Package 'meaRtools'

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Title Micro-Electro Array (MEA) Analysis
Version 1.0.4
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Description Core algorithms for MEA spike train analysis, feature extraction, statistical analy-
      sis and plotting of multiple MEA recordings with multiple genotypes and treatments, pub-
      lished by Gelfman et al (2017) at <a href="https://github.com/igm-team/meaRtools/">https://github.com/igm-team/meaRtools/</a>.
Depends R (>= 3.2.2)
Imports lattice,tcltk,emdist,ggplot2 (>= 2.2.1),
      gridExtra,reshape2,plyr,gtools, Rcpp (>= 0.12.11)
LinkingTo Rcpp
License GPL (>= 3)
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Type Package

${\sf R}$ topics documented:

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Description

Provide information about a new MEA plate format

Usage

```
add_plateinfo(arrayname, info)
```

Arguments

arrayname Name of the plate

info List of information to store about this plate

Details

Store information about a new platename called arrayname. If arrayname already has been used, overwrite it with this new information.

Value

Nothing.

Author(s)

Stephen Eglen

Description

Takes data from S object (MEA data structure) and makes a list of dataframes. Each dataframe corresponds to one feature, containing values for each well across each DIV of recording

Usage

```
aggregate_features(s, feat_type, parameters)
```

Arguments

s MEA data structure

feat_type Type of features (e.g. "spikes", "ns", "bursts")
parameters A list of parameters, see data("parameters")

Value

A list of dataframes for a given set of features

Examples

```
data("S")
data("parameters")
s<-list()
s[[1]]<-S
spike_features = suppressWarnings( aggregate_features(s, "spike", parameters))
ns_features = suppressWarnings( aggregate_features(s, "ns", parameters) )
burst_features = suppressWarnings( aggregate_features(s, "burst", parameters) )</pre>
```

```
calculate_burst_features
```

Filter spikes and bursts in recording objects

Description

Apply user defined filters on the spikes that were recorded and calculate spike features.

```
calculate_burst_features(s)
```

Arguments

S

A spikelist object returned from calling calculate_spike_features.

Value

Returns an 's' object containing all the spikes and bursts of all the loaded recording Robjects.

Author(s)

Diana Hall

```
calculate_entropy_and_mi
```

Calculate Entropy and mututal information for each treatment level

Description

Given an MEA recording, this function computes entropy and mutual information measures for each treatment level.

Usage

```
calculate_entropy_and_mi(mea, treatments, mult_factor = 1.5, bin_size = 0.1)
```

Arguments

mea The input mea spikelist object

treatments The treatment levels that MI and entropy will be computed.

mult_factor The multiplication factor relating to the inter quartile range used in the algo-

rithm. It serves as a tuning parameter with a default value of 1.5.

bin_size The bin size(in second) used to compute mutual information.

Value

A list object holding MI and Entropy for each treatment level.

Examples

```
library(meaRtools)

data(S)
S <- filter_nonactive_spikes(S,spikes_per_minute_min=1)

treatments <- c("treatX", "treatY")
## compute entropies and MI's
ENT.MI <- calculate_entropy_and_mi(S, treatments, mult_factor=1.5, bin_size=0.1)
data_dists <- ENT.MI[["data_dists"]]</pre>
```

6 calculate_isis

```
norm_mis_per_well <- ENT.MI[["norm_mis_per_well"]]</pre>
# test for difference in mean entropy between treatmentA, treatmentB
ent <- data_dists[["ENT"]]</pre>
ent.WT <- mean(ent[[treatments[1]]])</pre>
ent.MUT <- mean(ent[[treatments[2]]])</pre>
ent.res <- wilcox.test(ent[[treatments[1]]], ent[[treatments[2]]])</pre>
cat("entropy means (WT / MUT) :", ent.WT, "/", ent.MUT, "\n")
print(ent.res)
# test for diff in mutual info btwn treatmentA, treatmentB
mi <- data_dists[["MI"]]</pre>
mi.WT <- mean(mi[[treatments[1]]])</pre>
mi.MUT <- mean(mi[[treatments[2]]])</pre>
mi.res <- wilcox.test(mi[[treatments[1]]], mi[[treatments[2]]])</pre>
cat("mutual info means (WT / MUT) :", mi.WT, "/", mi.MUT, "\n")
print(mi.res)
  plot(density(mi[[treatments[1]]]))
  lines(density(mi[[treatments[2]]]), col="red")
```

calculate_isis

Calculate inter spike intervals

Description

The function calculates all the interspikes interval between all spikes of each of the channels recorded.

Usage

```
calculate_isis(s)
```

Arguments

S

MEA data structure

Value

Returns the MEA data structure (S object in the example) with the following new lists:

S\$isis list of all isis for each channel
S\$mean_isis mean isis for each channel
S\$sd_isis sd of isis for each channel

Examples

```
data("S")
S <- calculate_isis(S)</pre>
```

calculate_network_bursts

Compute network bursts for a list of MEA recordings.

Description

For a list of MEA recordings, ususally from the same plate at different time point, This function detects and report network burst features at the well level.

Usage

```
calculate_network_bursts(s,sigmas, min_electrodes, local_region_min_nae)
```

Arguments

s A list of MEA recordings, typically from the same MEA plate at different time

point.

sigmas The window size used to generate network bursts.

min_electrodes Minimum number of electrodes to call a network burst

local_region_min_nae

Indicates if an adaptive threthold method should be used.

Value

Returns an object containing summary, nb_all, nb_features, result, and nb_features_merged.

summary brief summary

nb_all Each well has 3 data frames with nb times, one for each smoothing window

nb_features a list containing a data-frame for each DIV analyzed

result for each DIV analyzed, information on the DIV, times of nb for each well and

each smoothing window

nb_features_merged

data frame with nb related features averaged across DIVs

Author(s)

Quanli Wang

References

Add reference to Yi-Fan Lu's paper when it is in press.

calculate_network_spikes

Compute the netwrok spikes statistics from spike lists.

Description

Taken a spike list object for a set of electrodes, this function searches network spikes returns a list of all network spikes.

Usage

```
calculate_network_spikes(e, sur = 100,ns_n, ns_t)
```

Arguments

е	A spike list object for a set of electrodes.
sur	This parameter is related to the number of datapoints to be used in summmarizing mean network spikes, which will be only used for network spike diagnostics. The default value of 100 will usually be sufficient.
ns_t	global variable, time window of a network spike
ns_n	global variable, minimum number of coincident electrodes

Value

Returns a list of object, containing network spikes.

wells A list of wells that network spikes were found and defined.

ns_all A list of network spikes computed from the spike lists.

well_layout The plate/well layout identified by the function.

References

Need to find the paper describe this method.

```
calculate_spike_features
```

Filter spikes and bursts in recording objects

Description

Apply user defined filters on the spikes that were recorded and calculate spike features.

```
calculate_spike_features(r_object_files, parameters)
```

calc_burst_distributions 9

Arguments

```
r_object_files A list of recording Robject files
parameters A list of parameters, see data("parameters")
```

Value

Returns an 's' object containing all the spikes and bursts of all the loaded recording Robjects.

Author(s)

Diana Hall

```
calc_burst_distributions
```

calculate and plot burst featues distributions

Description

The function calculates normalized distributions of selected bursting features and plots distribution graphs of all treatments in a recording. The function also prints csv output in the /Analysis directory for downstream stats such as permutation test of treatment labels

Usage

```
calc_burst_distributions(s, min_vals = 1, xlimit = 25, bins_in_sec = 5,
feature = "non", filter_values_by_min = 0, min_values = 0, per_well = 0,
outputdir = tempdir(), min_electrodes = 4, time_stamp = "DATE_TIME")
```

Arguments

S	MEA data structure	
min_vals	minimum values number per electrode, electrodes with a smaller number of values than that are discarded	
xlimit	max limit of values, for example: xlimit = 25 for IBI analysis means that IBIs longer than 25 seconds will not be part of distribution calculations	
bins_in_sec	how many bins to cut each of the segments. For example: IBI analysis has 25 seconds as xlimit, to analyse in a 0.1 sec resolution bins_in_sec should be set to 10, for 1 sec resolution set bins_in_sec to 1	
feature	what feature to analyze, options are "ibi", "isi, "nspikes_in_burst", "duration", "spikes_density_in_burst"	
filter_values_by_min		
	should analysis dispaged values with lower than filter values by min number	

should analysis disregard values with lower then filter_values_by_min number of values? (0/1, default is 0). For example, if set to 1 for duration analysis, should analysis consider also bursts shorter than filter_values_by_min?

10 calc_burst_summary

min_values disregards values with lower then filter_values_by_min, only if filter_values_by_min

set to 1

per_well should distribution analysis be performed by testing treatment differences on

well level means (1) or electrode level means(0)

outputdir output directory

min_electrodes minimum electrodes for an active well

time_stamp time stamp for the output files

Details

Plot distributions calculates normalized distributions of bursting features. 'Normalized distribution' are a way to handle biases caused by noisy electrodes/wells. The function will calculate a normalized histogram (values 0-1) of each feature for each electrode. Next, it will average histogram values either per well and then average all wells per treatment, or directly per treatment. All comparisons between treatments will be then made by plotting the normalized histograms of each treatment and running a K-S test between them.

Note

Output is a made of: 1) Plots of all selected burst features distributions. 2) CSV files ending with _distributions.csv that harbor all electrodes per treatment for all the recordings loaded in the meaRtools pipeline for a specific MEA plate

Author(s)

Sahar Gelfman

Examples

calc_burst_summary

Calculate average and standard deviation of the bursting features.

Description

The function calculates a summary of all the bursting features and returns a data.frame with those values.

```
calc_burst_summary(s, bursty_threshold = 1)
```

calc_burst_summary 11

Arguments

s MEA data structure

bursty_threshold

min number of bursts/minute to count as a bursty unit.

Value

A data frame with the following columns:

channels electrode name

spikes #spikes

mean_freq firing rate (Hz)

nbursts #bursts detected

 $bursts_per_sec \ \#bursts/second.matrix(nrow=0,ncol=1)$

bursts_per_min #bursts/min

bursty is bursts_per_min >bursty_threshold (defaults to 1 burst/min)

mean_dur mean burst duration

sd_dur sd

mean_spikes mean #spikes in a burst

sd_spikes sd
per_spikes_in_burst

% of spikes in a burst

per_spikes_out_burst

% of spikes not in a burst

mean_si mean Surprise Index (only for poisson .surprise measure)

mean_isis mean ISI within a burst

sd_mean_isis sd

mean_ibis mean IBI

sd_ibis sd

cv_ibis Coefficient of variation of IBI (= mean_ibi/sd_ibi)

Examples

```
# Load exapmple of recording Robject (MEA data structure)
data("S")
S$bs<-calc_burst_summary(S)</pre>
```

Description

Creates a data frame with columns for well firing rate, mean electrode firing rate, well name and DIV. See details for computations.

Usage

```
compute_mean_firingrate_by_well(s)
```

Arguments

S

Well firing rate= total spikes per well/recording time.

Details

Well firing rate= total spikes per well/recording time. Electrode level firing rate= average across all electrodes in a well(total spikes on electrode/recording time)

Examples

```
data("S")
res<-compute_mean_firingrate_by_well(S)
res[1:4,]</pre>
```

```
{\tt compute\_mean\_sttc\_by\_well}
```

Compute the mean STTC averaged across all pairwise electrodes in well

Description

Compute the mean STTC averaged across all pairwise electrodes in well

```
compute_mean_sttc_by_well(s, dt = 0.05, beg = NULL, end = NULL)
```

compute_sttc_by_well

13

Arguments

S	structure storing the well information
dt	Time window for STTC (default = 0.05 seconds)
beg	Start time in seconds (defaults to start of recording)
end	End time in seconds (defaults to end of recording)

Details

For each pair of electrodes, we calculate the STTC. We then take the mean of these pairs, excluding autocorrelations. If a well has one (or no) electrodes, the value returned for that well is NULL.

Warning: taking the mean over a well is useful only if you do not suspect distance-dependent correlations in your firing. (For activity like retinal waves, we find that correlations are strongly dependent on the distance separating electrodes.)

Value

A vector giving the mean of all pairwise STTCs on each well.

Author(s)

Stephen Eglen

Description

Compute the STTC across all pairwise electrodes in well

Usage

```
compute_sttc_by_well(s, dt = 0.05, beg = NULL, end = NULL)
```

Arguments

S	structure storing the well information
dt	Time window for STTC (default = 0.05 seconds)
beg	Start time in seconds (defaults to start of recording)
end	End time in seconds (defaults to end of recording)

Details

For each pair of electrodes (excluding autocorrelations), we calculate the STTC. If a well has one (or no) electrodes, no STTCs are calculated for that well.

14 count_ns

Value

A data frame giving all pairwise STTCs (and distance separating electrodes) on each well.

Author(s)

Stephen Eglen

count_ns	Count number of spikes within evenly spaced time intervals(bins) from
	input spike trains.

Description

Given a list of spike trains, this function creates evenly spaced bins and returns number of spikes from all spike trains for each bins.

Usage

```
count_ns(spikes, beg, end, wid, nbins)
```

Arguments

sp1kes	The input list	of spike trains.
--------	----------------	------------------

beg Start time of recording in seconds.
end End time of recording in seconds.

wid Bin width in seconds.

nbins Number of evenly spaced bins for given time interval.

Value

Return a vector of counts of spikes from all spike trains for user-defined, evenly spaced bins.

Author(s)

Stephen Eglen

dist_perm 15

dist_perm	Burst distribution permutations	

Description

Perform two statistical tests to quantify difference between two burst probability distributions using burst probability distribution data. Performed test are the Maximum Distance between cumulative distributions and Earth Movers Distance between the original probability distributions.

Usage

```
dist_perm(datafile,np,type,kotype)
```

Arguments

datafile	A $_$ distributions.csv input file. Format as the output of calc $_$ burst $_$ distributions
np	Number of permutations to perform
type	Name of first genotype
kotype	Name of second genotype

Value

A list containing results of two statistical tests for the input probability distributions data.

data.EMD	Original value of EMD distance
data.EMD	Original value of maximum distance
perm.EMD	A permuted p.value of the EMD distance
perm_p	A permuted p.value of the maximum distance
outp	Maximum distances between genotypes for all permutations performed
out_emd	Maximum Earth Movers Distance between genotypes for all permutations performed
	Torrined
data.wt	Cumulative probabilities of the first genotype
data.ko	Cumulative probabilities of the second genotype
data.wt.Origina	1
	Probabilities distribution of the first genotype
data.ko.Origina	1
	Probabilities distribution of the second genotype

References

See https://redmine.igm.cumc.columbia.edu/projects/mea/wiki for further details

Examples

```
result <- dist_perm(distributionFilePath,10000,"WT","KO")</pre>
```

16 filter_wells

```
filter_nonactive_spikes
```

Filter nonactive spikes from recordings

Description

Given an input MEA recording, this function removes spike trains that are deemed as nonactive based on the number of spikes per minutes.

Usage

```
filter_nonactive_spikes(mea, spikes_per_minute_min = 1)
```

Arguments

```
mea The input MEA spikelist object.
```

spikes_per_minute_min

Minimum number of spikes per minute for a spike train to be considered as active.

Value

An MEA spikelist object with nonactive spike trains removed.

filter_wells

Filter wells

Description

Filter out wells for which the number of active electrodes is less than 4, at least 70 percent of the time

Usage

```
filter_wells(unfiltered_df, nae,min_electrodes = 4,
well_max_div_inactive_ratio = 0.5)
```

Arguments

unfiltered_df Dataframe generated by the spike_features() function

nae A dataframe containing the number of active electrodes for the recording

min_electrodes Minimum number of active electrode to consider a well for analysis

well_max_div_inactive_ratio

The DIV inactive/active well ratio below which a well will be considered active for a set of DIVs

frate_counts 17

Value

A dataframe identical in format to the input, except that wells that do not meet the filtering criteria are removed.

Examples

```
data("S")
data("parameters")
s<-list(); s[[1]]<-S
spike_features<-aggregate_features(s, feat_type="spike", parameters )
nae = spike_features$nae
  filtered.spike.features = lapply(spike_features, function(x) filter_wells(x, nae))</pre>
```

frate_counts

Estimate population firing rate using fixed-width time bins.

Description

Estimate the population firing rate, averaging over all spikes.

Usage

```
frate_counts(spikes, beg, end, wid, nbins)
```

Arguments

spikes	List of simultaneously recorded spike trains		
beg	Start of the recording, in seconds.		
end	The start time of the last bin, in seconds.		
wid	The duration of each bin		
nbins	The number of bins to generate.		

Details

We compute the array-wide average activity for a list of spike trains. The duration of the recording is given in seconds by BEG and END. Time is divided up into NBINS bins, each of duration WID. Each spike is then placed in the appropriate bin and then we return the average count in each bin.

Value

The population firing rate (in Hz) for each bin.

Author(s)

Stephen Eglen

18 generate_raster_plot

```
generate_raster_plot generate_raster_plot
```

Description

Creates a pdf raster plot of selected user selected well from an 's' object. Options include verticle lines showing network spike times, vertical bars showing bursts as well as # showing count of spikes in burst and network spikes.

Usage

Arguments

window_size

Sumeries	
r_object_file	Default value is NULL, in which case tcltk pop-up file chooser will prompt user to select an 's' object. Otherwise, provide a full path to to a .RData 's' object that contains burst and network data.
outputdir	A directory (character string in quotes) where pdf is to be saved. Default is NULL, in which case the plot will be saved in the directory r_object_file location.
well_for_raster	
	A well name, character string, from plate. e.g. well_for_raster="A3". Default is NULL, in which case first well in plate will appear in plot.
interval_for_ra	aster
	A vector of min and max time (s) for raster marks. e.g. interval_for_raster=c(30,60) Default is NULL, in which case the whole recording interval will be used.
show_bursts	A boolean value sets whether bursts are indicated by red horizontal line (TRUE/FALSE) e.g. show_bursts=FALSE Default=FALSE
show_burst_numb	per
	A boolean value sets whether # spikes/bursts are indicated (TRUE/FALSE). show_bursts must be set to true in order that show_burst_number=T e.g. show_burst_number=FALSE Default=FALSE
show_networkspi	
	A boolean value sets whether network spikes are indicated by green vertical line (TRUE/FALSE) e.g. show_networkspikes=FALSE Default=FALSE
show_ns_number	A boolean value sets whether # electrodes in network spikes are indicated (TRUE/FALSE) e.g. show_ns_number=FALSE Default=FALSE
show_nb	A boolean value sets whether network bursts should be indicated in raster by or-

ange horizontal lines (TRUE/FALSE) e.g. show_ns_number=FALSE Default=FALSE

R-object should be used in network burst identification e.g. show_ns_number=10Default=NULL

A numeric value indicating which of the three smoothing sizes available in the

get_burst_info

Value

A pdf raster plot will be displayed in system viewer.

Author(s)

Diana Hall

Examples

get_burst_info

get burst feature information

Description

The function returns a list of values of a burst feature for a desired channel

Usage

```
get_burst_info(allb, index)
```

Arguments

allb The bursting features matrix of a channel (located in recording object - S object

in example: S\$allb[[channel number]]

index Name of the requested burting feature. Can be "beg", "end", "ibi", "len", "durn",

"mean_isis" or "si"".

Value

List of values of the requested feature (index) for the desired channel.

Examples

```
data("S")
S$allb[[1]]
```

get_data

get_data

Description

pop up file chooser with caption. Also, sets directory of analysis output.

Usage

```
get_data(caption = "")
```

Arguments

caption

text to display in pop-up file chooser to prompt user to select appropriate file. Default is no caption.

Value

Creates 2 directories:

'Analysis' directory in the parent directory of user selected file.

'R_objects' a subdirectory of 'Analysis'

Examples

```
get_data(caption="Please select a spike-list file for analysis")
```

Description

Extract data from experimental log file: a csv file with columns for well, treatment, dose, size and units.

```
get_experimental_log_file(file, master_chem_file = master_chem_file)
```

Arguments

file

spike-list csv file, one of the possible plate recording file formats available from Axion. Format: one spike and corresponding electrode name per row. See Axion biosystems website for details.

```
master_chem_file
```

A csv file containing the following columns: "Project", "Experiment.Date", "Plate.SN", "DIV", "Well", "Treatment", "Size", "Dose", and "Units". Empty wells must still be represented in file. If column is irrelavent to a given data set, then 'NA' or blank is sufficient. "Project" column must match the first character string preceding "_" in spike-list file name. e.g. exampleRecording_1012016_plate1_DIV1_spike_list.csv". Similarly, "Experiment.Data" and "Plate.SN" must match second and third character strings as separated by "_" in spike-list file name. "DIV" column does not need to be matched.

Value

list containing character vector of experimental log information.

well name e.g. "A4""

treatment on well e.g. 'WT'

size size information of chemical treatment

dose information for treatment

units units of dosage e.g. uL/g

References

See http://www.axionbiosystems.com/products/software/ for details on spike-list csv file format

Examples

get_num_ae

get_file_basename

get_file_basename

Description

Retreives the first 4 character strings separated by '_' from from a file path to a .RData object.

Usage

```
get_file_basename(filename)
```

Arguments

filename

a file name or full file path. filename must have file extension '.RData'.

Details

filename must have file extension '.RData'.

Value

Returns the first 4 character strings separated by '_' from from a file path to a .RData object.

Author(s)

Diana Hall

Examples

```
data("S") # load data
get_file_basename(S$file)
```

get_num_ae

get_num_ae

Description

Adds a field to a 's' spike object 'nae' that lists for each well the # of active electrodes (electodes firing > 5spike/minute).

```
get_num_ae(s2)
```

get_plateinfo 23

Arguments

s2

an 's' object containing spike trains, channel names, etc.

Value

returns 'nae' field in 's' which is a vector of # of active electrodes (electodes firing > 5 spikes/minute). Each vector entry is named by the well to which the data corresponds.

Author(s)

Diana Hall

Examples

```
data("S") # load data
b<-get_num_ae(S)
b$nae</pre>
```

get_plateinfo

Return information about an MEA plate format

Description

Return information about an MEA plate format

Usage

```
get_plateinfo(arrayname)
```

Arguments

arrayname

Plate name

Details

Given a plate name, return a list of information. If the plate name is not recognised, an error is generated.

Value

A list storing information about that plate.

Author(s)

Stephen Eglen

24 get_wt

Description

returns the first portion of file .RData spike object named according to convention of Project name, experiment date (MMDDYYYY format) and plate serial number separated by a '_' as in "exampleRecording_1012016_plate1_DIV1_spike_list.csv" in data package directory.

Usage

```
get_project_plate_name(file)
```

Arguments

file

a full file path or file name

Value

Returns a character string of the project name, experiment date and plate serial number in a .RData file path. see example.

Examples

```
data("S") # load data
get_project_plate_name(S$file)
```

get_wt

Get WT

Description

Extracts all treatments/genotypes and allows user to choose single treatment as wild type/reference for downstream analyses

Usage

```
get_wt(s)
```

Arguments

S

MEA dataframe structure

Value

A string corresponding to the user's choice

has_network_spikes 25

Examples

```
data("S")
s<-list()
s[[1]]<-S
wt <- get_wt(s)</pre>
```

has_network_spikes

A utility function to check if network spikes are detected.

Description

For an returned object from calcualte.network.spikes, this function provides a utility checking if it contains any network spikes from any well.

Usage

```
has_network_spikes(nspikes)
```

Arguments

nspikes

The network spike object returned by calling calcualte.network.spikes.

Value

Return a boolean value indicating if any network spikes are found from the network spikes object.

isi *isi*

Description

calculates the isi (inter-spike interval) (s) between sucessive spikes in a input spike train.

Usage

```
isi(train)
```

Arguments

train

spike train: a set of non-decreasing timestamps (s)

Value

a vector of isis: first entry is ISI between first & second spike in input spike train and so forth. Total length is 1 less than input spike train.

26 mi_find_bursts

Author(s)

Diana Hall

Examples

```
data("S") # load data
b<-isi(S$spikes[[1]])
S$spikes[[1]][1:4]
b[1:3]</pre>
```

load_spikelist

Load Robject File

Description

Loads a previously saved Rdata file of a recording.

Usage

```
load_spikelist(spk_data_file)
```

Arguments

spk_data_file MEA recording Rdata file

Value

loaded R object

 ${\tt mi_find_bursts}$

Find bursts

Description

For one spike train, find the bursts using the maximum interval method.

```
mi_find_bursts(spikes,mi_par)
```

Arguments

spikes A spike train of one channel, located in MEA data structure (example S\$spikes[[1]]).

mi_par A list of burst features:

beg_isi Beginning inter spike intervalend_isi Ending inter spike interval

min_ibi Minimum inter burst interval to combine burstsmin_durn Minimum duration to consider as burstmin_spikes Minimum spikes to consider as burst

Value

Returns a matrix of burst information for a specific channel. Matrix columns are:

beg the number of spike that is first in the burst
end number of the last spike in the burst
ibi time interval from previous burst
durn durarion of burst in seconds

mean_isis average inter spike interval within the burst si surprise index, allways 1 for mi algorithm

Author(s)

Stephen Eglen

References

Eytan and Marom (2006) J Neuroscience.

Examples

```
data("S")
allb <- lapply(S$spikes, mi_find_bursts, S$parameters$mi_par )</pre>
```

```
nb_matrix_to_feature_dfs
```

Convert network burst data matrix to a list of data frames.

Description

Convert network burst data matrix to a list of dataframes. Each dataframe has rows representing wells while columns representing different timepoints(DIVs). The dataframe format alllows well level permutaiton based tests to be done much easier.

28 parameters

Usage

```
nb_matrix_to_feature_dfs(matrix_and_feature_names)
```

Arguments

matrix_and_feature_names

The data matrix return by calling function calculate_network_bursts.

Value

Returns a list of dataframes, ith each representing a feature matrix, with rows for wells and columns for different timepoints(DIVs).

Author(s)

Quanli Wang

See Also

calculate_network_bursts

parameters

A list of parameters with default values that user can customize.

Description

A list of parameters with default values that user can customize.

Usage

```
data("parameters")
```

Format

The format is: List of 20 \$ spike.csv : logi TRUE \$ spike.plot : logi TRUE \$ burst.csv : logi TRUE \$ ns.csv : logi TRUE \$ burst_type : chr "mi" \$ s_min : num 5 \$ ns.csv : logi TRUE \$ ns.plot : logi TRUE \$ elec_min_rate : num 0.0167 \$ elec_max_rate : num 1000 \$ well_min_rate : num 0 \$ mi_par :List of 5 ..\$ beg_isi : num 0.1 ..\$ end_isi : num 0.25 ..\$ min_ibi : num 0.8 ..\$ min_durn : num 0.05 ..\$ min_spikes: num 5 \$ ns_t : num 0.01 \$ ns_n : num 3 \$ sur : num 100 \$ burst_distribution_ibi :List of 7 ..\$ perform : num 1 ..\$ min_cases : num 15 ..\$ x_axis_lim : num 20 ..\$ bins_in_sec : num 5 ..\$ min_values : num 0 ..\$ filter_by_min: num 0 ..\$ per_well : num 0 \$ burst_distribution_durn :List of 7 ..\$ perform : num 1 ..\$ min_cases : num 15 ..\$ x_axis_lim : num 18 ..\$ bins_in_sec : num 10 ..\$ min_values : num 0 ..\$ filter_by_min: num 0 ..\$ per_well : num 0 \$ burst_distribution_isi :List of 7 ..\$ perform : num 1 ..\$ min_cases : num 15 ..\$ x_axis_lim : num 0.5 ..\$ bins_in_sec : num 100 ..\$ min_values : num 0 ..\$ filter_by_min: num 0 ..\$ per_well : num 0 \$ burst_distribution_nspikes :List of 7 ..\$ perform : num 1 ..\$ min_cases : num 5 ..\$ x_axis_lim : num 0 \$ burst_distribution_nspikes :List of 7 ..\$ perform : num 0 ..\$ filter_by_min: num 0 ..\$ per_well : num 0 \$ burst_distribution_spikes :List of 7 ..\$ perform : num 1 ..\$ min_cases : num 5 ..\$ x_axis_lim : num 0 ..\$ bins_in_sec : num 1 ..\$ min_values : num 0 ..\$ filter_by_min: num 0 ..\$ per_well : num 0 \$ burst_distribution_spike_freq:List of 7 ..\$ perform : num 1 ..\$ min_cases : num 1 ..\$ min_cases : num 15 ..\$

```
x_axis_lim: num 300 ..$ bins_in_sec: num 1 ..$ min_values: num 0 ..$ filter_by_min: num 0 ..$ per_well: num 0
```

Examples

```
data(parameters)
```

```
\begin{tabular}{ll} {\tt permute\_features\_and\_plot} \\ {\tt \it Write\ PDF} \end{tabular}
```

Description

Generates a PDF containing plots and p-values for each feature. P-values are generating using Mann Whitney and permutation tests. This function requires that you create a list of dataframes for a given feature type (e.g. spikes) using the aggregate.data() function

Usage

```
permute_features_and_plot(s, wt, np, features_list, type, output_dir)
```

Arguments

MEA	data	structure
	MEA	MEA data

wt The treatment that will act as the wildtype/reference for the Mann Whitney and

Permutation tests

np Number of permutations to be performed

features_list A list of dataframes containing data for a given feature

type Type of features contained in features_list (e.g. spikes, ns, or bursts)

output_dir Directory where output files will be generated

Value

A PDF file containing the plots and p-values.

Author(s)

Ryan Dhindsa

Examples

```
data("S")
spike_features<-aggregate_features(S, feat_type="spike" )
wt <- "untreated"
output_dir = tempdir()
   print(paste0("Creating output folders under ",output_dir))
permute_features_and_plot(S, wt, np, spike_features, "spikes", output_dir)</pre>
```

30 plot.sttcp

plateinfo

MEA plate information

Description

MEA plate information

Usage

plateinfo

Format

An object of class list of length 2.

plot.sttcp

Plot the STTCP

Description

Plot the STTCP

Usage

```
## S3 method for class 'sttcp' plot(x, ...)
```

Arguments

x A list containing the sttc

... Other arguments to pass to the plot function

Details

Plot the STTCP.

Value

nothing.

Author(s)

Stephen Eglen

Description

Plots related to network spike for each well with network spikes in format of users choosing.

Usage

```
plot_active_wells_network_spikes(nspikes)
```

Arguments

nspikes

list of attributes related to network spikes: wells, plate layout and network spike information for each well. See calculate_network_spikes for further details.

Value

returns a multi-page plot.

See Also

```
calculate_network_spikes xyplot_network_spikes
```

Examples

```
data("S")
data('parameters')
nspikes <- calculate_network_spikes( S, parameters$sur ,parameters$ns_n, parameters$ns_t )

pdf(file=NSPlotPath)
    xyplot.network.spikes(nspikes)
    plot_active_wells_network_spikes(nspikes)
    dev.off()</pre>
```

Description

Displays average firing rate by well and by electrode for each DIV available.

Usage

```
plot_mean_firingrate_by_eletrode_by_div(s)
```

Arguments

S

's' object. must be a list, with each DIV a different entry.

Examples

```
data("S")
s<-list()
s[[1]]<-S

plot_mean_firingrate_by_eletrode_by_div(s)</pre>
```

Description

Displays average firing rate by well for each DIV available. First plot well rate in average Hz/electrode and second plot is Hz/total spikes well.

Usage

```
plot_mean_firingrate_by_well_by_div(s)
```

Arguments

s

's' object. must be a list, with each DIV a different entry.

Value

Plot is output, location and path to plot may be controlled by R's plotting apparatus e.g. 'pdf()'

Author(s)

Diana Hall

plot_network_spikes 33

Examples

```
data("S")
s<-list()
s[[1]]<-S

plot_mean_firingrate_by_well_by_div(s)</pre>
```

plot_network_spikes

Generic method for plotting network spikes.

Description

The generic plotting function for network spikes.

Usage

```
plot_network_spikes(ns, ...)
```

Arguments

ns The network spike object returned after running calculate_network_spikes.

... Additional plotting options that is general to plot functions.

Value

None. network spikes related plots will be generated in current plotting device.

Description

Plots all bursting features in a _burst_plot.pdf under the output directory.

Usage

```
plot_plate_summary_for_bursts(s, outputdir,parameters)
```

Arguments

s MEA data structure outputdir Output directory

parameters meaRtools basic parameter list

Details

The plot function will plot all the features calculated for the bursts in the recording. Those include: Mean Firing Rate by Plate (Hz), Mean firing rate, Mean Duration, Number of bursts by channel and well, Mean Inter Burst Interval, Mean ISI within bursts, Mean burst per minute, Mean spikes in a burst and % spikes in a burst. The function also calls calc_burst_distributions to calculate and plot burst feature distributions.

Value

A _burst_plot.pdf is printed under the output directory

Examples

```
data("S")
plot_plate_summary_for_bursts(S,"/Analysis")
```

Description

Diana needs to add document here.

Usage

```
plot_plate_summary_for_spikes(s, outputdir)
```

Arguments

```
s 's' .RData object. Each DIV must constitute one entry in list. outputdir directory path where plot will be saved to.
```

Value

Multiple page plot in pdf format containing data on which electrodes have recorded any spikes, ISI (inter-spike interval) histogram by plate and by well by electrode, log ISI histogram by plate and by electrode, average electrode firing rate by well, & binned electrode firing rate over recording duration.

Author(s)

Diana Hall

publications 35

Examples

```
data("S")
s<-list()
s[[1]]<-S

plot_plate_summary_for_spikes(s, outputdir="/Desktop")</pre>
```

publications

Show list of publications that have used this package

Description

Show list of publications that have used this package

Usage

```
publications()
```

Details

Simple wrapper function to show the publications.md file, documenting papers that have used previous versions of this package. In RStudio, the file will appear in its own window; otherwise it will appear in a pager run within the R session

Author(s)

Stephen Eglen

read_spikelist

Axion convert spk_list to r_object

Description

Converts the Axion spk_list file to a Rdata object and initializes it with all spike and plate info

```
read_spikelist(key, spk_list_file, chem_info ,r_object_dir)
```

36 read_spikelist_text

Arguments

key base name of spk_list file

spk_list_file The full spk_list file name (including path)

chem_info plate layout information list as loaded using function chem_info_2

r_object_dir Directory of r_object files

Value

save_file Full path of the saved r_object data file

See Also

chem.info.2

Examples

Description

Construct an MEA object by importing from text files.

```
read_spikelist_text(spike_text_file, channel_text_file, chem_info, array,
  div = NULL)
```

read_spikelist_text 37

Arguments

Details

This function can be used to read in spike times from text files.

Value

S the MEA object

Author(s)

Stephen Eglen

```
demas_platelayout = list(n_well = 6,
                        wells = paste0("w", 1:6),
                        n_{well_r} = 2,
                        n_{well_c} = 3,
                        layout = c(3, 2),
                        n_elec_r = 8,
                        n_elec_c = 8,
                        xlim = c(-100, 7200),
                        ylim = c(0, 6000),
                        spacing = 200,
                        corr_breaks = 0
add_plateinfo("demas-6well", demas_platelayout)
times = system.file("extdata/textreader/demas.times", package="meaRtools")
pos = system.file("extdata/textreader/demas.pos", package="meaRtools")
s = read_spikelist_text(times, pos, array="demas-6well")
meaRtools:::.plot_mealayout(s$layout, use_names = TRUE, cex=0.3)
```

38 remove_spikes

remove_spikes

remove_spikes

Description

removes all spikes and associated meta data from 's' spike object except those specified by 'ids'.

Usage

```
remove_spikes(s, ids)
```

Arguments

s

's' list object, needs to contain a 'spikes' field with spike train

ids

Name or index of channel(s) to be kept, all other channels removed. either name of channel, e.g. "E5_12" or an vector of idices c(1,2) corresponding to channel index. If a negative index is given, then that channel and associated data will be removed.

Value

's' object.

See Also

construct.s

```
data("S") # load data
r<-remove_spikes(S, c(-1, -2))

$$channels[1:2] # original 's' object first 2 channels
r$channels[1:2] # first 2 channels have been removed

$$NCells # original count of channels
r$NCells # count of channels after 2 channels removed

$$nspikes # original spike count of first 2 channels
r$nspikes # spike count of first 2 channels after 2 channels removed

# OR keep only first 2 channels
t<-remove_spikes(S, c(1, 2))
t$channels</pre>
```

run_TMcpp 39

run_TMcpp

Compute STCC direct in Cpp

Description

```
run the STTC code for a spike train (Cpp version)
```

Usage

```
run_TMcpp(dt, start, end, spike_times_1, spike_times_2)
```

Arguments

dt bin width for

start start time in seconds end end time in seconds

spike_times_1 spike train 1
spike_times_2 spike train 2

Details

Internal computation

Value

STTC value

Author(s)

Stephen Eglen

S

example 'S' object

Description

An example 'S' list object containing multiple fields describing 1 minute recording on a 48 well plate.

Usage

```
data("S")
```

40

Format

```
channels electrode names
spikes a list of spike trains for each channel
nspikes # spikes for each channel
NCells total # electrodes
meanfiringrate mean firing rate by channel
file full path of file
layout electrodes grid positions for all electrodes on plate
rates list with average count and firing per time_interval (s) as well as plate average
rec_time 2 element vector of first and last spike time of recording
goodwells well names for all wells meeting minimum firing criteria
treatment treatments for each well
size chemical compound size for each treatment
units units of dose of treatment
dose dose of treatment
well well names
nae # active electrodes (firing>5spikes/min)
cw wells that each channel belongs to
parameters A list of parameters, see data("parameters")
allb for each electrode, a matrix of burst related information
bs burst summary, a data frame containing burst endpoints by electrode
ns_all for each well, a list of network spike information
isis list of inter-spike interval (isi) (s) by channel
mean_isis list of average isi by channel
sd_isis list of standard deviation of isi by channel
well_stats data frame containing well level firing rate information
```

Details

Created by use of functions available in package.

```
data('S')
names(S)
```

si_find_bursts 41

rsts

Description

For one spike train, find the bursts using the Poisson surprise method.

Usage

```
si_find_bursts(spikes,s_min,burst_isi_max)
```

Arguments

spikes A spike train of one channel, located in MEA data structure (example S\$spikes[[1]]).

s_min A minimum value for the surprise index

Value

Returns a matrix of burst information for a specific channel. Matrix columns are:

beg the number of spike that is first in the burst
end number of the last spike in the burst
ibi time interval from previous burst
durn durarion of burst in seconds
mean_isis average inter spike interval within the burst

si surprise index

Author(s)

Stephen Eglen

References

Eytan and Marom (2006) J Neuroscience.

```
data("S")
allb <- lapply(S$spikes, si_find_bursts, S$parameters$s_min )</pre>
```

42 sttc

sttc

Compute STTC for a pair of spike trains

Description

Compute STTC for a pair of spike trains

Usage

```
sttc(a, b, dt = 0.05, rec_time = NULL)
```

Arguments

a	first spike train
b	second spike train
dt	bin size in seconds
rec_time	2-element vector: start and end time

Details

The Spike Time Tiling correlation (STTC) is computed for a pair of spike trains. The method is defined in Cutts and Eglen (2014). We assume that the spike trains are ordered, smallest-time first.

Value

STTC a scalar bounded between -1 and +1.

Author(s)

Stephen J Eglen

```
a = c(1, 2, 3, 4, 5)
b = a+0.01
c = a+0.5
sttc(a, b)==1
sttc(a, c)==0
```

sttcp 43

Description

Compute STTC profile for a pair of spike trains

Usage

```
sttcp(a, b, dt = 0.05, tau_max = 5, tau_step = 0.1, beg = NULL,
end = NULL)
```

Arguments

а	spike train 1
b	spike train 2
dt	time window for STTC
tau_max	maximum time shift
tau_step	step size in tau
beg	start of recording. When NULL use the minimum spike time from the two trains.
end	end of recording. When NULL use the maximum spike time from the two trains.

Details

We extend the STTC to a profile (or correlogram) by shifting one spike train by amount tau, where tau varies in [-tau_max, +tau_max] in steps of tau_step.

Value

List containing the STTC profile.

Author(s)

Stephen Eglen

```
t1 <- -cumsum(log(runif(1000)) / 2)
t2 <- -cumsum(log(runif(1000)) / 2)
corr <- sttcp(t1, t2)
plot(corr, main="cross correlation")
autocorr <- sttcp(t1, t1)
plot(autocorr, main="auto correlation")</pre>
```

sttc_allspikes1

sttcp_ab

Compute STTC profile for two spike trains

Description

Compute STTC profile for two spike trains

Usage

```
sttcp_ab(a, b, start, end, dt, tau_sep, tau_max)
```

Arguments

a	Spike train 1
b	Spike train 2
start	Start time
end	End time

dt coincidence window for STTC

tau_sep step size for tau in [-tau_max, +tau_max]

tau_max maximum tau value

Details

Compute the STTC profile for two spike trains using C++.

Value

obj An object of type "sttcp", containing the tau values and correlations.

Author(s)

Stephen Eglen

sttc_allspikes1

Compute STTC for all pairs of spike trains

Description

Compute STTC for all unique pairs of spike trains

Usage

```
sttc_allspikes1(spikes, dt, beg, end)
```

Arguments

spikes List of spike trains dt tiling window beg start time end end time

Details

Return a matrix of all STTC values

Value

Matrix of STTC values. Upper diagonal matrix only; diagonal elements should be 1.

Author(s)

Stephen Eglen

summarize_network_spikes

Generate network spikes based features.

Description

This function takes the returned object from calcualte.network.spikes function and parse and filter them using customed filters to regenerate features used by IGM MEA projects.

Usage

```
summarize_network_spikes(e, nspikes, ns_e, sur)
```

Arguments

e A spike list object for a set of electrodes.

nspikes The spike list object returned from calling calculate_network_spikes.

ns_e Minumum number of spikes for each electrode within the network spike win-

dow. Most IGM MEA projects use a value of 2.

sur This parameter is related to the number of datapoints to be used in summmariz-

ing mean network spikes, which will be only used for network spike diagnostics.

The default value of 100 will usually be sufficient.

Value

Returns a new spikes object with filtered and re-calcualted features.

Author(s)

Quanli Wang

tiling_correlogramcpp Compute all STTPs for a set of spike trains

Description

Compute all STTPs for a set of spike trains

Usage

```
tiling_correlogramcpp(spikes, n, nspikes, first_spike, start, end, dt, tau_sep,
   tau_max)
```

Arguments

spikes Concatenated list of spike trains

n number of spike trains

nspikes Vector containing the number of spikes in each train

first_spike Index to the first spike in each train.

start Start time of recording in seconds

end End time of recording in seconds

dt Coincidence window for STTC

tau_sep Step size for taus.

tau_max Maximum absolute tau value.

Details

This computes all pairwise STTPs for spike trains. (This may be of use for Tom's internal code, rather than for production use.)

Value

Pairwise STTPs for all spike trains

Author(s)

Tom Edinburgh

tiling_correlogramcpp_index

Compute STTPs for just two spike trains, A and B

Description

Compute STTP for just one pair of trains

Usage

```
tiling_correlogramcpp_index(spikes, n, nspikes, first_spike, start, end, dt,
  tau_sep, tau_max, a, b)
```

Arguments

trains
tı

n number of spike trains

nspikes Vector containing the number of spikes in each train

first_spike Index to the first spike in each train.

start Start time of recording in seconds

end End time of recording in seconds

dt Coincidence window for STTC

tau_sep Step size for taus.

tau_max Maximum absolute tau value.
a Number of first spike train
b Number of second spike train

Details

If you have the spikes from an array in a flattened form, you can compute the STTP for just two of the spike trains, rather than computing all pairwise STTPs.

Value

STTP for spike trains a and b

Author(s)

Tom Edinburgh

```
write_features_to_files
```

Write feature data to an output file

Description

Takes in list of dataframes (one per feature) from an MEA data structure that is produced by aggregate_features and writes output to Files. Each dataframe corresponds to one feature, containing values for each well across each DIV of recording

Usage

```
write_features_to_files(s, features_list, output_dir, type)
```

Arguments

```
s MEA data structure
```

features_list list of dataframes, one for each feature.

output_dir Output directory)

type Type of features (e.g. "spikes", "ns", "bursts")

Value

Write one csv per feature for the feature type requested.

Examples

```
data("S")
s<-list()
s[[1]]<-S
spike_features = aggregate_features(s, "spike")

write_features_to_files(s, spike_features, analysis$output_dir, "spikes")</pre>
```

```
write_network_spikes_to_csv
```

Summarize and write netowrk spikes features into a csv file.

Description

Summarize and write netowrk spikes features into a csv file.

Usage

```
write_network_spikes_to_csv(s, nspikes, outputdir)
```

Arguments

s A list of MEA recordings, typically from the same MEA plate at different time

point.

nspikes The spike list object returned from calling calculate_network_spikes.

outputdir The user defined output directory while the cvs file to be writen. There should

not have a file sperator at the end of the outputdir.

Value

None.

 $write_plate_summary_for_bursts$

Prints bursting features

Description

The function reads the MEA data structure and uses the 'allb' list built using mi_find_bursts. It then prints all bursting features summary per well and per channel in _bursts.csv and _well_bursts.csv

Usage

```
write_plate_summary_for_bursts(s, outputdir)
```

Arguments

s MEA data structure outputdir Output directory

Value

Output file _bursts.csv holds all features generated for bursts per well and per channel:

treatment the treatment/genotype based on the experimental log file plan

well number

nae number of active electrodes

nAB number of electrodes with bursts

duration total duration of bursts mean_dur mean duration of bursts

mean_freq firing rate (Hz)
nbursts number of bursts

bursts_per_sec bursts/second.matrix(nrow=0,ncol=1)

bursts_per_min bursts/min

```
sd of burst duration
sd_dur
mean_freq_in_burst
                  average frequency of spikes in a burst
sd_freq_in_burst
                  sd of frequency of spikes in a burst
mean_spikes_in_burst
                  mean number of spikes in a burst
sd_spikes_in_burst
                  sd of number of spikes in a burst
total_spikes_in_burst
                  total number of spikes in a bursts
per_spikes_in_burst
                  percent of spikes in a burst
                  mean ISI within a burst
mean_isis
                  sd ISI within a burst
sd_isis
mean_ibis
                  mean IBI
sd_ibis
                  sd of ibis
                  Coefficient of variation of IBI (= mean_ibi/sd_ibi)
cv_ibis
file
                  input recording file
```

Examples

```
data("S")
output_dir = file.path(tempdir(),"Analysis")
print(paste0("Creating output folders under ",output_dir))
dir.create(output_dir)

s<-list(); s[[1]]<-S
write_plate_summary_for_bursts(s, output_dir)</pre>
```

Description

Produces csv output related to firing rate by DIV to directory of user specified output directory

Usage

```
write_plate_summary_for_spikes(s, outputdir)
```

Arguments

```
s 's' spike .RData object. Must be a list with one entry per DIV. outputdir
```

Value

One .csv file for each DIV is output and one additional file comprising all DIVs. Quantification of activity levels including total spike count, well and electrode level firing rate, as well as ISI and standard deviation of applicable features.

Author(s)

Diana Hall

Examples

```
data("S")
s<-list()
s[[1]]<-S

path<-tempdir()
write_plate_summary_for_spikes(s , path)</pre>
```

xyplot_network_spikes xyplot for network spikes at the plate level.

Description

xyplot for network spikes at the plate level. It will detech the plate layout and plot individual wells according to plate layout.

Usage

```
xyplot_network_spikes(nspikes)
```

Arguments

nspikes

The returned obect from calling summary.network.spikes.

Value

Return the handle of xyplot.

Author(s)

Quanli Wang

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