Package ‘AssayCorrector’

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Type Package

Title Detection and Correction of Spatial Bias in HTS Screens

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Description Allows to correct bias in high-throughput screening (HTS) assays. It (1) Detects plate-specific spatial bias by identifying rows and columns of all plates of the assay affected by this bias (following the results of the Mann-Whitney U test) as well as assay-specific spatial bias by identifying well locations (i.e., well positions scanned across all plates of a given assay) affected by this bias (also following the results of the Mann-Whitney U test); (2) Allows one to correct plate-specific spatial bias using either of the three additive or either of the three multiplicative PMP (Partial Mean Polish) methods (the most appropriate spatial bias model can be either specified by the user or determined by the program following the results of the Kolmogorov-Smirnov, Anderson-Darling or Cramer-von-Mises two-sample test) to correct the assay measurements as well as to correct assay-specific spatial bias by carrying out robust Z-scores within each plate of the assay and then traditional Z-scores across well locations.

Depends R (>= 3.3.0), RColorBrewer, lattice, latticeExtra, kSamples, RVAideMemoire

License GPL-3

LazyData TRUE

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**Description**

`correct_bias()` (1) uses either of the three additive or either of the three multiplicative PMP (Partial Mean Polish) methods (the most appropriate spatial bias model can be either specified or determined by the program following the results of the Kolmogorov-Smirnov, Anderson-Darling or Cramer-von-Mises two-sample test) to correct the assay measurements if the plate-specific correction is specified; (2) carries out the assay-specific correction if specified.

**Usage**

```r
correct_bias(assay, method = NULL, alpha = 0.05, type = "PA")
```

**Arguments**

- **assay**: The assay to be corrected. Has to be an `assay` object.
- **method**: `NULL`: autodetect (default), 1: additive, 2: multiplicative
- **alpha**: Significance level threshold (defaults to 0.05)
- **type**: P: plate-specific, A: assay-specific, PA: plate then assay-specific, AP: assay then plate-specific

**Value**

The corrected assay (`assay` object)

**Examples**

```r
assay <- create_assay(m)
detected <- detect_bias(assay)
corrected <- correct_bias(detected, method=2)
```
**Description**

`create_assay` makes a new object of class assay. You should pass this object to `detect_bias()` and `correct_bias()` methods.

**Usage**

```r
create_assay(m, ctrl = NA)
```

**Arguments**

- `m` The assay you want to be corrected.
- `ctrl` An optional boolean array of the same dimensions as `m`. Each entry is 1 if the well is a control well, 0 otherwise. All control wells are excluded from all computations.

**Value**

- `assay` The created assay object. It contains the following fields:
  - `n` The HTS matrix of raw measurements.
  - `ctrl` The binary matrix of control wells.
  - `biasPositions` The binary matrix where 1: well is biased, 0: well is unbiased, as suggested by Mann-Whitney test.
  - `mCorrected` The HTS matrix of corrected measurements, initialized to a zero array, and subsequently storing the corrected version of `m` via `correct_bias()`.
  - `biasType` Vector of length `p`, where `p` is the number of plates. It tells, for each plate of the assay, A: Additive trend, M: Multiplicative trend, U: Undetermined trend and C: Error-free plate.
  - `biasModel` Vector of length `p`, where `p` is the number of plates. It tells, for each plate of the assay, the most likely spatial bias model (1 through 6).
  - `biasConf` Vector of length `p`, where `p` is the number of plates. It tells, for each plate of the assay, the confidence in the model, (0 - lowest to 3 - highest). It is computed by counting the number of bias models (additive or multiplicative) which agree together.

**Examples**

```r
# Fictive 8x12x5 assay
assay<-create_assay(m)
# Plate 7 taken from Carralot et al. 2012
assay<-create_assay(plate7)
```
**Description**

detect (1) identifies rows and columns of all plates of the assay affected by spatial bias (following the results of the Mann-Whitney U test); (2) identifies well locations (i.e., well positions scanned across all plates of a given assay) affected by spatial bias (also following the results of the Mann-Whitney U test).

**Usage**

detect_bias(assay, alpha = 0.01, type = "p", test = "ad")

**Arguments**

- **assay**: The assay to be corrected. Has to be an assay object.
- **alpha**: Significance level threshold (defaults to 0.01)
- **type**: P: plate-specific, A: assay-specific, PA: plate then assay-specific, AP: assay then plate-specific

**Value**

The corrected assay (assay object)

**Examples**

```r
assay <- create_assay(m)
detected <- detect_bias(assay)
```

---

**Artificially generated HTS assay**

**Description**

A 8x12x5 assay (class array) that was generated with partial column bias in the last column. Gaussian noise was then added.

**Usage**

m

**Format**

An object of class array of dimension 8 x 12 x 5.
Plate 7 of raw measurements obtained by Carralot et al. 2012 (Institut Pasteur Korea)

**Description**

The seventh plate taken from an experimental assay, which showed the evidence of existence of multiplicative kind of bias in screening technologies.

**Usage**

`plate7`

**Format**

An object of class `array` of dimension 16 x 20 x 1.

**plot.assay**

*Plot assay plate-wise*

**Description**

`plot.assay` plots a hit map of the assay (only one plate at a time)

**Usage**

```r
## S3 method for class 'assay'
plot(x, ..., plate = 1, type = "R")
```

**Arguments**

- `x` The assay you want to plot
- `...` Ellipsis to be passed to the `levelplot()` function from the `lattice` package
- `plate` The plate number (Default: 1)
- `type` Either "R" - raw assay, "C" - corrected assay (if it exists) or "P" - spatial bias position

**Value**

None
print.assay  

Print assay summary

Description

print.assay simply prints a summary of the HTS assay

Usage

```r
## S3 method for class 'assay'
print(x, ..., plate = 1)
```

Arguments

- `x`  
  The assay you want to print
- `...`  
  Ellipsis to be passed to the default `print()` function
- `plate`  
  The plate number (Default: 1)

Value

None
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