Package ‘MDimNormn’

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Title Multi-Dimensional MA Normalization for Plate Effect
Version 0.8.0
Author Mun-Gwan Hong
Maintainer Mun-Gwan Hong <mun-gwan.hong@scilifelab.se>
Depends R (>= 3.2.0)
Description Normalize data to minimize the difference between sample plates (batch effects). For given data in a matrix and grouping variable (or plate), the function ‘normn_MA’ normalizes the data on MA coordinates. More details are in the citation. The primary method is ‘Multi-MA’. Other fitting functions on MA coordinates can also be employed e.g. loess.
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**normn MA**

*Multi-dimensional MA normalization for plate effect*

**Description**

Normalize data to minimize the difference among the subgroups of the samples generated by experimental factor such as multiple plates (batch effects)

- the primary method is Multi-MA, but other fitting function, $f$ in manuscript (e.g. loess) is available, too.

This method is based on the assumptions stated below

1. The geometric mean value of the samples in each subgroup (or plate) for a single target is ideally same as those from the other subgroups.

2. The subgroup (or plate) effects that influence those mean values for multiple observed targets are dependent on the values themselves. (intensity dependent effects)

**Usage**

```r
normn_MA(mD, expGroup, represent_FUN= function(x) mean(x, na.rm= T),
            fitting_FUN= NULL, isLog= TRUE)
```

**Arguments**

- **mD** a matrix of measured values in which columns are the measured molecules and rows are samples
- **expGroup** a vector of experimental grouping variable such as plate. The length of code-expGroup must be same as the number of rows of mD.
- **represent_FUN** a function that computes representative values for each experimental group (e.g. plate). The default is mean ignoring any NA
- **fitting_FUN** NULL or a function that fits to data in MA-coordinates. If it is NULL as the default, ‘Multi-MA’ method is employed. If a function is used, two arguments of $m_j$ and $A$ are required, which are $m_j$ coordinate in $M_d$ and $A$ coordinate, respectively.
- **isLog** TRUE or FALSE, if the normalization should be conducted after log-transformation. The affinity proteomics data from suspension bead arrays is recommended to be normalized using the default, isLog = TRUE.

**Value**

The data after normalization in a matrix

**Author(s)**

Mun-Gwan Hong <mun-gwan.hong@scilifelab.se>
References
Hong M-G, Lee W, Pawitan Y, Schwenk JM (201?) Multi-dimensional normalization of plate effects for multiplexed applications unpublished

Examples
data(sba)
B <- normn_MA(sba$X, sba$plate) # Multi-MA normalization

# MA-loess normalization
B <- normn_MA(sba$X, sba$plate, fitting_FUN= function(m_j, A) loess(m_j ~ A)$fitted)

# weighted linear regression normalization
B <- normn_MA(sba$X, sba$plate, fitting_FUN= function(m_j, A) {
  beta <- lm(m_j ~ A, weights= 1/A)$coefficients
})

# robust linear regression normalization
if(any(search() == "package:MASS")) { # excutable only when MASS package was loaded.
  B <- normn_MA(sba$X, sba$plate, fitting_FUN= function(m_j, A) {
    beta <- rlm(m_j ~ A, maxit= 100)$coefficients
  })
}

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SBA

Artificially generated data alike that of Suspension bead arrays

Description
The data that has similarity to Suspension bead arrays data.

Usage
data(sba)

Format
A list that consists of "plate" which is a factor of plate number, "X" that contains measured values where columns are targets and rows are samples (or observations).

Examples
data(sba)

# plot to check difference of geometric mean of every target between plates
sba_gm <- by(sba$X, sba$plate, apply, 2, function(x) exp(mean(log(x))))
par(mfrow= c(2, 3))
```r
apply(combn(4, 2), 2, function(ea) {
plot(sba_gm[[ea[1]]], sba_gm[[ea[2]]], xlab= names(sba_gm)[ea[1]],
     ylab= names(sba_gm)[ea[2]], log="xy", asp= 1)
abline(0, 1, col="cadetblue")
})

# show first 10 observations in plate 1 and plate 2
print(sba$X[c(1:10, 97:106), 1:10])
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