Package 'kronos'

April 26, 2023

Title Microbiome Oriented Circadian Rhythm Analysis Toolkit
Version 1.0.0
<pre>URL https://github.com/thomazbastiaanssen/kronos</pre>
Description The goal of 'kronos' is to provide an easy-to-use framework to analyse circadian or otherwise rhythmic data using the familiar R linear modelling syntax, while taking care of the trigonometry under the hood.
Depends R (>= 3.5.0)
Imports stats, methods, ggplot2
License GPL (>= 3)
Encoding UTF-8
LazyData true
RoxygenNote 7.2.3
NeedsCompilation no
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Repository CRAN
Date/Publication 2023-04-26 06:00:02 UTC
R topics documented:
bigdata bigmeta bigmeta build_kronos_formula delistKronos_groupwise delistKronos_pairwise fit_cosinor_model fit_groupwise_model fw_kronos getKronos getKronos getKronos_fit

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Description

Snippet of example data to demonstrate the functionality of 'kronos' between and among three different groups

Usage

bigdata

Format

A long format data.frame object with three 113 columns, features, and 94 rows, samples.

Source

Dummy data modified from untargeted hippocampal metabolomics over the day to demonstrate rhythmicity between multiple groups in a large dataset.

bigmeta 3

bigmeta	Descriptional metadata for the 'bigdata' object, for the purpose of demonstration.

Description

Descriptional metadata for the 'bigdata' object, for the purpose of demonstration.

Usage

bigmeta

Format

A long format data.frame object with three 113 columns and 94 rows.

Source

Dummy metadata modified from untargeted hippocampal metabolomics over the day

Description

Update 'kronos' formula.

Usage

```
build_kronos_formula(formula, time, verbose)
```

Arguments

formula A formula. Use the time function to designate which variable represents time.

time A string. Should be the column name containing the time values.

verbose A boolean. Toggles whether to print diagnostic information while running. Use-

ful for debugging errors on large data sets.

delistKronos_groupwise

Get Results from list of KronosOut Objects

Description

These functions provides a unified wrapper to retrieve results from a list of kronosOut objects.

Usage

```
delistKronos_groupwise(kronos_list, padjust = TRUE)
```

Arguments

kronos_list a list of preferrably named kronosOut objects.

padjust a boolean. Toggles FDR using Benjamini Hochbergs procedure.

Value

A table with circadian output stats per group per feature.

```
delistKronos_pairwise Get Results from list of KronosOut Objects
```

Description

These functions provides a unified wrapper to retrieve results from a list of kronosOut objects.

Usage

```
delistKronos_pairwise(kronos_list, padjust = TRUE)
```

Arguments

kronos_list a list of preferrably named kronosOut objects.

padjust a boolean. Toggles FDR using Benjamini Hochbergs procedure.

Value

ANOVA-like adjusted p-values for how each factor interacts with time.

fit_cosinor_model 5

fit_cosinor_model	Fit cosinor model
TIC_COSTITOT_INDUCT	i ii cosmoi moaci

Description

Fit cosinor model for totality of data

Usage

```
fit_cosinor_model(
  formula,
  data,
  time = NULL,
  verbose = verbose,
  for_pw = FALSE
)
```

Arguments

	formula	A formula.	Use the time	e function to	designate v	which	variable represents time
--	---------	------------	--------------	---------------	-------------	-------	--------------------------

data Input data

time A string. Should be the column name containing the time values.

verbose A boolean. Toggles whether to print diagnostic information while running. Use-

ful for debugging errors on large datasets.

for_pw A boolean. Toggles whether to perform pairwise ANOVAs as a TukeyHSD-like

post-hoc.

fit_groupwise_model Fit cosinor model

Description

Fit cosinor model for one aspect of data. Called by main 'kronos' function.

Usage

```
fit_groupwise_model(data, group, time, period, verbose)
```

Arguments

data	input data
group	A character string. Signifies which group will be assessed.
time	A string. Should be the column name containing the time values.
period	A numeric. The length of a period, in the same format as the time parameter.
verbose	A boolean. Toggles whether to print diagnostic information while running. Useful for debugging errors on large data sets.

fw_kronos

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fw	ΚI	ro	n	o	S

Fit a cosinor model and extract relevant parameters on a feature table.

Description

This wrapper applies kronos(), the main workhorse function in the 'kronos' package. It manages the individual functionalities of 'kronos', including rhythmicity analysis and differential rhythmicity.

Usage

```
fw_kronos(
    x,
    formula,
    metadata,
    time = NULL,
    period = 24,
    verbose = FALSE,
    pairwise = FALSE
)
```

Arguments

X	Input data. A table with rows being features and columns being samples
formula	A formula. Use the time function to designate which variable represents time. Leave the left-hand side of the formula empty as it will be sequentially replaced by every feature in the table.
metadata	A metadata table, with rows being samples and columns being metadata entries
time	A string. Should be the column name containing the time values.
period	A numeric. The length of a period, in the same format as the time parameter.
verbose	A boolean. Toggles whether to print diagnostic information while running. Useful for debugging errors on large datasets.
pairwise	A boolean. Toggles whether to perform pairwise ANOVAs as a TukeyHSD-like post-hoc.

Value

A list of kronosOut S4 objects containing coefficients and all operations.

```
#Load prepared data stored in 'kronos' library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:</pre>
```

getKronos 7

```
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)

#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)

#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)

#Extracting data from the output object:
kronosListToTable(out_list)

#Plotting:
gg_kronos_acrogram(out_list)
```

getKronos

Get Results from KronosOut Object

Description

These functions provides a unified wrapper to retrieve results from a kronosOut object.

Usage

```
getKronos(kronosOut, target)
```

Arguments

kronos0ut a kronos0ut output object.

target the specific entry of the kronosOut object to be extracted.

Value

A data.frame of results.

```
#Load prepared data stored in 'kronos' library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)</pre>
```

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```
getKronos_groupwise(output)

#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)

#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)

#Extracting data from the output object:
kronosListToTable(out_list)

#Plotting:
gg_kronos_acrogram(out_list)
```

getKronos_fit

Get Results from KronosOut Object

Description

These functions provides a unified wrapper to retrieve results from a kronosOut object.

Usage

```
getKronos_fit(kronosOut)
```

Arguments

kronosOut

a kronos0ut output object.

Value

The model fit used.

```
#Load prepared data stored in 'kronos' library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)
#Plotting:</pre>
```

getKronos_groupwise 9

```
gg_kronos_circle(output)
gg_kronos_sinusoid(output)

#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)

#Extracting data from the output object:
kronosListToTable(out_list)

#Plotting:
gg_kronos_acrogram(out_list)
```

getKronos_groupwise

Get Results from KronosOut Object

Description

These functions provides a unified wrapper to retrieve results from a kronosOut object.

Usage

```
getKronos_groupwise(kronosOut)
```

Arguments

kronosOut

a kronos0ut output object.

Value

Rhythmicity parameters per group.

```
#Load prepared data stored in 'kronos' library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)

#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)

#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)

#For high-dimensional data, use fw_kronos:</pre>
```

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```
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)

#Extracting data from the output object:
kronosListToTable(out_list)

#Plotting:
gg_kronos_acrogram(out_list)
```

getKronos_input

Get Results from KronosOut Object

Description

These functions provides a unified wrapper to retrieve results from a kronos0ut object.

Usage

```
getKronos_input(kronosOut)
```

Arguments

kronosOut

a kronos0ut output object.

Value

The data used as input for the model.

```
#Load prepared data stored in 'kronos' library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)

#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)

#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)

#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)</pre>
```

getKronos_pairwise 11

```
#Extracting data from the output object:
kronosListToTable(out_list)

#Plotting:
gg_kronos_acrogram(out_list)
```

getKronos_pairwise

Get Results from KronosOut Object

Description

These functions provides a unified wrapper to retrieve results from a kronosOut object.

Usage

```
getKronos_pairwise(kronosOut)
```

Arguments

kronos0ut

a kronos0ut output object.

Value

Pairwise comparisons between groups.

```
#Load prepared data stored in 'kronos' library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),</pre>
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)
#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)
#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)
#Extracting data from the output object:
kronosListToTable(out_list)
```

```
#Plotting:
gg_kronos_acrogram(out_list)
```

```
getKronos_pairwise_p Get Results from KronosOut Object
```

Description

These functions provides a unified wrapper to retrieve results from a kronosOut object.

Usage

```
getKronos_pairwise_p(kronosOut)
```

Arguments

kronos0ut a kronos0ut output object.

Value

ANOVA-like adjusted p-values for how each factor interacts with time.

```
#Load prepared data stored in 'kronos' library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),</pre>
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)
#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)
#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)
#Extracting data from the output object:
kronosListToTable(out_list)
```

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```
#Plotting:
gg_kronos_acrogram(out_list)
```

getKronos_params

Get Results from KronosOut Object

Description

These functions provides a unified wrapper to retrieve results from a kronosOut object.

Usage

```
getKronos_params(kronosOut)
```

Arguments

kronos0ut

a kronos0ut output object.

Value

The names and values of additional circadian model parameters, mostly for plotting purposes.

```
#Load prepared data stored in 'kronos' library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),</pre>
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)
#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)
#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)
#Extracting data from the output object:
kronosListToTable(out_list)
#Plotting:
gg_kronos_acrogram(out_list)
```

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getKronos_trace

Get Results from KronosOut Object

Description

These functions provides a unified wrapper to retrieve results from a kronosOut object.

Usage

```
getKronos_trace(kronosOut)
```

Arguments

kronos0ut

a kronos0ut output object.

Value

The traces per group for plotting.

```
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),</pre>
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)
#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)
#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)
#Extracting data from the output object:
kronosListToTable(out_list)
#Plotting:
gg_kronos_acrogram(out_list)
```

get_cos_sine 15

get_cos_sine Get sine and cosine components

Description

Based on 'cosinor' and 'limorhyde' packages

Usage

```
get_cos_sine(data, period, colnamePrefix = NULL)
```

Arguments

data input data

period A numeric. The length of a period, in the same format as the time parameter.

colnamePrefix A character string. Typically the name of the "Time" variable.

get_vars	Figure out what variable represents time. function.	Called by main 'kronos'
----------	---	-------------------------

Description

Extracts time from the formula and from the time argument. Also handles inconsistencies.

Usage

```
get_vars(formula, time, data, verbose = verbose)
```

Arguments

formula A formula. Use the time function to designate which variable represents time.

time A string. Should be the column name containing the time values.

data input data

verbose A boolean. Toggles whether to print diagnostic information while running. Use-

ful for debugging errors on large data sets.

gg_kronos_acrogram

gg_kronos_acrogram

A plotting method for acrophase circleplots using 'ggplot2'.

Description

Wrapper around 'ggplot2' to make circadian circleplots.

Usage

```
gg_kronos_acrogram(kronosOutList)
```

Arguments

kronosOutList A list of KronosOut output objects from the main kronos function.

Value

```
a 'ggplot2' compatible object.
```

```
#Load prepared data stored in Kronos library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),</pre>
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)
#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)
#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)
#Extracting data from the output object:
kronosListToTable(out_list)
#Plotting:
gg_kronos_acrogram(out_list)
```

gg_kronos_circle 17

gg_kronos_circle

A plotting method for circadian plots using 'ggplot2'.

Description

Wrapper around 'ggplot2' to make circadian circleplots.

Usage

```
gg_kronos_circle(kronosOut)
```

Arguments

kronos0ut

an output object from the main kronos function.

Value

```
a 'ggplot2' compatible object.
```

```
#Load prepared data stored in Kronos library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),</pre>
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)
#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)
#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)
#Extracting data from the output object:
kronosListToTable(out_list)
#Plotting:
gg_kronos_acrogram(out_list)
```

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gg_kronos_sinusoid

A plotting method for circadian plots using 'ggplot2'.

Description

Wrapper around 'ggplot2' to make figures with a sinusoid trace.

Usage

```
gg_kronos_sinusoid(kronosOut, fill = "unique_group")
```

Arguments

kronosOut

an output object from the main kronos function.

fill

The name of the variable that should be used to mark different groups. In the

case of a single group, leave empty.

Value

a 'ggplot2' compatible object.

```
#Load prepared data stored in Kronos library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),</pre>
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)
#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)
#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)
#Extracting data from the output object:
kronosListToTable(out_list)
#Plotting:
gg_kronos_acrogram(out_list)
```

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groupdata

Snippet of example data to demonstrate the functionality of 'kronos' between and among three different groups

Description

Snippet of example data to demonstrate the functionality of 'kronos' between and among three different groups

Usage

groupdata

Format

A long format data.frame object with three columns, and 94 rows, samples.

Source

Dummy data modified from PCR analysis of mouse ileum over the day to demonstrate rhythmicity between multiple groups.

kronos

Fit a cosinor model and extract relevant parameters

Description

This is the main workhorse function in the 'kronos' package. It manages the individual functionalities of 'kronos', including rhythmicity analysis and differential rhythmicity.

Usage

```
kronos(
  formula,
  data,
  time = NULL,
  period = 24,
  verbose = TRUE,
  pairwise = TRUE
)
```

20 kronosListToTable

Arguments

formula A formula. Use the time function to designate which variable represents time.

data input data

time A string. Should be the column name containing the time values.

period A numeric. The length of a period, in the same format as the time variable

verbose A boolean. Toggles whether to print diagnostic information while running. Use-

ful for debugging errors on large data sets.

pairwise A boolean. Toggles whether to perform pairwise ANOVAs as a TukeyHSD-like

post-hoc.

Value

A kronosOut S4 object containing coefficients and all operations.

Examples

```
#Load prepared data stored in Kronos library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),</pre>
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)
#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)
#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)
#Extracting data from the output object:
kronosListToTable(out_list)
#Plotting:
gg_kronos_acrogram(out_list)
```

kronosListToTable

Wrangle results from list of KronosOut Objects to publication ready table.

kronosOut-class 21

Description

These functions provides a unified wrapper to retrieve results from a list of kronosOut objects.

Usage

```
kronosListToTable(kronos_list, padjust = TRUE)
```

Arguments

```
kronos_list a list of preferrably named kronosOut objects.

padjust a boolean. Toggles FDR using Benjamini and Hochbergs procedure.
```

Value

A table with circadian output stats per group per feature.

Examples

```
#Load prepared data stored in 'kronos' library
data("kronos_demo")
output <- kronos(formula = Variable_1 ~ time(Timepoint),</pre>
data = onevariable, period = 24, verbose = TRUE, pairwise = FALSE)
#Extracting data from the output object:
getKronos_fit(output)
getKronos_trace(output)
getKronos_groupwise(output)
#Plotting:
gg_kronos_circle(output)
gg_kronos_sinusoid(output)
#For high-dimensional data, use fw_kronos:
out_list = fw_kronos(x = bigdata[1:50,], formula = ~ Group + time(Timepoint),
metadata = bigmeta, period = 24, verbose = FALSE, pairwise = TRUE)
#Extracting data from the output object:
kronosListToTable(out_list)
#Plotting:
gg_kronos_acrogram(out_list)
```

kronosOut-class

An S4 class to contain all output parameters and plotting information from the 'kronos' main pipeline

22 kronos_predict

Description

kronosOut is the main output container of the main 'kronos' functions.

Slots

input A data.frame with the data that was fed to the main workhorse function as 'x' fit An lm fit for the entire model for the purpose of assessing differential rhytmicity. to_plot A data.frame with the traces required to plot individual sinusoid curves ind_fit A data.frame with the parameters from individual rhythmic model fits. pairwise_t A data.frame with the p.values for pairwise comparisons, if applicable.

kronos_anova

Extract p-value from full fit

Description

Compute p-values from full fit.

Usage

```
kronos_anova(fit, time)
```

Arguments

fit A lm model fit.

time A string. Should be the column name containing the time values.

kronos_predict

Give tracing information for plotting purposes

Description

Generate data needed to plot cosinor trace line.

Usage

```
kronos_predict(fit, period, time, factors, verbose = verbose)
```

Arguments

fit	A model fit
period	A numeric. The length of a period, in the same format as the time parameter.
time	A string. Should be the column name containing the time values.
factors	A vector. The names of the independent variables.
verbose	A boolean. Toggles whether to print diagnostic information while running. Use-

ful for debugging errors on large data sets.

onevariable 23

onevariable	Snippet of example data to demonstrate the functionality of 'kronos' in the most simple scenario.

Description

Snippet of example data to demonstrate the functionality of 'kronos' in the most simple scenario.

Usage

onevariable

Format

A long format data.frame object with three columns, and 31 rows, samples.

Source

Dummy data modified from metagenomic analysis of mouse caecal contents over the day to demonstrate rhythmicity within one group.

```
pairwise_cosinor_model
```

Fit pairwise cosinor models as some sort of TukeyHSD.

Description

Fit cosinor model for subset of data. Called by main 'kronos' function.

Usage

```
pairwise_cosinor_model(data, formula, time, verbose)
```

Arguments

data	input data
formula	A formula. Use the time function to designate which variable represents time.
time	A string. Should be the column name containing the time values.
verbose	A boolean. Toggles whether to print diagnostic information while running. Useful for debugging errors on large data sets.

24 twowaydata

show, kronosOut-method Show method for kronosOut object.

Description

method to print kronosOut object by calling show. Since kronosOut objects are typically unwieldy, also gives some tips on how to handle it.

Usage

```
## S4 method for signature 'kronosOut'
show(object)
```

Arguments

object

An kronos0ut object.

Value

Does not return anything, for efficiency reasons. The obvious side effect is output to the terminal.

twowaydata

Snippet of example data to demonstrate the functionality of 'kronos' in the two-factor design scenario.

Description

Snippet of example data to demonstrate the functionality of 'kronos' in the two-factor design scenario.

Usage

twowaydata

Format

A wide format data.frame object with nine columns, and 150 rows, samples.

Source

Dummy data modified from metagenomic analysis of mouse caecal contents over the day to demonstrate rhythmicity within one group.

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