Package ‘nlive’

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Description Estimation of relatively complex nonlinear mixed-effects models, including the Sigmoidal Mixed Model and the Piecewise Linear Mixed Model with abrupt or smooth transition, through a single intuitive line of code and with automated generation of starting values.
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The dataCog contains 1200 individuals with one line per visit. Repeated measures of global cognition (cognition) were collected over a maximum period of 30 years. Information on the age at death is also provided (ageDeath, ageDeath90).

A data frame with 11867 observations over 1200 subjects and 5 variables:

- **ID**  subject identification number
- **time** the retrospective (negative) time before death (in years)
- **cognition** composite score of global cognition
- **ageDeath** age at death (in years)
- **ageDeath90** age at death centered by the mean

```
summary(dataCog)
```
Description

The nlive() function allows to fit a Sigmoidal Mixed Model with 4 parameters, a Piecewise Linear Mixed Model with abrupt change, or a Piecewise Linear Mixed Model with a smooth polynomial transition in the context of longitudinal Gaussian outcomes. This function was designed to be intuitive enough to the less sophisticated users, while using recent developments such as the stochastic approximation expectation-maximization (SAEM) algorithm for efficient estimation. It was designed to optimize the initial values of the main parameters and help interpretation of the output by providing different features such as annotated outputs and graphs.

Usage

```r
nlive(  
  model,  
  dataset,  
  ID,  
  outcome,  
  time,  
  predictor.all = NULL,  
  predictor.par1 = NULL,  
  predictor.par2 = NULL,  
  predictor.par3 = NULL,  
  predictor.par4 = NULL,  
  start = NULL,  
  plot.xlabel = NULL,  
  plot.ylabel = NULL,  
  traj.marg = FALSE,  
  traj.marg.group = NULL,  
  spag.plot.title = NULL,  
  traj.marg.title = NULL,  
  traj.marg.group.title = NULL,  
  traj.marg.group.val = NULL  
)
```

Arguments

- **model**: indicator of the model to fit (1=Sigmoidal Mixed Model, 2=Piecewise Mixed Model with abrupt change, 3=Piecewise Mixed Model with smooth transition)
- **dataset**: data frame containing the variables ID, outcome, time, predictor.all, and predictor.par1 to predictor.par4.
- **ID**: name of the variable representing the grouping structure specified with " (e.g., "ID" representing the unique identifier of participants).
outcome name of the time-varying variable representing the longitudinal outcome specified with " (e.g., "outcome").

time name of the variable representing the timescale specified with " (e.g., "time"), which can be negative or positive.
predictor.all optional vector indicating the name of the variable(s) that the four main parameters of the model of interest will be adjusted to (e.g. predictor.all=c("X1","X2")). Default to NULL.
predictor.par1 optional vector indicating the name of the variable(s) that the first main parameter of the model of interest will be adjusted to (e.g. predictor.all=c("X1","X2")). For model 1, the first parameter = last level. For models 2 and 3, first parameter = intercept. Default to NULL.
predictor.par2 optional vector indicating the name of the variable(s) that the second main parameter of the model of interest will be adjusted to (e.g. predictor.all=c("X1","X2")). For model 1, the second parameter = initial level. For models 2 and 3, second parameter = slope before the change-point. Default to NULL.
predictor.par3 optional vector indicating the name of the variable(s) that the third main parameter of the model of interest will be adjusted to (e.g. predictor.all=c("X1","X2")). For model 1, the third parameter = midpoint. For models 2 and 3, third parameter = slope after the change-point. Default to NULL.
predictor.par4 optional vector indicating the name of the variable(s) that the fourth main parameter of the model of interest will be adjusted to (e.g. predictor.all=c("X1","X2")). For model 1, the fourth parameter is the Hill slope. For models 2 and 3, the fourth parameter is the changepoint. Default to NULL.
start optional vector to override the specification of the four initial values for the main parameters. For model 1, the values must be included in the following order: last level, initial level, midpoint, Hill slope. For models 2 and 3, the values must be included in the following order: intercept, slope before the changepoint, slope after the changepoint, changepoint. Default to NULL.
plot.xlabel optional text for the title of the x-axis of all plots
plot.ylabel optional text for the title of the y-axis of all plots
traj.marg optional logical indicating if the marginal estimated trajectory should be plotted for the most common profile of covariates, if any. Default to FALSE.
traj.marg.group optional name of the grouping variable listed in one of the predictor arguments to plot and contrast the estimated marginal trajectories between two specific groups, specified with " (e.g., traj.marg.group="X1"). If the variable is binary, the trajectories are contrasted between the two groups of interest. If the variable is continuous, the 10th and 90th percentile values will automatically be considered. The default value is NULL.
spag.plot.title optional text for the title of the spaghetti plot
traj.marg.title optional text for the title of the marginal estimated trajectory
traj.marg.group.title optional text for the title of the marginal estimated trajectories contrasted between groups
optional vector that can be used when `traj.marg.group` receives a quantitative variable and that allows to manually specify two percentile values to be considered for contrasting the `traj.marg.group`. The two values must be between 0 and 1 (e.g., `traj.marg.group.val=c(0.2,0.8)`; for percentiles 20th and 80th). Default to 10th and 90th percentiles (i.e., `traj.marg.group.val=c(0.1,0.9)`).

Details

**CAUTIONS REGARDING THE USE OF THE FUNCTION**

`traj.marg`: if "TRUE", this argument automatically plots the estimated marginal trajectories of the longitudinal outcome for the most common profile of covariates, if any (i.e., ref "1" for binary variables and mean values for continuous variables). Thus, users must ensure that continuous variables are centered on the mean.

Value

An object of class `SaemixObject` (from the existing `saemix` R package) containing the results of the fit of the data by the non-linear mixed model of interest. The `nlive` function automatically provides (i) a spaghetti plot of the observed outcome for 70 randomly selected statistical units in the dataset and (ii) the standard `saemix` output, including the fixed effects estimates, the variance of random effects, and Likelihood of the fitted model. The outputs are printed on the terminal and the numerical and graphical outputs are stored in a directory.

Author(s)

Maude Wagner, Ana W. Capuano, Emmanuelle Comets

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References


Examples

```r
### Fitting a sigmoidal mixed model - with no covariate
## Not run:
head(dataCog)
requireNamespace('nlraa')
smm.fit = nlife(model=1, dataset=dataCog, ID="ID", outcome="cognition", time="time")
## End(Not run)
```
nlive.inspect

Description

The nlive.inspect() function allows to generate basic graphs to describe the longitudinal observed measures of a variable of interest in the dataset.

Usage

```r
nlive.inspect(
    dataset,
    ID,
    variable,
    time,
    plot.xlabel = NULL,
    plot.ylabel = NULL,
    spag.plot.title = NULL
)
```

Arguments

dataset data frame containing the ID, variable, and time.
nlive.pmma

ID  name of the variable representing the grouping structure specified with " (e.g., "ID" representing the unique identifier of participants).
variable name of the time-varying variable of interest specified with " (e.g., "variable").
time name of the variable representing the timescale specified with " (e.g., "time"). Can be negative or positive.
plot.xlabel optional text for the title of the x-axis of all plots.
plot.ylabel optional text for the title of the y-axis of all plots.
spag.plot.title optional text for the title of the spaghetti plot.

Value

The nlive.inspect function automatically provides (i) an histogram of all the repeated measures of the variable available over time, (ii) a spaghetti plot of the longitudinal observed variable for 70 randomly selected statistical units, (iii) repeated boxplots of the longitudinal observed variable for each time unit. The outputs are printed on the terminal and the numerical and graphical outputs are stored in a directory

Author(s)

Maude Wagner, Ana W. Capuano, Emmanuelle Comets
<maude_wagner@rush.edu>

References


Examples

```r
## Not run:
nlive.inspect(dataset=dataCog, ID="ID", variable="cognition", time="time")
## End(Not run)
```

nlive.pmma  Automated Estimation of the Piecewise Linear Mixed Model with Abrupt Change

Description

The nlive.pmma() function allows to fit a Piecewise Linear Mixed Models with abrupt change in the context of longitudinal Gaussian outcomes. This function was designed to be intuitive enough to the less sophisticated users, while using recent developments such as the stochastic approximation expectation-maximization (SAEM) algorithm for efficient estimation. It was designed to optimize the initial values of the main parameters and help interpretation of the output by providing different features such as annotated outputs and graphs.
Usage

```r
nlive.pmma(
  dataset,
  ID, outcome, time,
  var.all = NULL,
  var.last.level = NULL,
  var.slope1 = NULL,
  var.slope2 = NULL,
  var.changepoint = NULL,
  start = NULL,
  plot.xlabel = NULL,
  plot.ylabel = NULL,
  traj.marg = FALSE,
  traj.marg.group = NULL,
  traj.marg.title = NULL,
  traj.marg.group.title = NULL,
  traj.marg.group.val = NULL
)
```

Arguments

- **dataset**: data frame containing the variables ID, outcome, time, var.all, and all other var. arguments.
- **ID**: name of the variable representing the grouping structure specified with " (e.g., "ID" representing the unique identifier of participants).
- **outcome**: name of the time-varying variable representing the longitudinal outcome specified with " (e.g., "outcome").
- **time**: name of the variable representing the timescale specified with " (e.g., "time"), which can be negative or positive.
- **var.all**: optional vector indicating the name of the variable(s) that the four main parameters of the model will be adjusted to (e.g. var.all=c("X1","X2")). Default to NULL.
- **var.last.level**: optional vector indicating the name of the variable(s) that the last level parameter of the model of interest will be adjusted to (e.g. var.last.level=c("X1","X2")). Default to NULL.
- **var.slope1**: optional vector indicating the name of the variable(s) that the slope1 (before changepoint) parameter of the model of interest will be adjusted to (e.g. var.slope1=c("X1","X2")). Default to NULL.
- **var.slope2**: optional vector indicating the name of the variable(s) that the slope2 (after changepoint) parameter of the model of interest will be adjusted to (e.g. var.slope2=c("X1","X2")). Default to NULL.
- **var.changepoint**: optional vector indicating the name of the variable(s) that the changepoint parameter of the model of interest will be adjusted to (e.g. var.changepoint=c("X1","X2")). Default to NULL.
optional vector to override the specification of the four initial values for the main parameters - values must be included in the following order: intercept, slope before the changepoint, slope after the changepoint, changepoint. Default to NULL.

plot.xlabel optional text for the title of the x-axis of all plots.

plot.ylabel optional text for the title of the y-axis of all plots.

traj.marg optional logical indicating if the marginal estimated trajectory should be plotted for the most common profile of covariates, if any. Default to FALSE.

traj.marg.group optional name of the grouping variable listed in one of the predictor arguments to plot and contrast the estimated marginal trajectories between two specific groups, specified with " (e.g., traj.marg.group="X1"). If the variable is binary, the trajectories are contrasted between the two groups of interest. If the variable is continuous, the 10th and 90th percentile values will automatically be considered. The default value is NULL.

traj.marg.title optional text for the title of the marginal estimated trajectory

traj.marg.group.title optional text for the title of the marginal estimated trajectories contrasted between groups

traj.marg.group.val optional vector that can be used when traj.marg.group receives a quantitative variable and that allows to manually specify two percentile values to be considered for contrasting the traj.marg.group. The two values must be between 0 and 1 (e.g., traj.marg.group.val=c(0.2,0.8); for percentiles 20th and 80th). Default to 10th and 90th percentiles (i.e., traj.marg.group.val=c(0.1,0.9)).

Details

CAUTIONS REGARDING THE USE OF THE FUNCTION

traj.marg: if "TRUE", this argument automatically plots the estimated marginal trajectories of the longitudinal outcome for the most common profile of covariates, if any (i.e., ref "1" for binary variables and mean values for continuous variables). Thus, users must ensure that continuous variables are centered on the mean.

Value

An object of class SaemixObject (from the existing saemix R package) containing the results of the fit of the data by the PMM-abrupt. The nlive.pmma function automatically provides the standard saemix output, including the fixed effects estimates, the variance of random effects, and Likelihood of the fitted model. The outputs are printed on the terminal and the numerical and graphical outputs are stored in a directory.

Author(s)

Maude Wagner, Ana W. Capuano, Emmanuelle Comets

<maude_wagner@rush.edu>
References


Examples

```r
# Fitting a piecewise mixed model with abrupt change - with no covariate
## Not run:
head(dataCog)
pmm.abrupt.fit = nlive.pmma(dataset=dataCog, ID="ID", outcome="cognition", time="time")
## End(Not run)

# plot(pmm.abrupt.fit): diagnostic plots to assess the goodness-of-fit of pmm.abrupt.fit
# psi(pmm.abrupt.fit): estimates of individual parameters
```

nlive.pmms

Automated Estimation of the Piecewise Linear Mixed Model with Smooth Change

Description

The nlive.pmms() function allows to fit a Piecewise Linear Mixed Models with smooth change in the context of longitudinal Gaussian outcomes. This function was designed to be intuitive enough to the less sophisticated users, while using recent developments such as the stochastic approximation expectation-maximization (SAEM) algorithm for efficient estimation. It was designed to optimize the initial values of the main parameters and help interpretation of the output by providing different features such as annotated outputs and graphs.

Usage

```r
nlive.pmms(
  dataset,
  ID,
  outcome,
  time,
  var.all = NULL,
  var.last.level = NULL,
  var.slope1 = NULL,
  var.slope2 = NULL,
  var.changepoint = NULL,
  start = NULL,
  plot.xlabel = NULL,
)```
plot.ylabel = NULL,
traj.marg = FALSE,
traj.marg.group = NULL,
traj.marg.title = NULL,
traj.marg.group.title = NULL,
traj.marg.group.val = NULL
)

Arguments

dataset data frame containing the variables ID, outcome, time, var.all, and all other var.
arguments.

ID name of the variable representing the grouping structure specified with " (e.g., "ID" representing the unique identifier of participants).

outcome name of the time-varying variable representing the longitudinal outcome specified with " (e.g., "outcome").

time name of the variable representing the timescale specified with " (e.g., "time"), which can be negative or positive.

var.all optional vector indicating the name of the variable(s) that the four main parameters of the model will be adjusted to (e.g. var.all=c("X1","X2")). Default to NULL.

var.last.level optional vector indicating the name of the variable(s) that the last level parameter of the model of interest will be adjusted to (e.g. var.last.level=c("X1","X2")). Default to NULL.

var.slope1 optional vector indicating the name of the variable(s) that the slope1 (before changepoint) parameter of the model of interest will be adjusted to (e.g. var.slope1=c("X1","X2")). Default to NULL.

var.slope2 optional vector indicating the name of the variable(s) that the slope2 (after changepoint) parameter of the model of interest will be adjusted to (e.g. var.slope2=c("X1","X2")). Default to NULL.

var.changepoint optional vector indicating the name of the variable(s) that the changepoint parameter of the model of interest will be adjusted to (e.g. var.changepoint=c("X1","X2")). Default to NULL.

start optional vector to override the specification of the four initial values for the main parameters - values must be included in the following order: intercept, slope before the changepoint, slope after the changepoint, changepoint. Default to NULL.

plot.xlabel optional text for the title of the x-axis of all plots
plot.ylabel optional text for the title of the y-axis of all plots
traj.marg optional logical indicating if the marginal estimated trajectory should be plotted for the most common profile of covariates, if any. Default to FALSE.

traj.marg.group optional name of the grouping variable listed in one of the predictor arguments to plot and contrast the estimated marginal trajectories between two specific
groups, specified with " (e.g., traj.marg.group="X1"). If the variable is binary, the trajectories are contrasted between the two groups of interest. If the variable is continuous, the 10th and 90th percentile values will automatically be considered. The default value is NULL.

**traj.marg.title**
optional text for the title of the marginal estimated trajectory

**traj.marg.group.title**
optional text for the title of the marginal estimated trajectories contrasted between groups

**traj.marg.group.val**
optional vector that can be used when traj.marg.group receives a quantitative variable and that allows to manually specify two percentile values to be considered for contrasting the traj.marg.group. The two values must be between 0 and 1 (e.g., traj.marg.group.val=c(0.2,0.8); for percentiles 20th and 80th). Default to 10th and 90th percentiles (i.e., traj.marg.group.val=c(0.1,0.9)).

**Details**

**CAUTIONS REGARDING THE USE OF THE FUNCTION**

traj.marg: if "TRUE", this argument automatically plots the estimated marginal trajectories of the longitudinal outcome for the most common profile of covariates, if any (i.e., ref "1" for binary variables and mean values for continuous variables). Thus, users must ensure that continuous variables are centered on the mean.

**Value**

An object of class SaemixObject (from the existing saemix R package) containing the results of the fit of the data by the PMM-smooth. The nlive.pmms function automatically provides the standard saemix output, including the fixed effects estimates, the variance of random effects, and Likelihood of the fitted model. The outputs are printed on the terminal and the numerical and graphical outputs are stored in a directory.

**Author(s)**

Maude Wagner, Ana W. Capuano, Emmanuelle Comets

<maude_wagner@rush.edu>

**References**

Examples

#### Fitting a piecewise mixed model with abrupt change - with no covariate

```r
## Not run:
head(dataCog)
pmm.smooth.fit = nlive.pmms(dataset=dataCog, ID="ID", outcome="cognition", time="time")

## End(Not run)

#### plot(pmm.smooth.fit): diagnostic plots to assess the goodness-of-fit of pmm.smooth.fit
#### psi(pmm.smooth.fit): estimates of individual parameters
```

---

### nlive.smm

**Automated Estimation of the Sigmoidal Mixed Model**

**Description**

The `nlive.smm()` function allows to fit a Sigmoidal Mixed Model with 4 parameters in the context of longitudinal Gaussian outcomes. This function was designed to be intuitive enough to the less sophisticated users, while using recent developments such as the stochastic approximation expectation-maximization (SAEM) algorithm for efficient estimation. It was designed to optimize the initial values of the main parameters and help interpretation of the output by providing different features such as annotated outputs and graphs.

**Usage**

```r
nlive.smm(
  dataset,
  ID,
  outcome,
  time,
  var.all = NULL,
  var.first.level = NULL,
  var.last.level = NULL,
  var.midpoint = NULL,
  var.Hslope = NULL,
  start = NULL,
  plot.xlabel = NULL,
  plot.ylabel = NULL,
  traj.marg = FALSE,
  traj.marg.group = NULL,
  traj.marg.title = NULL,
  traj.marg.group.title = NULL,
  traj.marg.group.val = NULL
)
```
Arguments

data frame containing the variables ID, outcome, time, var.all, and all other var.

ID name of the variable representing the grouping structure specified with " (e.g., "ID" representing the unique identifier of participants).

outcome name of the time-varying variable representing the longitudinal outcome speci-
fied with " (e.g., "outcome").

time name of the variable representing the timescale specified with " (e.g., "time"),
which can be negative or positive.

var.all optional vector indicating the name of the variable(s) that the four main param-
eters of the model will be adjusted to (e.g. var.all=c("X1","X2")). Default to NULL.

var.first.level

var.last.level

var.midpoint

var.Hslope

start

plot.xlabel optional text for the title of the x-axis of all plots

plot.ylabel optional text for the title of the y-axis of all plots

traj.marg optional logical indicating if the marginal estimated trajectory should be plotted

traj.marg.group

traj.marg.title

traj.marg.group.title
traj.marg.group.val
optional vector that can be used when traj.marg.group receives a quantitative variable and that allows to manually specify two percentile values to be considered for contrasting the traj.marg.group. The two values must be between 0 and 1 (e.g., traj.marg.group.val=c(0.2,0.8); for percentiles 20th and 80th). Default to 10th and 90th percentiles (i.e., traj.marg.group.val=c(0.1,0.9)).

Details

CAUTIONS REGARDING THE USE OF THE FUNCTION

traj.marg: if "TRUE", this argument automatically plots the estimated marginal trajectories of the longitudinal outcome for the most common profile of covariates, if any (i.e., ref "1" for binary variables and mean values for continuous variables). Thus, users must ensure that continuous variables are centered on the mean.

Value

An object of class SaemixObject (from the existing saemix R package) containing the results of the fit of the data by the SMM. The nlive.smm function automatically provides the standard saemix output, including the fixed effects estimates, the variance of random effects, and Likelihood of the fitted model. The outputs are printed on the terminal and the numerical and graphical outputs are stored in a directory.

Author(s)

Maude Wagner, Ana W. Capuano, Emmanuelle Comets
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References


Examples

```r
### Fitting a sigmoidal mixed model - with no covariate
## Not run:
head(dataCog)
requireNamespace("nlraa")
smm.fit = nlive.smm(dataset=dataCog, ID="ID", outcome="cognition", time="time")
## End(Not run)
### plot(smm.fit): diagnostic plots to assess the goodness-of-fit of smm.fit
### psi(smm.fit): estimates of individual parameters
```
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