancing covariates
```



```
colData <- DataFrame(Treatment=rep(c("ChIP", "Input"), 3),
                    row.names=LETTERS[1:6])

sset <- SummarizedExperiment(assays=SimpleList(counts=counts),
                             rowRanges=rowRanges, colData=colData)

s.list <- list(sset[,1:3], sset[,4:6])

simmodels <- simData(s.list, 20, type="two-steps")
```

simTime

simTime

Description

simTime is a function to perform the parametric-bootstrap step, where we use the true coefficients and cumulative hazard to simulate survival and censoring.

Usage

```
simTime(simmodels, result)
```

Arguments

simmodels	a list in the form of the return value of simData() which consists of three lists: obj: a list of ExpressionSets, matrices or RangedSummarizedExperiments setsID: a list of set labels indicating which original set the simulated one is from indices: a list of patient labels to tell which patient in the original set is drawn
result	a list in the form of return of getTrueModel() which consists of five lists: Beta: a list of coefficients obtained by grid: timeline grid corresponding to hazard estimations censH and survH survH: cumulative hazard for survival times distribution censH: cumulative hazard for censoring times distribution lp: true linear predictors

Value

survival time is saved in phenodata, here the function still returns the ExpressionSets

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

Examples

```
library(curatedOvarianData)

data(GSE17260_eset)

data(E.MTAB.386_eset)

data(GSE14764_eset)

esets <- list(GSE17260=GSE17260_eset, E.MTAB.386=E.MTAB.386_eset, GSE14764=GSE14764_eset)

esets.list <- lapply(esets, function(eset){

  return(eset[1:500, 1:20])

})

## simulate on multiple ExpressionSets

set.seed(8)

y.list <- lapply(esets.list, function(eset){

  time <- eset$days_to_death

  cens.chr <- eset$vital_status
```

```
cens <- c()

for(i in seq_along(cens.chr)){

  if(cens.chr[i] == "living") cens[i] <- 1

  else cens[i] <- 0

}

y <- Surv(time, cens)

return(y)

})

# To perform both parametric and non-parametric bootstrap, you can call simBootstrap()

# or, you can divide the steps into:

res <- getTrueModel(esets.list, y.list, 100)

simmodels <- simData(obj=esets.list, y.vars=y.list, n.samples=10)

# Then, use this function

simmodels <- simTime(simmodels=simmodels, result=res)

# it also supports performing only the parametric bootstrap step on a list of expressionsets

# but you need to construct the parameter by scratch
```

```
res <- getTrueModel(esets.list, y.list, 100)

setsID <- seq_along(esets.list)

indices <- list()

for(i in setsID){

  indices[[i]] <- seq_along(sampleNames(esets.list[[i]]))

}

simmodels <- list(obj=esets.list, y.vars=y.list, indices=indices, setsID=setsID)

new.simmodels <- simTime(simmodels=simmodels, result=res)
```

zmatrix

zmatrix

Description

generate a matrix of c statistics

Usage

```
zmatrix(obj, y.vars, fold, trainingFun = masomenos, cvFun = funCV,

        cvSubsetFun = cvSubsets)
```

Arguments

obj	a list of ExpressionSet, matrix or RangedSummarizedExperiment objects. If its elements are matrices, columns represent samples
y.vars	a list of response variables, all the response variables should be matrix, data.frame(with 2 columns) or Surv object
fold	cvFun parameter, in this case passes to funCV()
trainingFun	training function
cvFun	function to perform cross study within one set
cvSubsetFun	function to divide the expression sets into subsets for cross validation

Value

outputs one matrix of validation statistics

Author(s)

Yuqing Zhang, Christoph Bernau, Levi Waldron

Examples

```
library(curatedOvarianData)

library(GenomicRanges)

data(GSE17260_eset)

data(E.MTAB.386_eset)

data(GSE14764_eset)

esets <- list(GSE17260=GSE17260_eset, E.MTAB.386=E.MTAB.386_eset, GSE14764=GSE14764_eset)

esets.list <- lapply(esets, function(eset){

  return(eset[1:500, 1:20])

})

## simulate on multiple ExpressionSets

set.seed(8)

y.list <- lapply(esets.list, function(eset){

  time <- eset$days_to_death
```

```
cens.chr <- eset$vital_status

cens <- c()

for(i in seq_along(cens.chr)){

  if(cens.chr[i] == "living") cens[i] <- 1

  else cens[i] <- 0

}

y <- Surv(time, cens)

return(y)

})

# generate on original ExpressionSets

z <- zmatrix(esets.list, y.list, 3)

# generate on simulated ExpressionSets

simmodels <- simBootstrap(esets.list, y.list, 10, 100)

z <- zmatrix(simmodels$obj.list, simmodels$y.vars.list, 3)

# support matrix

X.list <- lapply(esets.list, function(eset){
```

```
newx <- exprs(eset) ### columns represent samples !!

return(newx)

})

z <- zmatrix(X.list, y.list, 3)

# support RangedSummarizedExperiment

nrows <- 200; ncols <- 6

counts <- matrix(runif(nrows * ncols, 1, 1e4), nrows)

rowRanges <- GRanges(rep(c("chr1", "chr2"), c(50, 150)),

                      IRanges(floor(runif(200, 1e5, 1e6)), width=100),

                      strand=sample(c("+", "-"), 200, TRUE))

colData <- DataFrame(Treatment=rep(c("ChIP", "Input"), 3),

                    row.names=LETTERS[1:6])

sset <- SummarizedExperiment(assays=SimpleList(counts=counts),

                             rowRanges=rowRanges, colData=colData)

time <- sample(4500:4700, 6, replace=TRUE)

cens <- sample(0:1, 6, replace=TRUE)

y.vars <- Surv(time, cens)
```

```
z <- zmatrix(list(sset[,1:3], sset[,4:6]), list(y.vars[1:3,],y.vars[4:6,]), 3)
```

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