

Package ‘mx FDA’

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Title A Functional Data Analysis Package for Spatial Single Cell Data

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Description Methods and tools for deriving spatial summary functions from single-cell imaging data and performing functional data analyses. Functions can be applied to other single-cell technologies such as spatial transcriptomics. Functional regression and functional principal component analysis methods are in the 'refund' package <<https://cran.r-project.org/package=refund>> while calculation of the spatial summary functions are from the 'spatstat' package <<https://spatstat.org/>>.

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URL <https://github.com/julia-wrobel/mxfda/>,
<http://juliawrobel.com/mxfda/>

BugReports <https://github.com/julia-wrobel/mxfda/issues/>

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add_summary_function *Add Summary Function*

Description

Sometimes other ways of calculating summary functions is wanted and is done in other packages, in this instance the data can be loaded into the mxFDA object.

Usage

```
add_summary_function(mxFDAobject, summary_function_data, metric)
```

Arguments

mxFDAobject object of class mxFDA
 summary_function_data
 data frame with summary_key from mxFDA object as key column for summary
 function
 metric character vector with either 'uni' or 'bi' and 'k', 'l', or 'g'; e.g. 'uni g'

Value

an updated mxFDA object with a derived value added. See [make_mxfda\(\)](#) for more details.

Author(s)

Alex Soupir <alex.soupir@moffitt.org>

 bivariate

bivariate

Description

Internal function called by `extract_summary_functions` to calculate a bivariate spatial summary function for a single image.

Usage

```

bivariate(
  mximg,
  markvar,
  mark1,
  mark2,
  r_vec,
  func = c(Kcross, Lcross, Gcross, entropy),
  edge_correction,
  breaks = NULL
)

```

Arguments

mximg Dataframe of cell-level multiplex imaging data for a single image. Should have
 variables x and y to denote x and y spatial locations of each cell.
 markvar The name of the variable that denotes cell type(s) of interest. Character.
 mark1 Character string that denotes first cell type of interest.
 mark2 Character string that denotes second cell type of interest.
 r_vec Numeric vector of radii over which to evaluate spatial summary functions. Must
 begin at 0.

func	Spatial summary function to calculate. Options are c(Kcross, Lcross, Gcross) which denote Ripley's K, Besag's L, and nearest neighbor G function, respectively, or entropy from Vu et al, 2023.
edge_correction	Character string that denotes the edge correction method for spatial summary function. For Kcross and Lcross choose one of c("border", "isotropic", "Ripley", "translate", "none"). For Gcross choose one of c("rs", "km", "han")
breaks	an integer for the number of breaks used for entropy

Details**[Stable]****Value**

A data.frame containing:

r	the radius of values over which the spatial summary function is evaluated
sumfun	the values of the spatial summary function
csr	the values of the spatial summary function under complete spatial randomness
fundiff	sumfun - csr, positive values indicate clustering and negative values repulsion

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

References

Xiao, L., Ruppert, D., Zipunnikov, V., and Crainiceanu, C. (2016). Fast covariance estimation for high-dimensional functional data. *Statistics and Computing*, 26, 409-421. DOI: 10.1007/s11222-014-9485-x.

Vu, T., Seal, S., Ghosh, T., Ahmadian, M., Wrobel, J., & Ghosh, D. (2023). FunSpace: A functional and spatial analytic approach to cell imaging data using entropy measures. *PLOS Computational Biology*, 19(9), e1011490.

entropy

*Entropy***Description**

Entropy

Usage

entropy(X, i, j, r_vec, correction)

Arguments

X	object of class ppp from spatstat with 2 marks
i	ignored
j	ignored
r_vec	vector of length wanted for breaks (will be rescaled) with max value at max for measuring entropy
correction	ignored

Details**[Experimental]****Value**

data frame with entropy calculated for `length(r_vec)` bins within 0 to `max(r_vec)`

Author(s)

Thao Vu <thao.3.vu@cuanschutz.edu>
Alex Soupir <alex.soupir@moffitt.org>

References

Vu, T., Seal, S., Ghosh, T., Ahmadian, M., Wrobel, J., & Ghosh, D. (2023). FunSpace: A functional and spatial analytic approach to cell imaging data using entropy measures. *PLOS Computational Biology*, 19(9), e1011490.

Altieri, L., Cocchi, D., & Roli, G. (2018). A new approach to spatial entropy measures. *Environmental and ecological statistics*, 25, 95-110.

extract_fpca_object *Extract FPCA object*

Description

Function that extracts the FPCA object created either by `run_fpca()` or `run_mfpca()` from the `mxFDA` object

Usage

```
extract_fpca_object(mxFDAobject, what)
```

Arguments

mxFDAobject	object of class mxFDA
what	what functional PCA data to extract, e.g. 'uni k'

Details

[Stable]

Output object can be visualized with `refund.shiny::plot_shiny()`

Value

fpca object created with `run_fcm()`

Author(s)

Alex Soupir <alex.soupir@moffitt.org>

Examples

```
#load ovarian mxFDA object
data('ovarian_FDA')

#run the FPCA
ovarian_FDA = run_fpca(ovarian_FDA, metric = "uni g", r = "r", value = "fundiff",
                      lightweight = TRUE,
                      pve = .99)

#extract the fpca object
obj = extract_fpca_object(ovarian_FDA, "uni g fpca")
```

extract_fpca_scores *Extract FPCA scores*

Description

Extract FPCA scores

Usage

```
extract_fpca_scores(mxFDAobject, what)
```

Arguments

mxFDAobject	object of class mxFDA
what	what functional PCA data to extract, e.g. 'uni k'

Details

[Stable]

Value

fpca object

Author(s)

Alex Soupir <alex.soupir@moffitt.org>

Examples

```
#load ovarian mxFDA object
data('ovarian_FDA')

#run ghe lfc model
ovarian_FDA = run_fPCA(ovarian_FDA, metric = "uni g", r = "r",
                      value = "fundiff",
                      analysis_vars = c("age", "survival_time"))

#extract uni fpc scores
fpc = extract_fPCA_scores(ovarian_FDA, 'uni g fPCA')
```

extract_model

Extract Model

Description

Currently only extracts functional cox models not mixed functional cox models.

Usage

```
extract_model(mxFDAobject, metric, type, model_name)
```

Arguments

mxFDAobject	object of class mxFDA
metric	metric functional PCA data to extract, e.g. 'uni k'
type	one of "cox", "mcox", or "sofr" to specify the type of model to extract
model_name	character string of the model name to retrieve

Details

[Stable]

Value

fit functional model

Author(s)

Alex Soupir <alex.soupir@moffitt.org>

Examples

```
#load ovarian mxFDA object
data('ovarian_FDA')

#run the lfc model
ovarian_FDA = run_fcm(ovarian_FDA, model_name = "fit_lfc",
                      formula = survival_time ~ age, event = "event",
                      metric = "uni g", r = "r", value = "fundiff",
                      analysis_vars = c("age", "survival_time"),
                      afcm = FALSE)

#extract model
mod = extract_model(ovarian_FDA, 'uni g', 'cox', 'fit_lfc')
```

extract_spatial_summary

Summarise spatial data in mxFDA object

Description

Summarise spatial data in mxFDA object

Usage

```
extract_spatial_summary(mxFDAobject, columns, grouping_columns = NULL)
```

Arguments

mxFDAobject	object of class mxFDA
columns	character vector for column heading for cells to summarise
grouping_columns	character vector of other columns to use as grouping, such as region classification column

Details

[Experimental]

Currently this function is experimental as it only handles data that has text in the columns. Eventually, will be able to handle any data inputs such as those from HALO where cells are designated as positive (1) or negative (0) for a cell phenotypes.

Value

data frame with percent of total points per spatial sample columns. If multiple levels are present in columns columns, multiple output columns will be provided.

Author(s)

Alex Soupir <alex.soupir@moffitt.org>

Examples

```
#load data
data(lung_df)

#create data frames for `mxFDA` object
clinical = lung_df %>%
  dplyr::select(image_id, patient_id, patientImage_id, gender,
               age, survival_days, survival_status, stage) %>%
  dplyr::distinct()
#make small, just need to make sure it runs
spatial = lung_df %>%
  dplyr::select(-image_id, -gender, -age, -survival_days, -survival_status, -stage) %>%
  dplyr::filter(patientImage_id %in% clinical$patientImage_id[1:10])

#create `mxFDA` object
mxFDAobject = make_mx FDA(metadata = clinical,
                          spatial = spatial,
                          subject_key = "patient_id",
                          sample_key = "patientImage_id")

#get markers
markers = colnames(mxFDAobject@Spatial) %>%
  grep("pheno", ., value = TRUE)

#extract summary
df = extract_spatial_summary(mxFDAobject, markers)
```

extract_summary_functions

Extract Summary Functions

Description

Function to extract spatial summary functions from the Spatial slot of an mxFDA object

Usage

```
extract_summary_functions(
  mxFDAobject,
  r_vec = seq(0, 100, by = 10),
  extract_func = c(univariate, bivariate),
  summary_func = c(Kest, Lest, Gest),
  markvar,
  mark1,
```

```

    mark2 = NULL,
    edge_correction,
    breaks = NULL
  )

```

Arguments

<code>mxFDAobject</code>	object of class <code>mxFDA</code>
<code>r_vec</code>	Numeric vector of radii over which to evaluate spatial summary functions. Must begin at 0.
<code>extract_func</code>	Defaults to <code>univariate</code> , which calculates univariate spatial summary functions. Choose <code>bivariate</code> for bivariate spatial summary functions.
<code>summary_func</code>	Spatial summary function to calculate. Options are <code>c(Kest, Lest, Gest)</code> which denote Ripley's K, Besag's L, and nearest neighbor G function, respectively.
<code>markvar</code>	The name of the variable that denotes cell type(s) of interest. Character.
<code>mark1</code>	Character string that denotes first cell type of interest.
<code>mark2</code>	Character string that denotes second cell type of interest for calculating bivariate summary statistics. Not used when calculating univariate statistics.
<code>edge_correction</code>	Character string that denotes the edge correction method for spatial summary function. For <code>Kest</code> and <code>Lest</code> choose one of <code>c("border", "isotropic", "Ripley", "translate", "none")</code> . For <code>Gest</code> choose one of <code>c("rs", "km", "han")</code>
<code>breaks</code>	integer value for number of breaks in <code>r_vec</code> . Used only for entropy measure

Details

[Stable]

Value

an object of class `mxFDA` containing the corresponding spatial summary function slot filled. See [make_mxfda\(\)](#) for object structure details.

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>
 Alex Soupir <alex.soupir@moffitt.org>

References

Xiao, L., Ruppert, D., Zipunnikov, V., and Crainiceanu, C. (2016). Fast covariance estimation for high-dimensional functional data. *Statistics and Computing*, 26, 409-421. DOI: 10.1007/s11222-014-9485-x.

[spatstat.explore::Kest\(\)](#)

[spatstat.explore::Gest\(\)](#)

[spatstat.explore::Lest\(\)](#)

```

spatstat.explore::Kcross()
spatstat.explore::Gcross()
spatstat.explore::Lcross()

```

Examples

```

#load ovarian FDA object
data('ovarian_FDA')

#run function
ovarian_FDA = extract_summary_functions(ovarian_FDA, r_vec = 0:100,
                                       extract_func = univariate,
                                       summary_func = Kest,
                                       markvar = "immune",
                                       mark1 = "immune",
                                       edge_correction = "trans")

```

extract_surface	<i>Extract Surface</i>
-----------------	------------------------

Description

Function that transforms functional models from linear or additive functional cox models into afcmSurface or lfcmSurface objects to be plotted.

Usage

```

extract_surface(
  mxFDAobject,
  metric,
  model = NULL,
  r = "r",
  value = "fundiff",
  grid_length = 100,
  analysis_vars,
  p = 0.05,
  filter_cols = NULL
)

```

Arguments

mxFDAobject	object of class mxFDA with model model calculated within
metric	spatial summary function to extract surface for
model	character string for the name of the model for metric data
r	Character string, the name of the variable that identifies the function domain (usually a radius for spatial summary functions). Default is "r".

value	Character string, the name of the variable that identifies the spatial summary function values. Default is "fundiff".
grid_length	Length of grid on which to evaluate coefficient functions.
analysis_vars	Other variables used in modeling FCM fit.
p	numeric p-value used for predicting significant AFCM surface
filter_cols	a named vector of factors to filter summary functions to in <code>c(Derived_Column = "Level_to_Filter")</code> format

Value

a 4 element list of either class `lfcmsurface` or `afcmsurface` depending on the class of model

Surface	<code>data.frame</code> for term predictions for the surface of the metric * radius area
Prediction	<code>data.frame</code> for standard error of the terms for the above surface. AFCM models use the <code>p</code> to set the upper and lower standard errors of β_1
Metric	character of the spatial summary function used; helps keep track if running many models
P-value	a numeric value of the input p-value

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

Alex Soupier <alex.soupier@moffitt.org>

Examples

```
#load ovarian mxFDA object
data('ovarian_FDA')

#run the lfcmsurface model
ovarian_FDA = run_fcm(ovarian_FDA, model_name = "fit_lfcmsurface",
                      formula = survival_time ~ age, event = "event",
                      metric = "uni g", r = "r", value = "fundiff",
                      analysis_vars = c("age", "survival_time"),
                      afcm = FALSE)

#extract surface
model_surface = extract_surface(ovarian_FDA, metric = 'uni g',
                                model = 'fit_lfcmsurface',
                                analysis_vars = 'age') #variables in model
```

filter_spatial	<i>Filter Spatial data</i>
----------------	----------------------------

Description

function to filter the spatial data slot of the mxFDA object.

Usage

```
filter_spatial(mxFDAobject, ..., based_on = "meta", force = FALSE)
```

Arguments

mxFDAobject	object of class mxFDA
...	expressions that return a logical TRUE/FALSE value when evaluated on columns of the meta data slot. These expressions get passed to <code>dplyr::filter()</code> so must be compatible.
based_on	character for which data slot to use for filtering, either 'meta', or 'spatial'. Default to 'meta'.
force	logical whether or not to return empty spatial data <i>if</i> filtering results in 0 rows

Value

object of class mxFDA with the spatial slot filtered. See `make_mxfda()` for more details on object

Author(s)

Alex Soupir <alex.soupir@moffitt.org>

References

`dplyr::filter()`

Examples

```
#load ovarian mxFDA object
data(ovarian_FDA)

#filter ages greater than 50
ovarian_FDA_age50 = filter_spatial(ovarian_FDA, age >= 50, based_on = 'meta')
```

`lung_df`*Multiplex imaging data from a non-small cell lung cancer study.*

Description

This data is adapted from the VectraPolarisData Bioconductor package. There are multiple ROIs for each patient. Data was filtered to include only the cells in the tumor compartment.

Usage`lung_df`**Format**`lung_df`:

A data frame with 879,694 rows and 19 columns:

image_id Image id for a given patient

patient_id Unique patient id

age Patient age at time of cancer diagnosis

survival_days Survival time from diagnosis, in days

survival_status Censoring variable, 1 = death, 0 = censor

x Cell x position

y Cell y position ...

Source

<https://bioconductor.org/packages/release/data/experiment/html/VectraPolarisData.html>

`lung_FDA`*Multiplex imaging data from a non-small cell lung cancer study*

Description

This data is adapted from the VectraPolarisData Bioconductor package. There are multiple ROIs for each patient.

Usage`lung_FDA`

Format

lung_FDA:

An mxFDA object with augmented non-small cel lung cancer multiplex immunofluorescence data, and NN $G(r)$ calculated:

Metadata information about the spatial samples with column `sample_key` column in both
Spatial cell-level information with `x` and `y` columns along with `sample_key` to link to Metadata
subject_key column in Metadata that may have multiple `sample_key` values for each, akin to patient IDs

sample_key column in both Metadata and Spatial that is a 1:1 with the samples (unique per sample)

univariate_summaries univariate summary slot with nearest neighbor G calculated

bivariate_summaries empty slot available for bivariate summaries

functional_pca empty slot for functional PCA data of summaries

functional_cox empty slot for functional models

Details

Spatial summary functions of lung cancer multiplex imaging data.

This data is adapted from the `VectraPolarisData` Bioconductor package. Signal between the survival outcome and spatial summary functions has been augmented for teaching purposes. Spatial relationship is summarized using the nearest neighbor G function.

Includes only spatial samples that had 10 or more radii with calculable G function

Source

<https://bioconductor.org/packages/release/data/experiment/html/VectraPolarisData.html>

make_mxfda

Make mxFDA class object

Description

Used to create an object of class `mxFDA` that can be used with the `mxFDA` package for functional data analysis.

Usage

```
make_mxfda(metadata, spatial = NULL, subject_key, sample_key)
```

Arguments

metadata	metadata with columns <code>subject_key</code> and <code>sample_key</code>
spatial	spatial information, either list or df, with column <code>sample_key</code> . <code>Spatial</code> can be empty if inputting data already derived. See add_summary_function() for more details.
subject_key	column name in Metadata for subject ID
sample_key	column linking Metadata to Spatial data

Details**[Stable]****Value**S4 object of class `mxFDA`

Metadata	slot of class <code>data.frame</code> that contains sample and subject level information
Spatial	slot of class <code>data.frame</code> that contains point level information within samples. An example would be cells belonging to TMA cores
subject_key	slot of class <code>character</code> that corresponds to a column in the Metadata slot that groups samples at a subject level. An example would be <code>"patient_id"</code>
sample_key	slot of class <code>character</code> that corresponds to a column both in the Metadata and Spatial slots that links samples to characteristics
univariate_summaries	slot of class <code>list</code> where univariate summary functions calculated on Spatial would be stored
bivariate_summaries	slot of class <code>list</code> where bivariate summary functions calculated on Spatial would be stored
functional_pca	slot of class <code>list</code> where FPCA results are stored
functional_mzca	slot of class <code>list</code> where MFPCA results are stored
functional_cox	slot of class <code>list</code> where functional cox model results are stored
functional_mcox	slot of class <code>list</code> where mixed functional cox model results are stored
scalar_on_function	slot of class <code>list</code> where functional models are fit to scalar responses

Author(s)

Alex Soupir <alex.soupir@moffitt.org>

Examples

```

#select sample metadata
clinical = lung_df %>%
  dplyr::select(image_id, patient_id, patientImage_id,
                gender, age, survival_days, survival_status, stage) %>%
  dplyr::distinct()
#select the spatial information
spatial = lung_df %>%
  dplyr::select(-image_id, -gender, -age, -survival_days, -survival_status, -stage)
sample_id_column = "patientImage_id"
#create the mxFDA object
mxFDAobject = make_mxfda(metadata = clinical,
                          spatial = spatial,
                          subject_key = "patient_id",
                          sample_key = sample_id_column)

```

 ovarian_FDA

Multiplex imaging data from an ovarian cancer tumor microarray

Description

This data is adapted from the VectraPolarisData Bioconductor package and comes from a tumor-microarray of tissue samples from 128 patients with ovarian cancer. There is one patient per subject.

Usage

```
ovarian_FDA
```

Format

ovarian_FDA:

An mxFDA object with augmented ovarian cancer multiplex immunofluorescence data, and NN G(r) calculated:

Metadata information about the spatial samples with column sample_key column in both

Spatial cell-level information with x and y columns along with sample_key to link to Metadata
subject_key column in Metadata that may have multiple sample_key values for each, akin to patient IDs

sample_key column in both Metadata and Spatial that is a 1:1 with the samples (unique per sample)

univariate_summaries univariate summary slot with nearest neighbor G calculated

bivariate_summaries empty slot available for bivariate summaries

functional_pca empty slot for functional PCA data of summaries

functional_cox empty slot for functional models

Details

Spatial summary functions of ovarian cancer multiplex imaging data.

This data is adapted from the VectraPolarisData Bioconductor package. Signal between the survival outcome and spatial summary functions has been augmented for teaching purposes. Spatial relationship is summarized using the nearest neighbor G function.

Source

<https://bioconductor.org/packages/release/data/experiment/html/VectraPolarisData.html>

plot.afcmSurface	<i>Plot afcm object</i>
------------------	-------------------------

Description

Plot afcm object

Usage

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

Arguments

x	object of class afcmSurface to be plotted
...	currently ignored

Value

object compatible with ggplot2

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

Alex Soupir <alex.soupir@moffitt.org>

plot.lfcmSurface	<i>Plot lfcm surface</i>
------------------	--------------------------

Description

Plot lfcm surface

Usage

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

Arguments

x	object of class lfcmSurface to be plotted
...	currently ignored

Value

object compatible with ggplot2

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>
Alex Soupir <alex.soupir@moffitt.org>

plot.mxFDA	<i>Plot mxFDA object</i>
------------	--------------------------

Description

Plot mxFDA object

Usage

```
## S3 method for class 'mxFDA'  
plot(x, filter_cols = NULL, ...)
```

Arguments

x	object of class mxFDA to be plotted
filter_cols	column key to filter
...	additional parameters including y, what, and sampleID to inform what to be plotted

Details**[Stable]**

If there are multiple metrics that are included in the derived table, an extra parameter `filter_cols` in the format of `c(Derived_Column = "Level_to_Filter")` will return curves from the `Derived_Column` with the level `Level_to_Filter`

When plotting `mFPCA` objects, additional arguments `level1` and `level2` help indicate which FPCA from level 1 and level 2 to plot

Value

object of class `ggplot` compatible the `ggplot2` aesthetics

Author(s)

Alex Soupir <alex.soupir@moffitt.org>

Examples

```
#set seed
set.seed(333)
#plotting summary
data("ovarian_FDA")
plot(ovarian_FDA, y = 'fundiff', what = 'uni g')
#running fpca
ovarian_FDA = run_fpca(ovarian_FDA, metric = "uni g", r = "r", value = "fundiff",
                      lightweight = TRUE,
                      pve = .99)
#plot fpca
plot(ovarian_FDA, what = 'uni g fpca', pc_choice = 1)
```

plot.sofr

Plot sofr object

Description

Plot sofr object

Usage

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

Arguments

`x` object of class `sofr` to be plotted
`...` currently ignored

Value

object compatible with ggplot2

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

Alex Soupir <alex.soupir@moffitt.org>

plot_fpc

Create plot of mean +/- scaled eigenfunctions from FPCA

Description

Produces a ggplot with mean plus or minus two standard deviations of a selected FPC.

Usage

```
plot_fpc(obj, pc_choice)
```

Arguments

obj fPCA object to be plotted.

pc_choice FPC to be plotted.

Details

[Superseded]

Value

object of class ggplot

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

plot_mfpc	<i>Create plot of mean +/- scaled eigenfunctions from FPCA</i>
-----------	--

Description

Produces a ggplot with mean plus or minus two standard deviations of a selected FPC.

Usage

```
plot_mfpc(obj, pc_choice_level1, pc_choice_level2)
```

Arguments

obj	fPCA object to be plotted.
pc_choice_level1, pc_choice_level2	FPC to be plotted.

Details

[Superseded]

Value

list of objects of class ggplot

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

run_fcm	<i>Run Function Cox Models</i>
---------	--------------------------------

Description

Fit a functional Cox regression model.

Usage

```
run_fcm(  
  mxFDAobject,  
  model_name,  
  formula,  
  event = "event",  
  metric = "uni k",  
  r = "r",  
  value = "fundiff",
```

```

    afcm = FALSE,
    smooth = FALSE,
    filter_cols = NULL,
    ...,
    knots = NULL
  )

```

Arguments

mxFDAobject	Dataframe of spatial summary functions from multiplex imaging data, in long format. Can be estimated using the function <code>extract_summary_functions</code> or provided separately.
model_name	character string to give the fit model in the functional cox slot
formula	Formula to be fed to <code>mgcv</code> in the form of <code>survival_time ~ x1 + x2</code> . Does not contain functional predictor. Character valued. Data must contain censoring variable called "event".
event	character string for the column in Metadata that contains 1/0 for the survival event
metric	name of calculated spatial metric to use
r	Character string, the name of the variable that identifies the function domain (usually a radius for spatial summary functions). Default is "r".
value	Character string, the name of the variable that identifies the spatial summary function values. Default is "fundiff".
afcm	If TRUE, runs additive functional Cox model. If FALSE, runs linear functional cox model. Defaults to linear functional cox model.
smooth	Option to smooth data using FPCA. Defaults to FALSE.
filter_cols	a named vector of factors to filter summary functions to in <code>c(Derived_Column = "Level_to_Filter")</code> format
...	Optional other arguments to be passed to <code>fpca.face</code>
knots	Number of knots for defining spline basis.

Details

[Stable]

Value

A list which is a linear or additive functional Cox model fit. See `mgcv::gam` for more details.

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

Alex Soupier <alex.soupier@moffitt.org>

Examples

```
#load ovarian mxFDA object
data('ovarian_FDA')

#run the lfcM model
ovarian_FDA = run_fcm(ovarian_FDA, model_name = "fit_lfcM",
                      formula = survival_time ~ age, event = "event",
                      metric = "uni g", r = "r", value = "fundiff",
                      afcm = FALSE)
```

run_fpca

run_fpca

Description

This is a wrapper for the function `fpca.face` from the `refund` package. EXPAND

Usage

```
run_fpca(
  mxFDAobject,
  metric = "uni k",
  r = "r",
  value = "fundiff",
  knots = NULL,
  analysis_vars = NULL,
  lightweight = FALSE,
  filter_cols = NULL,
  ...
)
```

Arguments

<code>mxFDAobject</code>	object of class <code>mxFDA</code> created by <code>make_mxfda</code> with metrics derived with <code>extract_summary_functions</code>
<code>metric</code>	name of calculated spatial metric to use
<code>r</code>	Character string, the name of the variable that identifies the function domain (usually a radius for spatial summary functions). Default is "r".
<code>value</code>	Character string, the name of the variable that identifies the spatial summary function values. Default is "fundiff".
<code>knots</code>	Number of knots for defining spline basis. Defaults to the number of measurements per function divided by 2.
<code>analysis_vars</code>	Optional list of variables to be retained for downstream analysis.
<code>lightweight</code>	Default is <code>FALSE</code> . If <code>TRUE</code> , removes <code>Y</code> and <code>Yhat</code> from returned FPCA object. A good option to select for large datasets.

`filter_cols` a named vector of factors to filter summary functions to in `c(Derived_Column = "Level_to_Filter")` format

... Optional other arguments to be passed to `fpca.face`

Details

[Stable]

The `filter_cols` parameter is useful when the summary function was input by the user using `add_summary_function()` and the multiple marks were assessed; a column called "Markers" with tumor infiltrating lymphocytes as well as cytotoxic T cells. This parameter allows for filtering down to include only one or the other.

Value

A `mxFDA` object with the `functional_pca` slot filled for the respective spatial summary function containing:

`mxfundata` The original dataframe of spatial summary functions, with scores from FPCA appended for downstream modeling

`fpca_object` A list of class "fpca" with elements described in the documentation for `refund::fpca.face`

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

Alex Soupir <alex.soupir@moffitt.org>

References

Xiao, L., Ruppert, D., Zipunnikov, V., and Crainiceanu, C. (2016). Fast covariance estimation for high-dimensional functional data. *Statistics and Computing*, 26, 409-421. DOI: 10.1007/s11222-014-9485-x.

Examples

```
#load ovarian mxFDA object
data('ovarian_FDA')

#run the FPCA
ovarian_FDA = run_fpca(ovarian_FDA, metric = "uni g", r = "r", value = "fundiff",
                      lightweight = TRUE,
                      pve = .99)
```

run_mfcm

*Run function Cox models for data with multiple samples per subject***Description**

Fit a functional Cox regression model when there are multiple functions per subject, which arise from multiple samples per subject. It is not necessary for all subjects to have the same number of samples. The function first performs a multilevel functional principal components analysis (MF-PCA) decomposition to the spatial summary function. Then, the average curve for each subject is used in a functional Cox model (FCM). Variation around each subject's mean is captured by calculating the standard deviation of the level 2 scores from MFPCA, then including this as a scalar variable in the FCM called "level2_score_sd".

Usage

```
run_mfcm(
  mxFDAobject,
  model_name,
  formula,
  event = "event",
  metric = "uni k",
  r = "r",
  value = "fundiff",
  afcm = FALSE,
  filter_cols = NULL,
  pve = 0.99,
  ...,
  knots = NULL
)
```

Arguments

mxFDAobject	Dataframe of spatial summary functions from multiplex imaging data, in long format. Can be estimated using the function <code>extract_summary_functions</code> or provided separately.
model_name	character string to give the fit model in the functional cox slot
formula	Formula to be fed to <code>mgcv</code> in the form of <code>survival_time ~ x1 + x2</code> . Does not contain functional predictor. Character valued. Data must contain censoring variable called "event".
event	character string for the column in Metadata that contains 1/0 for the survival event
metric	name of calculated spatial metric to use
r	Character string, the name of the variable that identifies the function domain (usually a radius for spatial summary functions). Default is "r".

value	Character string, the name of the variable that identifies the spatial summary function values. Default is "fundiff".
afcm	If TRUE, runs additive functional Cox model. If FALSE, runs linear functional cox model. Defaults to linear functional cox model.
filter_cols	a named vector of factors to filter summary functions to in c(Derived_Column = "Level_to_Filter") format
pve	Proportion of variance explained by multilevel functional principal components analysis in mfpca step
...	Optional other arguments to be passed to fpc. face
knots	Number of knots for defining spline basis.

Details**[Stable]****Value**

A list which is a linear or additive functional Cox model fit. See `mgcv::gam` for more details.

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

Alex Soupir <alex.soupir@moffitt.org>

Examples

```
#load ovarian mxFDA object
data('lung_FDA')

# run the lfcm model
lung_FDA = run_mfcm(lung_FDA, model_name = "fit_mlfc",
  formula = survival_days ~ age,
  event = "survival_status",
  metric = "uni g", r = "r", value = "fundiff",
  pve = 0.99,
  afcm = FALSE)
```

run_mfpca

run_fpca

Description

This is a wrapper for the function `mfpca.face` from the `refund` package. EXPAND

Usage

```
run_mfpca(
  mxFDAobject,
  metric = "uni k",
  r = "r",
  value = "fundiff",
  knots = NULL,
  lightweight = FALSE,
  ...
)
```

Arguments

<code>mxFDAobject</code>	object of class <code>mxFDA</code> created by <code>make_mxfda()</code> with metrics derived with <code>extract_summary_functions</code>
<code>metric</code>	name of calculated spatial metric to use
<code>r</code>	Character string, the name of the variable that identifies the function domain (usually a radius for spatial summary functions). Default is "r".
<code>value</code>	Character string, the name of the variable that identifies the spatial summary function values. Default is "fundiff".
<code>knots</code>	Number of knots for defining spline basis. Defaults to the number of measurements per function divided by 2.
<code>lightweight</code>	Default is FALSE. If TRUE, removes Y and Yhat from returned mFPCA object. A good option to select for large datasets.
<code>...</code>	Optional other arguments to be passed to <code>mfpca.face</code>

Details

[Stable]

Value

A `mxFDA` object with the `functional_mPCA` slot for the respective spatial summary function containing:

<code>mxfundata</code>	The original dataframe of spatial summary functions, with scores from FPCA appended for downstream modeling
<code>fpc_object</code>	A list of class "fpc" with elements described in the documentation for <code>refund::fpc.face</code>

Author(s)

unknown <first.last@domain.extension>

Julia Wrobel <julia.wrobel@emory.edu>

Alex Soupier <alex.soupier@moffitt.org>

References

Xiao, L., Ruppert, D., Zipunnikov, V., and Crainiceanu, C. (2016). Fast covariance estimation for high-dimensional functional data. *Statistics and Computing*, 26, 409-421. DOI: 10.1007/s11222-014-9485-x.

Examples

```
#load data
data(lung_FDA)

#run mixed fpca
lung_FDA = run_mfpca(lung_FDA, metric = 'uni g')
```

run_sofr

Run Scalar on Function Regression

Description

Fit a scalar-on-function regression model. Uses `refund::pfr` under the hood for computations, and stores results in the `mxFDA` object.

Usage

```
run_sofr(
  mxFDAobject,
  model_name,
  formula,
  family = "gaussian",
  metric = "uni k",
  r = "r",
  value = "fundiff",
  smooth = FALSE,
  filter_cols = NULL,
  ...,
  knots = NULL
)
```

Arguments

<code>mxFDAobject</code>	Dataframe of spatial summary functions from multiplex imaging data, in long format. Can be estimated using the function <code>extract_summary_functions</code> or provided separately.
<code>model_name</code>	character string to give the fit model
<code>formula</code>	Formula to be fed to <code>mgcv</code> in the form of <code>outcome ~ x1 + x2</code> . Does not contain functional predictor. Character valued.

family	Exponential family distribution to be passed to <code>mgcv::gam</code> . Defaults to "gaussian". Select "binomial" for binary outcome.
metric	Name of calculated spatial metric to use
r	Character string, the name of the variable that identifies the function domain (usually a radius for spatial summary functions). Default is "r".
value	Character string, the name of the variable that identifies the spatial summary function values. Default is "fundiff".
smooth	Option to smooth data using FPCA. Defaults to FALSE.
filter_cols	a named vector of factors to filter summary functions to in <code>c(Derived_Column = "Level_to_Filter")</code> format
...	Optional other arguments to be passed to <code>fpca.face</code>
knots	Number of knots for defining spline basis.

Details**[Stable]****Value**

A list which is a linear or additive functional Cox model fit. See `mgcv::gam` for more details.

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

Alex Soupir <alex.soupir@moffitt.org>

Examples

```
#load ovarian mxFDA object
data('ovarian_FDA')

# run scalar on function regression model with a continuous outcome (age)
ovarian_FDA = run_sofr(ovarian_FDA,
                      model_name = "fit_sofr",
                      formula = age~stage,
                      metric = "uni g", r = "r", value = "fundiff")

# run scalar on function regression model with a binary outcome (stage)
# also known as functional logistic regression
ovarian_FDA = run_sofr(ovarian_FDA,
                      model_name = "fit_sofr",
                      formula = stage~age,
                      family = "binomial",
                      metric = "uni g", r = "r", value = "fundiff")
```

summary.mxFDA	<i>Summary method for object of class mxFDA</i>
---------------	---

Description

Summary method for object of class mxFDA

Usage

```
## S3 method for class 'mxFDA'
summary(object, ...)
```

Arguments

object	object of class mxFDA
...	unused currently

Details

[Stable]

Value

summary of object to the R console

Author(s)

Alex Soupir <alex.soupir@moffitt.org>

univariate	<i>univariate</i>
------------	-------------------

Description

Internal function called by [extract_summary_functions\(\)](#) to calculate a univariate spatial summary function for a single image.

Usage

```
univariate(
  mximg,
  markvar,
  mark1,
  mark2,
  r_vec,
  func = c(Kest, Lest, Gest),
```

```

    edge_correction,
    breaks = NULL
  )

```

Arguments

<code>mximg</code>	Dataframe of cell-level multiplex imaging data for a single image. Should have variables <code>x</code> and <code>y</code> to denote <code>x</code> and <code>y</code> spatial locations of each cell.
<code>markvar</code>	The name of the variable that denotes cell type(s) of interest. Character.
<code>mark1</code>	dummy filler, unused
<code>mark2</code>	dummy filler, unused
<code>r_vec</code>	Numeric vector of radii over which to evaluate spatial summary functions. Must begin at 0.
<code>func</code>	Spatial summary function to calculate. Options are <code>c(Kest, Lest, Gest)</code> which denote Ripley's <code>K</code> , Besag's <code>L</code> , and nearest neighbor <code>G</code> function, respectively.
<code>edge_correction</code>	Character string that denotes the edge correction method for spatial summary function. For <code>Kest</code> and <code>Lest</code> choose one of <code>c("border", "isotropic", "Ripley", "translate", "none")</code> . For <code>Gest</code> choose one of <code>c("rs", "km", "han")</code>
<code>breaks</code>	ignored

Details

[Stable]

Value

A `data.frame` containing:

<code>r</code>	the radius of values over which the spatial summary function is evaluated
<code>sumfun</code>	the values of the spatial summary function
<code>csr</code>	the values of the spatial summary function under complete spatial randomness
<code>fundiff</code>	<code>sumfun - csr</code> , positive values indicate clustering and negative values repulsion

Author(s)

Julia Wrobel <julia.wrobel@emory.edu>

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