

Package ‘geneClassifiers’

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Title Application of gene classifiers

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Description This packages aims for easy accessible application of classifiers which have been published in literature using an ExpressionSet as input.

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Author R Kuiper [cre, aut] (ORCID: <<https://orcid.org/0000-0002-3703-1762>>)

Maintainer R Kuiper <r.kuiper.emc@gmail.com>

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geneClassifiers-package

geneClassifiers: Application of gene classifiers

Description

This packages aims for easy accessible application of classifiers which have been published in literature using an ExpressionSet as input.

Details

Combining gene expression profiling data with survival data has led to the development of robust outcome predictors (gene classifiers).This package provides a method for running gene classifiers generating patient specific predictive outcomes. This package is intended to support and enable research. To yield stable results, this package requires a dataset of at least 20 patients.

For detail on how to use this package see the vignette: `vignette("geneClassifiers")`

Author(s)

Maintainer: R Kuiper <r.kuiper.emc@gmail.com> (0000-0002-3703-1762)

References

Kuiper R, Broyl A, de Knecht YA, Van Vliet MH, Van Beers EH, van der Holt B, el Jarari L, Mulligan G, Gregory W, Morgan G, Goldschmidt H. A gene expression signature for high-risk multiple myeloma. *Leukemia*. 2012 Nov;26(11):2406.

See Also

Useful links:

- <https://doi.org/doi:10.18129/B9.bioc.geneClassifiers>
- Report bugs at <https://github.com/rkuiper/geneClassifiers/issues>

ClassifierParameters *An S4 class to store classifier parameters.*

Description

This class stores classifier related information This is information on probe-sets used and their weightings, means, standard deviations and covariance structure as observed in the classifiers training data, and the description of the procedure on how to preprocess new data prior to application of the classifier.

Slots

`name` A character string indicating the name of the classifier
`description` A short description of the classifier
`citations` A character vector of citations to literature
`normalizationMethod` A character string indicating the normalization method to apply
`eventChain` A list of preprocessing steps
`probeNames` A character vector
`intercept` A numeric value
`weights` A numeric vector
`decisionBoundaries` A numeric vector with values that separate the risk-groups
`doRun` A function which is called for the actual classification
`means` A numeric vector of probe-set means as observed in the trainingsset (if available)
`sds` A numeric vector of probe-set standard deviations as observed in the trainingsset (if available)
`.geneClassifierVersion` An object of class `package_version`

ClassifierResults *An S4 class to store classifier results.*

Description

This class stores classifier results as obtained after running the `runClassifier` function.

Slots

`classifierParameters` An object of class `ClassifierParameters` in which the applied classifier parameters are stored.

`score` A numeric vector of resulting classifier scores

`batchCorrection` A character vector indicating whether batch correction was applied

`weightingType` A character string indicating whether the weighting type was complete (i.e. no missing data), reweighted (i.e. missing data was handled based on correction using the covariance structure in the classifiers training data), or reduced (i.e. missing data but not reweighting the original probeset weighting)

`.geneClassifierVersion` An object of class `package_version`

dim,FixedExpressionData-method
Dimensions of an Object

Description

Retrieve the dimension of an object.

Usage

```
## S4 method for signature 'FixedExpressionData'
dim(x)
```

Arguments

`x` an R object, for example a matrix, array or data frame.

Value

Retrieves the 'dim' attribute of the object. It is 'NULL' or a vector of mode 'integer'.

See Also

Other fixed data information extraction functions: `[,FixedExpressionData,ANY,ANY-method`, `getNormalizationMethod`, `getTargetValue`

Examples

```
data(exampleMAS5)
myData <- setNormalizationMethod(exampleMAS5, "MAS5.0", targetValue=500)
dim(myData)
dim(myData[1:10,1:3])
```

exampleMAS5

Example MAS5.0 ExpressionSet

Description

An [ExpressionSet](#). The data contains a sample of gene expression data from patients included in the HOVON65/GMMG-HD4 trial on multiple myeloma. The data was MAS5.0 normalized to a target value of 500.

Usage

```
exampleMAS5
```

Format

An object of class `ExpressionSet` with 374 rows and 25 columns.

FixedExpressionData

An S4 class to store classifier parameters.

Description

This class stores gene expression data together with information on the normalization method and additional normalization related parameters. In order to ensure the data is not manipulated in unforeseen ways, manipulation is strictly controlled through adding transformations which are pre-defined in the `TransformationProcess`-class. Upon reading the data by the `exprs` function, the transformations are performed in the order they were added.

Slots

`normalizationMethod` A character string indicating the normalization method that was applied to the data. Possible values are given by [getNormalizationMethods](#).

`expressionEnvironment` A locked environment in which the expression matrix is stored.

`normalizationParameters` A list with normalization specific values.

`transformationProcess` A locked environment to which the transformation processes are added.

`.geneClassifierVersion` An object of class [package_version](#)

getBatchCorrection *Obtain the batch correction status for a classifier result.*

Description

getBatchCorrection returns TRUE or FALSE indicating whether correction was applied

Usage

```
getBatchCorrection(object)
```

```
## S4 method for signature 'ClassifierResults'  
getBatchCorrection(object)
```

Arguments

object An object of class [ClassifierResults](#) as returned by [runClassifier](#)

Value

TRUE or FALSE

See Also

Other classifier results: [getClassifications](#), [getScores](#), [getWeightingType](#)

Examples

```
myData <- setNormalizationMethod(exampleMAS5, "MAS5.0",targetValue=500)  
results <- runClassifier('EMC92', myData)  
getBatchCorrection( results )
```

getCitations *Obtain citations to the classifier*

Description

getCitations Obtain citations to the classifier

Usage

```
getCitations(object)
```

```
## S4 method for signature 'ClassifierParameters'  
getCitations(object)
```

Arguments

object An object of class [ClassifierParameters](#) as returned by [getClassifier](#)

Value

A character vector

See Also

Other classifier information functions: [getClassifier](#), [getDecisionBoundaries](#), [getDescription](#), [getEventChain](#), [getIntercept](#), [getMeans](#), [getNormalizationMethod](#), [getProbeNames](#), [getSds](#), [getTrainingData](#), [getWeights](#)

Examples

```
aClassifier <- getClassifier("EMC92")
getCitations(aClassifier)
```

`getClassifications` *Obtain classifier classifications.*

Description

`getClassifications` returns the resulting classifications.

Usage

```
getClassifications(object)

## S4 method for signature 'ClassifierResults'
getClassifications(object)
```

Arguments

object An object of class [ClassifierResults](#)

Value

A vector of ordered factors with classifications per sample

See Also

Other classifier results: [getBatchCorrection](#), [getScores](#), [getWeightingType](#)

Examples

```
myData <- setNormalizationMethod(exampleMAS5, "MAS5.0",targetValue=500)
results <- runClassifier('EMC92', myData)
getScores( results )
getClassifications( results )
```

getClassifier	<i>Obtain a classifier definition.</i>
---------------	--

Description

getClassifier returns a requested classifier definition.

Usage

```
getClassifier(value)

## S4 method for signature 'ClassifierResults'
getClassifier(value)

## S4 method for signature 'character'
getClassifier(value)
```

Arguments

value	Either a text value indicating a classifier name (see showClassifierList), or an object of class ClassifierResults as returned by the runClassifier function.
-------	--

Value

The return value is a classifier definition which is encoded in an object of class [ClassifierParameters](#). This can be used as input argument for the [runClassifier](#) function.

See Also

[ClassifierParameters](#) and [runClassifier](#)

Other classifier information functions: [getCitations](#), [getDecisionBoundaries](#), [getDescription](#), [getEventChain](#), [getIntercept](#), [getMeans](#), [getNormalizationMethod](#), [getProbeNames](#), [getSds](#), [getTrainingData](#), [getWeights](#)

Examples

```
getClassifier("EMC92")
```

getDecisionBoundaries *Obtain the decision boundaries defined for the classifier.*

Description

getDecisionBoundaries returns the a numeric vector of boundary values that separate the risk groups.

Usage

```
getDecisionBoundaries(object)

## S4 method for signature 'ClassifierParameters'
getDecisionBoundaries(object)
```

Arguments

object An object of class [ClassifierParameters](#) as returned by [getClassifier](#)

Value

A numeric vector

See Also

Other classifier information functions: [getCitations](#), [getClassifier](#), [getDescription](#), [getEventChain](#), [getIntercept](#), [getMeans](#), [getNormalizationMethod](#), [getProbeNames](#), [getSds](#), [getTrainingData](#), [getWeights](#)

Examples

```
aClassifier <- getClassifier("EMC92")
getDecisionBoundaries(aClassifier)
```

getDescription *Obtain classifiers' description.*

Description

getDescription returns the descriptive text associated with the classifier.

Usage

```
getDescription(object)

## S4 method for signature 'ClassifierParameters'
getDescription(object)
```

Arguments

object An object of class `ClassifierParameters` as returned by `getClassifier`

Value

A character string describing the classifier

See Also

Other classifier information functions: `getCitations`, `getClassifier`, `getDecisionBoundaries`, `getEventChain`, `getIntercept`, `getMeans`, `getNormalizationMethod`, `getProbeNames`, `getSds`, `getTrainingData`, `getWeights`

Examples

```
aClassifier <- getClassifier("EMC92")
getDescription(aClassifier)
```

<code>getEventChain</code>	<i>Obtain classifiers' event chain.</i>
----------------------------	---

Description

`getEventChain` returns the event chain encoded in the in the classifier. The eventchain indicates what preprocessing steps are performed by the `runClassifier` function prior to classification.

Usage

```
getEventChain(object)

## S4 method for signature 'ClassifierParameters'
getEventChain(object)
```

Arguments

object An object of class `ClassifierParameters` as returned by `getClassifier`

Value

Returns the event chain encoded in the in the classifier encoded as a named list.

See Also

`showClassifierList` `getClassifier` `runClassifier`

Other classifier information functions: `getCitations`, `getClassifier`, `getDecisionBoundaries`, `getDescription`, `getIntercept`, `getMeans`, `getNormalizationMethod`, `getProbeNames`, `getSds`, `getTrainingData`, `getWeights`

Examples

```
aClassifier <- getClassifier("EMC92")
getEventChain(aClassifier)
```

<code>getIntercept</code>	<i>Obtain classifiers' intercept.</i>
---------------------------	---------------------------------------

Description

`getIntercept` returns the numeric value of the classifier's intercept.

Usage

```
getIntercept(object)

## S4 method for signature 'ClassifierParameters'
getIntercept(object)
```

Arguments

`object` An object of class [ClassifierParameters](#) as returned by [getClassifier](#)

Value

A numeric value

See Also

Other classifier information functions: [getCitations](#), [getClassifier](#), [getDecisionBoundaries](#), [getDescription](#), [getEventChain](#), [getMeans](#), [getNormalizationMethod](#), [getProbeNames](#), [getSds](#), [getTrainingData](#), [getWeights](#)

Examples

```
aClassifier <- getClassifier("EMC92")
getIntercept(aClassifier)
```

getMeans *Obtain classifiers' reference means.*

Description

getMeans returns the reference means encoded in the in the classifier.

Usage

```
getMeans(object)

## S4 method for signature 'ClassifierParameters'
getMeans(object)
```

Arguments

object An object of class [ClassifierParameters](#) as returned by [getClassifier](#)

Value

Returns a numeric vector of probe set means as observed in the reference data

See Also

[showClassifierList](#) [getClassifier](#) [runClassifier](#)

Other classifier information functions: [getCitations](#), [getClassifier](#), [getDecisionBoundaries](#), [getDescription](#), [getEventChain](#), [getIntercept](#), [getNormalizationMethod](#), [getProbeNames](#), [getSds](#), [getTrainingData](#), [getWeights](#)

Examples

```
aClassifier <- getClassifier("EMC92")
getMeans(aClassifier)
```

getName *Obtain object names.*

Description

getName returns the name associated with the requested object.

Usage

```
getName(object)

## S4 method for signature 'TransformationProcess'
getName(object)

## S4 method for signature 'ClassifierParameters'
getName(object)

## S4 method for signature 'ClassifierResults'
getName(object)
```

Arguments

object The object to get the name of.

Value

The return value is a character string

See Also

[ClassifierParameters](#)

[ClassifierResults](#)

Examples

```
aClassifier <- getClassifier("EMC92")
getName( aClassifier )
```

getNormalizationMethod

Obtain normalization method

Description

The function getNormalizationMethod returns the normalization method associated with the object

getNormalizationMethods returns a character vector of currently available normalization methods.

Usage

```

getNormalizationMethod(object)

getNormalizationMethods()

## S4 method for signature 'FixedExpressionData'
getNormalizationMethod(object)

## S4 method for signature 'ClassifierParameters'
getNormalizationMethod(object)

```

Arguments

object An object of class [FixedExpressionData](#) or [ClassifierParameters](#)

Details

The given normlization methods can be used in the

Value

A character string indicating the normalization method.

See Also

[getNormalizationMethods](#)

Other classifier information functions: [getCitations](#), [getClassifier](#), [getDecisionBoundaries](#), [getDescription](#), [getEventChain](#), [getIntercept](#), [getMeans](#), [getProbeNames](#), [getSds](#), [getTrainingData](#), [getWeights](#)

Other fixed data information extraction functions: [\[,FixedExpressionData,ANY,ANY-method](#), [dim,FixedExpressionData-method](#), [getTargetValue](#)

Other workflow functions: [runClassifier](#), [setNormalizationMethod](#), [showClassifierList](#)

Examples

```

data(exampleMAS5)
myData <- setNormalizationMethod(exampleMAS5, "MAS5.0", targetValue=500)
aClassifier <- getClassifier("EMC92")
getNormalizationMethod( myData )
getNormalizationMethod( aClassifier )
data(exampleMAS5)

showClassifierList()
getNormalizationMethods()

myData <- setNormalizationMethod(exampleMAS5, "MAS5.0",targetValue=500)
results <- runClassifier('UAMS70', myData)

getScores( results )

```

```
getClassifications( results )
```

getProbeNames	<i>Obtain probe-set names.</i>
---------------	--------------------------------

Description

getProbeNames returns the probe names associated with the requested classifier.

Usage

```
getProbeNames(object)  
  
## S4 method for signature 'ClassifierParameters'  
getProbeNames(object)
```

Arguments

object An object of class [ClassifierParameters](#) as returned by [getClassifier](#)

Value

The return value is a character vector of probe-set names.

See Also

[ClassifierParameters](#)

Other classifier information functions: [getCitations](#), [getClassifier](#), [getDecisionBoundaries](#), [getDescription](#), [getEventChain](#), [getIntercept](#), [getMeans](#), [getNormalizationMethod](#), [getSds](#), [getTrainingData](#), [getWeights](#)

Examples

```
aClassifier <- getClassifier("EMC92")  
getProbeNames( aClassifier )
```

getScores *Obtain classifier score.*

Description

getScores returns the resulting scores from a classifier run

Usage

```
getScores(object)

## S4 method for signature 'ClassifierResults'
getScores(object)
```

Arguments

object An object of class `ClassifierResults`

Value

A numeric vector with scores per sample

See Also

Other classifier results: [getBatchCorrection](#), [getClassifications](#), [getWeightingType](#)

Examples

```
data(exampleMAS5)
myData <- setNormalizationMethod(exampleMAS5, "MAS5.0", targetValue=500)
results <- runClassifier('EMC92', myData)
getScores( results )
getClassifications( results )
```

getSds *Obtain classifiers' reference standard deviations.*

Description

getSds returns the reference standard deviations encoded in the classifier.

Usage

```
getSds(object)

## S4 method for signature 'ClassifierParameters'
getSds(object)
```


Arguments

object An object of class [ClassifierParameters](#) as returned by [getClassifier](#)

Value

Returns a numeric vector of probe set standard deviations as observed in the reference data

See Also

[showClassifierList](#) [getClassifier](#) [runClassifier](#)

Other classifier information functions: [getCitations](#), [getClassifier](#), [getDecisionBoundaries](#), [getDescription](#), [getEventChain](#), [getIntercept](#), [getMeans](#), [getNormalizationMethod](#), [getProbeNames](#), [getTrainingData](#), [getWeights](#)

Examples

```
aClassifier <- getClassifier("EMC92")
getSds(aClassifier)
```

getTargetValue	<i>Obtain the targetValue</i>
----------------	-------------------------------

Description

getTargetValue returns the current applied targetValue in the MAS5.0 gene expression data.

Usage

```
getTargetValue(object)

## S4 method for signature 'FixedExpressionData'
getTargetValue(object)
```

Arguments

object An object of class [FixedExpressionData](#)

Value

A numeric value

See Also

Other fixed data information extraction functions: [\[,FixedExpressionData,ANY,ANY-method](#), [dim,FixedExpressionData-method](#), [getNormalizationMethod](#)

Examples

```
data(exampleMAS5)
myData <- setNormalizationMethod(exampleMAS5, "MAS5.0", targetValue=500)
getTargetValue( myData )
```

getTrainingData	<i>Obtain classifier training data.</i>
-----------------	---

Description

getTrainingData returns the training data that was used for building the classifier.

Usage

```
getTrainingData(object)

## S4 method for signature 'ClassifierParameters'
getTrainingData(object)
```

Arguments

object An object of class [ClassifierParameters](#) as returned by [getClassifier](#)

Value

An object of class [ExpressionSet](#)

See Also

Other classifier information functions: [getCitations](#), [getClassifier](#), [getDecisionBoundaries](#), [getDescription](#), [getEventChain](#), [getIntercept](#), [getMeans](#), [getNormalizationMethod](#), [getProbeNames](#), [getSds](#), [getWeights](#)

Examples

```
aClassifier <- getClassifier("EMC92")
getTrainingData(aClassifier)
```

getWeightingType	<i>Obtain the weighting type used to obtain a classifier result.</i>
------------------	--

Description

getWeightingType returns weighting type
getWeightingTypes returns weighting type

Usage

```
getWeightingType(object)  
  
getWeightingTypes()  
  
## S4 method for signature 'ClassifierResults'  
getWeightingType(object)
```

Arguments

object An object of class [ClassifierResults](#) as returned by [runClassifier](#)

Value

one of the values in [getWeightingTypes\(\)](#)
either "complete" or "reweighted"

See Also

Other classifier results: [getBatchCorrection](#), [getClassifications](#), [getScores](#)

Other classifier results: [getBatchCorrection](#), [getClassifications](#), [getScores](#)

Examples

```
myData <- setNormalizationMethod(exampleMAS5, "MAS5.0",targetValue=500)  
results <- runClassifier('EMC92', myData)  
getWeightingType( results )  
getWeightingTypes()
```

getWeights	<i>Obtain classifier weights.</i>
------------	-----------------------------------

Description

getWeights returns the probe weights associated with the classifier.

Usage

```
getWeights(object)

## S4 method for signature 'ClassifierParameters'
getWeights(object)
```

Arguments

object An object of class [ClassifierParameters](#) as returned by [getClassifier](#)

Value

A numeric vector.

See Also

Other classifier information functions: [getCitations](#), [getClassifier](#), [getDecisionBoundaries](#), [getDescription](#), [getEventChain](#), [getIntercept](#), [getMeans](#), [getNormalizationMethod](#), [getProbeNames](#), [getSds](#), [getTrainingData](#)

Examples

```
aClassifier <- getClassifier("EMC92")
getWeights(aClassifier)
```

runClassifier	<i>Perform classification.</i>
---------------	--------------------------------

Description

runClassifier performs classification by applying a classifier to gene expression data.

Usage

```
runClassifier(classifierParameters, fixedExpressionData, ...)

## S4 method for signature 'character,FixedExpressionData'
runClassifier(classifierParameters,
             fixedExpressionData, ...)

## S4 method for signature 'ClassifierParameters,FixedExpressionData'
runClassifier(classifierParameters,
             fixedExpressionData, ...)
```

Arguments

classifierParameters
Either a text value indicating a classifier name (see [showClassifierList](#)), or an object of class [ClassifierParameters](#) as returned by the [getClassifier](#) function.

fixedExpressionData
The data to be classified in the form of a [FixedExpressionData](#) object as returned by the [setNormalizationMethod](#) function.

...
see details

Details

A list of possible classifiers is obtained by [showClassifierList](#). The data to be classified is first to be processed by the [setNormalizationMethod](#) function. By default the data is assumed to contain many ($n \geq 25$) samples with corresponding probe-sets needed for classification. If one of these conditions is not met, a classifier outcome might be seriously affected. By default an error is given. Although strongly discouraged, it is possible to circumvent the security checks. If not all required probe-sets are included in the input set, you can explicitly pass the parameter `allow.reweighted = TRUE` to the `runClassifier` function in order to determine the classifier outcome using less probe-sets (e.g. possible if the missing probe-sets are known to have minimal contribution). See `vignette("MissingCovariates")` for more information. If the input data has a small number of samples, the default batch correction becomes ineffective. If you are aware of the possible negative effects you can force to not use batch correction by passing the parameter `do.batchcorrection=FALSE`.

Value

The classification results as an object of class [ClassifierResults](#).

See Also

Other workflow functions: [getNormalizationMethod](#), [setNormalizationMethod](#), [showClassifierList](#)

Examples

```
data(exampleMAS5)
myData<-setNormalizationMethod(exampleMAS5,"MAS5.0",targetValue=500)
runClassifier("EMC92",myData)
```

setNormalizationMethod

Prepare data.

Description

setNormalizationMethod is to be called prior to running a classifier.

Usage

```
setNormalizationMethod(expressionSet, method, ...)
```

Arguments

expressionSet	An object of class ExpressionSet containing the gene expression data.
method	A character string indicating the normalization that was applied to the data. Possible values are given by getNormalizationMethods() .
...	see details.

Details

The [FixedExpressionData](#) class forms together with the [ClassifierParameters](#) class the basis for input to the [runClassifier](#) function. The data inside the [FixedExpressionData](#)-class has to be stored as it is right after normalization. This function may require some additional arguments:

- `isLog2Transformed = TRUE` Use this argument if the data already underwent a log2transformation, as is common e.g. in case of MAS5.0 normalization.
- `targetValue = value` This is a MAS5.0 specific argument. It is the sample intensity mean when the lowest and highest 2% of intensities are discarded. If only part of the original expression set is given to this function, then this argument is required.

Value

An object of class [FixedExpressionData](#)

See Also

Other workflow functions: [getNormalizationMethod](#), [runClassifier](#), [showClassifierList](#)

Examples

```
data(exampleMAS5)
myData <- setNormalizationMethod(exampleMAS5, "MAS5.0",targetValue=500)
results <- runClassifier('EMC92', myData)
getScores( results )
getClassifications( results )
```

showClassifierList *Show classifier names and descriptions.*

Description

showClassifierList gives a data.frame of all implemented classifiers.

Usage

```
showClassifierList(normalizations)
```

Arguments

normalizations an optional text argument of one or more normalization methods in order to filter the classifiers to be shown.

Details

The names of the classifiers shown can be used as input for the [runClassifier](#) function and the [getClassifier](#) function.

Value

A data.frame with columns: "name", "normalizationMethod" and "description"

See Also

Other workflow functions: [getNormalizationMethod](#), [runClassifier](#), [setNormalizationMethod](#)

Examples

```
showClassifierList()
data(exampleMAS5)
myData <- setNormalizationMethod(exampleMAS5, "MAS5.0",targetValue=500)
results <- runClassifier('UAMS70', myData)
getScores( results )
getClassifications( results )
```

 [,FixedExpressionData,ANY,ANY-method

Extract

Description

Extract Parts of an Object

Usage

```
## S4 method for signature 'FixedExpressionData,ANY,ANY'
x[i, j, ..., drop = TRUE]

## S4 method for signature 'FixedExpressionData,ANY,missing'
x[i, j, ..., drop = TRUE]

## S4 method for signature 'FixedExpressionData,missing,ANY'
x[i, j, ..., drop = TRUE]

## S4 method for signature 'FixedExpressionData,ANY,missing'
x[[i, j, ...]]

## S4 method for signature 'FixedExpressionData,missing,ANY'
x[[i, j, ...]]

## S4 method for signature 'FixedExpressionData,ANY,ANY'
x[[i, j, ...]]
```

Arguments

x	An object of class FixedExpressionData
i	the rows index
j	the column index
...	unused
drop	unused

Value

An object of class [FixedExpressionData](#)

See Also

Other fixed data information extraction functions: [dim](#), [FixedExpressionData-method](#), [getNormalizationMethod](#), [getTargetValue](#)

Examples

```
data(exampleMAS5)
myData <- setNormalizationMethod(exampleMAS5, "MAS5.0", targetValue=500)
dim(myData)
dim(myData[1:10,1:3])
dim(myData[[1:10,1:3]])
```

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