

# Package ‘CytoDx’

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**Type** Package

**Title** Robust prediction of clinical outcomes using cytometry data  
without cell gating

**Version** 1.30.0

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**Description** This package provides functions that predict clinical outcomes using single cell data (such as flow cytometry data, RNA single cell sequencing data) without the requirement of cell gating or clustering.

**License** GPL-2

**Encoding** UTF-8

**LazyData** true

**Imports** doParallel, dplyr, glmnet, rpart, rpart.plot, stats,  
flowCore, grDevices, graphics, utils

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**VignetteBuilder** knitr, rmarkdown

**RoxygenNote** 6.1.0

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| CytoDx.fit | <i>Build the CytoDx model</i> |
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## Description

A function that builds the CytoDx model.

## Usage

```
CytoDx.fit(x, y, xSample, family = c("gaussian", "binomial", "poisson",
  "multinomial", "cox", "mgaussian"), type1 = "response",
  type2 = "response", parallelCore = 1, reg = FALSE, ...)
```

## Arguments

|              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| x            | The marker profile of cells pooled from all samples. Each row is a cell, each column is a marker.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| y            | The clinical outcomes associated with samples to which cells belong. Length must be equal to nrow(x). For family="binomial" should be either a factor with two levels, or a two-column matrix of counts or proportions (the second column is treated as the target class; for a factor, the last level in alphabetical order is the target class). For family="multinomial", can be a nc>=2 level factor, or a matrix with nc columns of counts or proportions. For either "binomial" or "multinomial", if y is presented as a vector, it will be coerced into a factor. For family="cox", y should be a two-column matrix with columns named 'time' and 'status'. The latter is a binary variable, with '1' indicating death, and '0' indicating right censored. The function Surv() in package survival produces such a matrix. For family="mgaussian", y is a matrix of quantitative responses. |
| xSample      | A vector specifying which sample each cell belongs to. Length must equal to nrow(x).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| family       | Response type. Must be one of the following: "gaussian", "binomial", "poisson", "multinomial", "cox", "                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| type1        | Type of first level prediction. Type of prediction required. Type "link" gives the linear predictors for "binomial", "multinomial", "poisson" or "cox" models; for "gaussian" models it gives the fitted values. Type "response" gives the fitted probabilities for "binomial" or "multinomial", fitted mean for "poisson" and the fitted relative-risk for "cox"; for "gaussian" type "response" is equivalent to type "link".                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| type2        | Type of second level prediction.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| parallelCore | The number of core to be used. Only used when reg is TRUE.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| reg          | If elastic net regularization will be used.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| ...          | Other parameters to be passed into the glmnet or the cv.glmnet function in the glmnet package.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |

**Value**

Returns a list. `train.Data.cell` contains the training data and the predicted `y` for the training data at the cell level. `model.cell` contains the cell stage statistical model. `Data.sample` contains the training data and the predicted `y` for the training data at the sample level. `model.sample` contains the sample stage statistical model. `family` specifies the regression type. `method` specifies the type of learning method. `type.cell` is the type of cell level prediction. `type.sample` is the type of sample level prediction.

**Examples**

```
# Find the table containing fcs file names in CytoDx package
path <- system.file("extdata", package="CytoDx")
# read the table
fcs_info <- read.csv(file.path(path, "fcs_info.csv"))
# Specify the path to the cytometry files
fn <- file.path(path, fcs_info$fcsName)
# Read cytometry files using fcs2DF function
train_data <- fcs2DF(fcsFiles=fn,
                     y=fcs_info$Label,
                     assay="FCM",
                     b=1/150,
                     excludeTransformParameters=
                       c("FSC-A", "FSC-W", "FSC-H", "Time"))
# build the model
fit <- CytoDx.fit(x=as.matrix(train_data[,1:7]),
                 y=train_data$y,
                 xSample = train_data$xSample,
                 reg=FALSE,
                 family="binomial")
# check accuracy for training data
pred <- CytoDx.pred(fit,
                    xNew=as.matrix(train_data[,1:7]),
                    xSampleNew=train_data$xSample)

boxplot(pred$xNew.Pred.sample$y.Pred.s0~
        fcs_info$Label)
```

CytoDx.pred

*Make prediction using the CytoDx model***Description**

A function that makes prediction using the CytoDx model.

**Usage**

```
CytoDx.pred(fit, xNew, xSampleNew)
```

**Arguments**

|                   |                                                                                                       |
|-------------------|-------------------------------------------------------------------------------------------------------|
| <code>fit</code>  | The two stage statistical model. Must be the object returned by <code>CytoDx.fit</code> .             |
| <code>xNew</code> | The marker profile of cells pooled from all new samples. Each row is a cell, each column is a marker. |

**xSampleNew** A vector specifying which sample each cell belongs to. Length must equal to `nrow(xNew)`.

### Value

Returns a list. `xNew.Pred1` contains the predicted  $y$  for the new data at the cell level. `xNew.Pred2` contains the predicted  $y$  for the new data at the sample level.

### Examples

```
# Find the table containing fcs file names in CytoDx package
path <- system.file("extdata", package="CytoDx")
# read the table
fcs_info <- read.csv(file.path(path, "fcs_info.csv"))
# Specify the path to the cytometry files
fn <- file.path(path, fcs_info$fcsName)
train_data <- fcs2DF(fcsFiles=fn,
                    y=fcs_info$Label,
                    assay="FCM",
                    b=1/150,
                    excludeTransformParameters=
                      c("FSC-A", "FSC-W", "FSC-H", "Time"))
# build the model
fit <- CytoDx.fit(x=as.matrix(train_data[,1:7]),
                 y=train_data$y,
                 xSample = train_data$xSample,
                 reg=FALSE,
                 family="binomial")
# check accuracy for training data
pred <- CytoDx.pred(fit,
                   xNew=as.matrix(train_data[,1:7]),
                   xSampleNew=train_data$xSample)

boxplot(pred$xNew.Pred.sample$y.Pred.s0~
        fcs_info$Label)
```

---

fcs2DF

*Convert fcs files to a data frame*

---

### Description

A function that convert fcs files to a data frame.

### Usage

```
fcs2DF(fcsFiles, y = NULL, assay = c("FCM", "CyTOF"), b = 1/200,
      fileSampleSize = 5000, compFiles = NULL, nameDict = NULL,
      excludeTransformParameters = c("FSC-A", "FSC-W", "FSC-H", "Time",
      "Cell_length"))
```

**Arguments**

|                            |                                                                                                                                                                                                                                                                                                                    |
|----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| fcsFiles                   | A vector specifying the location of fcs files (relative to working directory).                                                                                                                                                                                                                                     |
| y                          | A vector containing the clinical outcome of each sample. Must have the same length as fcsFiles. Null for testing data.                                                                                                                                                                                             |
| assay                      | Either "FCM" or "CyTOF" to indicate the type of cytometry data.                                                                                                                                                                                                                                                    |
| b                          | A positive number used to specify the arcsinh transformation. $f(x) = \text{asinh}(b \cdot x)$ where $x$ is the original value and $f(x)$ is the value after transformation. The suggested value is 1/150 for flow cytometry (FCM) data and 1/8 for CyTOF data.                                                    |
| fileSampleSize             | An integer specifying the number of events sampled from each fcs file. If NULL, all the events will be pre-processed and wrote out to the new fcs files.                                                                                                                                                           |
| compFiles                  | A vector specifying the paths of user supplied compensation matrix for each fcs file. The matrix must be stored in csv files.                                                                                                                                                                                      |
| nameDict                   | A vector used to change marker names. Each element in the vector is the preferred name of a marker. The name of each element is the marker name used in the fcs file. For example, a vector <code>c("CD8b"="CD8", "cd8"="CD8")</code> will change "CD8b" and "cd8" into "CD8", making annotations more consistent. |
| excludeTransformParameters | A vector specifying the name of parameters not to be transformed (left at linear scale).                                                                                                                                                                                                                           |

**Value**

Returns a data frame containing the preprocessed cytometry data. Cells from different fcs files are combined into one flow frame. A new column, xSample, is introduced to indicate the origin of each cell. The data frame also includes the clinical outcome y.

**Examples**

```
# Find the table containing fcs file names in CytoDx package
path <- system.file("extdata", package="CytoDx")
# read the table
fcs_info <- read.csv(file.path(path, "fcs_info.csv"))
# Specify the path to the cytometry files
fn <- file.path(path, fcs_info$fcsName)
# Read cytometry files using fcs2DF function
train_data <- fcs2DF(fcsFiles=fn,
  y=fcs_info$Label,
  assay="FCM",
  b=1/150,
  excludeTransformParameters=
    c("FSC-A", "FSC-W", "FSC-H", "Time"))
```

---

meanUnique

*Calulate mean or take unique elements of a vector*


---

**Description**

A function that calulate mean or take unique elements of a vector.

**Usage**

```
meanUnique(x)
```

**Arguments**

**x**                      a vector

**Value**

If **x** is numeric, returns the mean. Otherwise, returns the unique elements of **x**.

**Examples**

```
x <- 1:5
meanUnique(x)
x=c("a", "a", "b")
meanUnique(x)
```

---

pRank

*Percentile rank transformation of the data*


---

**Description**

A function that performs the rank transformation of the data.

**Usage**

```
pRank(x, xSample)
```

**Arguments**

**x**                      A data frame containing the pooled data from fcs files. Each row is a cell, each column is a marker.

**xSample**              A vector specifying which sample each cell belongs to. Length must equal to `nrow(x)`.

**Value**

Returns data frame containing rank transformed data.

**Examples**

```
x <- pRank(x=iris[,1:4], xSample=iris$Species)
```

---

|                 |                                                   |
|-----------------|---------------------------------------------------|
| rank.ub.average | <i>Percentile rank transformation of a vector</i> |
|-----------------|---------------------------------------------------|

---

**Description**

A function that performs the Percentile rank transformation of a vector

**Usage**

```
rank.ub.average(x)
```

**Arguments**

|   |                   |
|---|-------------------|
| x | A numeric vector. |
|---|-------------------|

**Value**

Returns the percentile rank of each element.

**Examples**

```
rank.ub.average(1:10)
```

---

|        |                                          |
|--------|------------------------------------------|
| set2DF | <i>convert a flowSet to a data frame</i> |
|--------|------------------------------------------|

---

**Description**

A function that convert a flowSet to a data frame.

**Usage**

```
set2DF(flowSet, fcsFiles, y = NULL)
```

**Arguments**

|          |                                                                            |
|----------|----------------------------------------------------------------------------|
| flowSet  | A flowSet object                                                           |
| fcsFiles | A vector containing the name of each fcs file included in flowSet.         |
| y        | The clinical outcome each fcs file associated with. Null for testing data. |

**Value**

Returns a data frame containing the cytometry data. Cells from different fcs files are combined into one flow frame. A new column, xSample, is introduced to indicate the origin of each cell. The data frame also includes the clinical outcome y.

## Examples

```
library(flowCore)
# Find the table containing fcs file names in CytoDx package
path <- system.file("extdata",package="CytoDx")
# read the table
fcs_info <- read.csv(file.path(path,"fcs_info.csv"))
# Specify the path to the cytometry files
fn <- file.path(path,fcs_info$fcsName)
fSet <- read.flowSet(fn)
df <- set2DF(flowSet=fSet,fcsFiles=fn,y = fcs_info$Label)
```

---

|          |                                                                                              |
|----------|----------------------------------------------------------------------------------------------|
| treeGate | <i>Use decision tree to find a group of cells that are associated with clinical outcome.</i> |
|----------|----------------------------------------------------------------------------------------------|

---

## Description

A function that sse decision tree to find a group of cells that are associated with clinical outcome.

## Usage

```
treeGate(P, x, ...)
```

## Arguments

|     |                                                                                                         |
|-----|---------------------------------------------------------------------------------------------------------|
| P   | The predicted association of each cell with a clinical outcome.                                         |
| x   | The marker profile of each cell. Each row is a cell, each column is a marker. Must have length(P) rows. |
| ... | Other parameters to be passed into the rpart function                                                   |

## Value

Returns a object created by rpart function. Also plots a graph of decision tree.

## Examples

```
# Find the table containing fcs file names in CytoDx package
path=system.file("extdata",package="CytoDx")
# read the table
fcs_info <- read.csv(file.path(path,"fcs_info.csv"))
# Specify the path to the cytometry files
fn <- file.path(path,fcs_info$fcsName)
# Read cytometry files using fcs2DF function
train_data <- fcs2DF(fcsFiles=fn,
                    y=fcs_info$Label,
                    assay="FCM",
                    b=1/150,
                    excludeTransformParameters=
                      c("FSC-A","FSC-W","FSC-H","Time"))
# build the model
fit <- CytoDx.fit(x=as.matrix(train_data[,1:7]),
                y=train_data$y,
                xSample = train_data$xSample,
```

```
      reg=FALSE,
      family="binomial")
# check accuracy for training data
pred <- CytoDx.pred(fit,
  xNew=as.matrix(train_data[,1:7]),
  xSampleNew=train_data$xSample)

boxplot(pred$xNew.Pred.sample$y.Pred.s0~
  fcs_info$Label)

# Find the associated population using treeGate
TG <- treeGate(P = fit$train.Data.cell$y.Pred.s0,
  x= train_data[,1:7])
```

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