

# Package ‘rain’

July 15, 2023

**Type** Package

**Title** Rhythmicity Analysis Incorporating Non-parametric Methods

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**Description** This package uses non-parametric methods to detect rhythms in time series. It deals with outliers, missing values and is optimized for time series comprising 10-100 measurements. As it does not assume expect any distinct waveform it is optimal or detecting oscillating behavior (e.g. circadian or cell cycle) in e.g. genome- or proteome-wide biological measurements such as: micro arrays, proteome mass spectrometry, or metabolome measurements.

**License** GPL-2

**Depends** R (>= 2.10), gmp, multtest

**biocViews** TimeCourse, Genetics, SystemsBiology, Proteomics, Microarray, MultipleComparison

**Suggests** lattice, BiocStyle

**Encoding** UTF-8

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**Description**

Package Description

**Details**

Start with function 'rain'

**Author(s)**

Paul Thaben &lt;paul.thaben@charite.de&gt;

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menetRNASeqMouseLiver	<i>Time courses of gene expression in mouse liver</i>
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**Description**

Temporal gene expression profiling in mouse liver, measured by high throughput sequencing. Profiles shows the changes in gene expression in mice under 12 h light: 12 h dark conditions. Data were originally published by Menet et. al. (2012) under Creative Commons License 3.0: <http://creativecommons.org/licenses/by/3.0/>. The data are available in the public domain at GEO <http://www.ncbi.nlm.nih.gov/geo/> as Dataset entry GSE36916.

**Usage**

menetRNASeqMouseLiver

**Format**

a data.frame containing the normalized expression values for each gene and time point in two repeats. First number shows the time of measurement in 'Zeitgeber Time' (ZT) whereas ZT\_0 is the time of light on. The second number specifies the biological replicate.

**Author(s)**

Paul F. Thaben &lt;paul.thaben@charite.de&gt;

**References**

Menet, J. S., Rodriguez, J., Abruzzi, K. C., & Rosbash, M. (2012). Nascent-Seq reveals novel features of mouse circadian transcriptional regulation. *eLife*, **1(0)**, e00011. doi:10.7554/eLife.00011

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rain	<i>Detection of rhythmic behavior in time series.</i>
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### Description

rain detects rhythms in time-series using non parametric methods. It uses an extension of the rank test for Umbrella Alternatives (Mack & Wolfe, 1981), based on on the Jonckheere-Terpstra test, which tests whether sets of groups have a trend or not. The Umbrella method extends this to independent rising and falling sets.

### Usage

```
rain(x, deltat, period, period.delta = 0, peak.border = c(0.3, 0.7),
     nr.series = 1, measure.sequence = NULL, method = "independent",
     na.rm = FALSE, adjp.method = "ABH", verbose = getOption("verbose"))
```

### Arguments

x	numeric array, containing the data. One row per time point, one column per sample. If more than one replicate is done, see nr.series for formatting.
deltat	numeric: sampling interval.
period	numeric: Period to search for. The given period is mapped to the best matching number of measurements. A set of periods can be defined by period and period.delta.
period.delta	numeric: width of period interval. A interval of different period-length to evaluate is defined by period $\$-\$$ period.delta and period $\$+\$$ period.delta. In this interval all possible numbers of time points according to the deltat are tested.
peak.border	vector c(min,max): defines the different form of the peak. min and max have to be $>0$ and $<1$ . The concrete interpretation depends on the chosen method (see Details). (default = c(0.3,0.7))
nr.series	numeric: Number of replicates of the whole time series. If using nr.series all series have to have the same length. These multiple time series contained in x must be organized timepoint by timepoint using the following format [r1t1, r2t1, r1t2, r2t2, ..., r1tn, r2tn] where ritj is the i'th repeat of the j'th time-point.
measure.sequence	numeric array: Numbers of replicates for each time point. By using 'measure.sequence', irregular time courses may be evaluated. A value of 0 is possible and handled correctly. The array determines how many values are present for each time piont. The values are ordered in the same format as specified above. measure.sequence overwrites nr.series if both are set.
method	string ('independent', 'longitudinal'): identify the method to use (see Details).
na.rm	boolean: calculate individual statistics for time series containign NAs. The time series of a sample containing NAs is treated as if the time points with NA are not measured. Using this option increases calculation time.

adjp.method	string (see <a href="#">mt.rawp2adjp</a> ): select the method wich is used for the multiple testing correction for the different phases and periods and shapes tested
verbose	status output

### Details

The method tests whether a the time course consists of alternating rising and falling slopes, repeated with a distinct period. The partitions of the rising part with respect to the whole period are given by `peak.border = c(min, max)`. The value `peak.shape` specifies this partition in the best matching model. The phase is defined as the time point with the peak. There are two versions of umbrella:

**independent** Multiple periods are interpreted as repeats of one period.

**logitudinal** The whole time series remains unaffected. Partial slopes in the beginning and end of the time series are evaluated as shorter slopes. This method implicitly rejects underlying trends. This should be used only with longitudinal samples, hat may contain strong trends

### Value

An array containing p-values and the description of the best matching model. Each row apply to a sample in `x`.

<code>pVal</code>	The p-Values
<code>phase</code>	The phase of the peak (see Details)
<code>peak.shape</code>	The shape of the curve depending on the method used (see Details)
<code>period</code>	The period length, same unit as <code>deltat</code>

### Author(s)

Paul F. Thaben

### References

Mack, G. A., & Wolfe, D. A. (1981). K-Sample Rank Tests for Umbrella Alternatives. *Journal of the American Statistical Association*, **76(373)**, 175–181.

### Examples

```
# create a dataset with different noise levels
noise.levels <- c(1, 0.5, 0.2, 0.1, 0.05, 0.02)
period <- 15
testset <- apply(matrix(noise.levels, nrow = 1), 2, function(noise){
  timecourse = 1 + 0.4 * cos((1:30) / period * 2 * pi) +
  rnorm(30, 0, noise)
})

results <- rain(testset, period=15, deltat=1, method='independent')

plot(-log(results$pVal) ~ noise.levels)
```

```
## Not run:
# testing a biological dataset
data(menetRNASeqMouseLiver)
menet.ossr <- rain(t(menetRNASeqMouseLiver), deltat = 4, period = 24,
  nr.series = 2, peak.border = c(0.3, 0.7), verbose=TRUE)
require('lattice')

best <- order(results$pVal)[1:10]

xyplot(as.matrix(menetRNASeqMouseLiver
  [best, (0:5 * 2 + rep(c(1, 2), each = 6))])
  ~rep(0:11 * 4 + 2, each = 10) |rownames(menetRNASeqMouseLiver)[best],
  scales = list(y = list(relation = 'free')),
  layout = c(2, 5), type = 'b', pch = 16, xlab = 'time',
  ylab = 'expression value', cex.lab = 1)

## End(Not run)
```

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