

# Package ‘flassomsm’

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**Type** Package

**Title** Penalized Estimation for Multi-State Models with Lasso and Fused Penalties

**Version** 0.1.0

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**Description** Provides a suite of methods for detecting influential subjects in longitudinal datasets, particularly when observations occur at irregular time points. The methods identify individuals whose response trajectories deviate significantly from the population pattern, enabling detection of anomalies or subjects exerting undue influence on model outcomes.

**Imports** dplyr, corpcor, future, future.apply, glmnet, mstate,numDeriv, penalized, progress, progressr, survival

**Suggests** ggplot2, rlang, mice

**License** GPL-3

**Encoding** UTF-8

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**RoxygenNote** 7.3.3

**NeedsCompilation** no

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covselec	<i>covselec</i>
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## Description

This function is used for state-wise weighted biomarker selection for both lasso and fused type penalty and is applicable for a multi-state model encompassing finite number of states and transitions.

## Usage

```
covselec(
  data,
  time_cols,
  status_cols,
  covariate_range,
  alphas,
  lambdas,
  method = "lasso",
  p_cut = 0.2,
  verbose = TRUE
)
```

## Arguments

<code>data</code>	Multi state dataset with multiple state and time column in the data
<code>time_cols</code>	time-to-event columns for each state in a MSM
<code>status_cols</code>	status columns for corresponding states in a MSM
<code>covariate_range</code>	range of high-dimensional biomarkers in the MSM dataset
<code>alphas</code>	penalty parameter for lasso type penalty
<code>lambdas</code>	penalty parameter for fused type penalty
<code>method</code>	method to be selected for covariate selection either "lasso" or "fused"
<code>p_cut</code>	association between variables
<code>verbose</code>	Logical indicating whether to print progress messages

**Details**

This function deals with biomarker selection for each state of a multi-state model each phase involves selecting significant biomarkers for that state from two sets: one comprising covariates from the preceding state, and another consisting of all covariates from the current state that were previously unselected. If the total number of biomarkers is referred to as the overall count, and each state in a multi-state model has its own number of selected biomarkers, then in a model with four states, the number of selected biomarkers for the fourth state is determined using a weighted combination. Specifically, it depends on the number of biomarkers selected in the third state, a modified set from the second state, another modified set from the first state

**Value**

list containing selected biomarkers for each state

**Author(s)**

Atanu Bhattacharjee, Gajendra Kumar Vishwakarma, Abhipsa Tripathy

**Examples**

```
##
set.seed(123)
covselec(data= highDmsm, time_cols = c("state1", "state2", "state3"),
status_cols = c("status1", "status2", "status3"),
covariate_range = 8:107, alphas=c(0.40, 0.45, 0.60),
lambdas = c(0.1, 0.15, 0.20), method = "lasso", p_cut = 0.2, verbose = TRUE)
##
```

---

flassomsm

*flassomsm*

---

**Description**

Fits a penalized regression model with combined Fusedlasso penalty using hybrid algorithm

**Usage**

```
flassomsm(
  msdata,
  X,
  p,
  lambda_lasso,
  lambda_fused,
  tol_outer = 1e-04,
  max_outer = 50,
  rho = 1,
  tol_admm = 1e-04,
  max_admm = 100,
```

```

    trace = TRUE,
    MSM_profile = FALSE,
    use_parallel = TRUE
  )

```

### Arguments

<code>msdata</code>	is a multi-state model in extended form having columns Tstart,Tstop,trans (covariates expanded transition wise)
<code>X</code>	expanded covariate matrix of the msdata
<code>p</code>	number of covariates in the dataset before expanding
<code>lambda_lasso</code>	parameter for lasso penalty
<code>lambda_fused</code>	parameter for fused penalty
<code>tol_outer</code>	tolerance limit in the outer loop of PIRLS algorithm to converge
<code>max_outer</code>	round of iterations until tolerance is reached for the outer loop
<code>rho</code>	augmented Lagrangian parameter
<code>tol_admm</code>	tolerance limit in the inner loop of ADMM algorithm to converge
<code>max_admm</code>	round of iterations until tolerance is reached for the inner loop
<code>trace</code>	logical triggering for status information
<code>MSM_profile</code>	logical triggering to return the results
<code>use_parallel</code>	logical flag to indicate whether to use parallel processing

### Details

This is the core function of the package. This function fits a penalized Cox-type regression model within the framework of a multi-state model. It is designed to handle transition-specific covariate effects across multiple states by incorporating a regularization approach that combines both the Lasso penalty and the Fused penalty. The penalization is of the L1 type, meaning it applies to the absolute values of the regression coefficients, encouraging sparsity in the model. Additionally, it penalizes the absolute differences between corresponding coefficients across different transitions, promoting similarity or grouping of effects across transitions when appropriate. This dual-penalty structure enables both variable selection and smoothing of covariate effects across related transitions, which is particularly useful in complex multi-state settings where covariate effects may share underlying patterns but still exhibit transition-specific behaviors. The parameters are estimated using a hybrid algorithm technique combining PIRLS and ADMM together.

### Value

A list with elements like matrix of estimated beta coefficients along with standard error and p value, number of iterations, aic (Akaike Information Criterion) value, gcv (GCV criterion) value and df (degrees of freedom)

### Author(s)

Atanu Bhattacharjee, Gajendra Kumar Vishwakarma, Abhipsa Tripathy

**Examples**

```
##
set.seed(123)
data(msdata_3state)
covs1 <- msdata_3state[,9:10]
flassomsm(msdata = msdata_3state,X=msdata_3state[,c(11:dim(msdata_3state)[[2]])],
p = length(covs1),lambda_lasso = 0.3,lambda_fused = 0.5,tol_outer = 1e-4,
max_outer = 50, rho = 1, tol_admm = 1e-4, max_admm = 100,trace = TRUE,
MSM_profile = FALSE)

# For 2 covariates and 3 number of transitions

# Simulate msdata_4state instead of loading from disk
msdata_4state <- simdata(seed=123,n=1000,dist="weibull",cdist="exponential",
  cparams=list(rate = 0.1),lambdas=c(0.1, 0.2, 0.3, 0.4),
  gammas=c(1.5, 2, 2.5, 2.6),beta_list=list(c(-0.05, 0.01, 0.5, 0.6),
  c(-0.03, 0.02, 0.07, 0.08),c(-0.04, 0.03, 0.04, -0.03),
  c(-0.05,0.05,0.6,0.8)),cov_means=c(0,10,2,3),cov_sds=c(1,20,5,1.05),
  trans_list=list(c(2, 3, 4, 5),c(3, 4, 5),c(4, 5), c(5), c()),
  state_names=c("Tx", "Rec", "Death", "Reldeath", "srv"))

set.seed(123)
sub_msdata_4state <- msdata_4state[msdata_4state$id %in% sample(unique(msdata_4state$id), 10), ]
covs1 <- sub_msdata_4state[,9:10]
flassomsm(msdata = sub_msdata_4state,X=sub_msdata_4state[,c(13:32)],
  p = length(covs1),lambda_lasso = 0.5,lambda_fused = 0.6,tol_outer = 1e-4,
  max_outer = 50, rho = 1, tol_admm = 1e-4, max_admm = 100,trace = TRUE,MSM_profile = FALSE)

# For 2 covariates and 10 number of transitions
##
```

---

flassomsm\_admm

*flassomsm\_admm*


---

**Description**

Fits a penalized regression model with combined Fusedlasso penalty using ADMM algorithm

**Usage**

```
flassomsm_admm(
  msdata,
  X,
  p,
  lambda_lasso,
  lambda_fused,
  tol_admm = 1e-04,
  max_admm = 100,
```

```

rho = 1,
trace = TRUE,
MSM_profile = FALSE
)

```

### Arguments

msdata	is a multi-state model in extended form having columns Tstart,Tstop,trans (covariates expanded transition wise)
X	expanded covariate matrix of the msdata
p	number of covariates in the dataset before expanding
lambda_lasso	parameter for lasso penalty
lambda_fused	parameter for fused penalty
tol_admm	tolerance limit in the algorithm to stop
max_admm	maximum number of iterations reached
rho	augmented Lagrangian parameter
trace	logical triggering for status information
MSM_profile	logical triggering to return the results

### Details

This function fits a penalized Cox type regression model to a multi-state setting, where the penalty is a combination of Lasso penalty and Fused penalty. It applies L1 type penalization with the penalty applied to absolute transition-specific effects and pairwise difference between the corresponding transition effects and alternating direction method of multipliers (ADMM) algorithm.

### Value

A list with elements like matrix of estimated beta coefficients along with standard error and p value,number of iterations, aic (Akaike Information Criterion) value, gcv (GCV criterion) value and df (degrees of freedom)

### Author(s)

Atanu Bhattacharjee,Gajendra Kumar Vishwakarma,Abhipsa Tripathy

### Examples

```

##
set.seed(123)
data(msdata_3state)
covs1 <- msdata_3state[,9:10]
flassomsm_admm(msdata = msdata_3state,X=msdata_3state[,c(11:dim(msdata_3state)[[2]])],
p = length(covs1),lambda_lasso = 0.3,lambda_fused = 0.5,tol_admm = 1e-4,max_admm = 10,
rho = 1, trace = TRUE, MSM_profile = FALSE)

# For 2 covariates and 3 number of transitions

```

```

# Simulate msdata_4state instead of loading from disk
msdata_4state <- simdata(seed=123,n=1000,dist="weibull",cdist="exponential",
  cparams=list(rate = 0.1),lambdas=c(0.1, 0.2, 0.3, 0.4),
  gammas=c(1.5, 2, 2.5, 2.6),beta_list=list(c(-0.05, 0.01, 0.5, 0.6),
  c(-0.03, 0.02, 0.07, 0.08)),c(-0.04, 0.03, 0.04, -0.03),
  c(-0.05, 0.05, 0.6, 0.8)),cov_means=c(0, 10, 2, 3),
  cov_sds=c(1, 20, 5, 1.05),trans_list=list(c(2, 3, 4, 5),
  c(3,4,5),c(4,5),c(5),c()),state_names=c("Tx","Rec","Death","ReIdeath","srv"))
set.seed(123)
sub_msdata_4state <- msdata_4state[msdata_4state$id %in% sample(unique(msdata_4state$id), 10), ]
covs1 <- sub_msdata_4state[,9:10]
flassomsm_admm(msdata = sub_msdata_4state,X=sub_msdata_4state[,c(13:32)],
  p = length(covs1),lambda_lasso = 0.5,lambda_fused = 0.6,
  tol_admm = 1e-4,max_admm = 10,rho = 1, trace = TRUE,
  MSM_profile = FALSE)

# For 2 covariates and 10 number of transitions
##

```

---

flassomsm\_pirls

*flassomsm\_pirls*


---

## Description

Fits a penalized regression model with combined Fusedlasso penalty using PIRLS algorithm

## Usage

```

flassomsm_pirls(
  msdata,
  X,
  p,
  lambda_lasso,
  lambda_fused,
  tol_lim = 1e-04,
  max_iter = 50,
  trace = TRUE,
  MSM_profile = FALSE,
  use_parallel = TRUE
)

```

## Arguments

msdata	is a multi-state model in extended form having columns Tstart,Tstop,trans (covariates expanded transition wise)
X	expanded covariate matrix of the msdata
p	number of covariates in the dataset before expanding

lambda_lasso	parameter for lasso penalty
lambda_fused	parameter for fused penalty
tol_lim	tolerance limit in the algorithm to stop
max_iter	maximum number of iterations reached
trace	logical triggering for status information
MSM_profile	logical triggering to return the results
use_parallel	logical flag to indicate whether to use parallel processing

### Details

This function fits a penalized Cox type regression model to a multi-state model, where the penalty is a combination of Lasso penalty and Fused penalty. It implements L1 type penalization with the penalty applied to absolute transition-specific effects and pairwise difference between the corresponding transition effects.

### Value

A list with elements like matrix of estimated beta coefficients along with standard error and p value, number of iterations, aic (Akaike Information Criterion) value, gcv (GCV criterion) value and df (degrees of freedom)

### Author(s)

Atanu Bhattacharjee, Gajendra Kumar Vishwakarma, Abhipsa Tripathy

### Examples

```
##
set.seed(123)
data(msdata_3state)
covs1 <- msdata_3state[,9:10]
flassomsm_pirls(msdata = msdata_3state, X=msdata_3state[,c(11:dim(msdata_3state)[[2]])],
p = length(covs1), lambda_lasso = 0.3, lambda_fused = 0.5, tol_lim = 1e-4,
max_iter = 10, trace = TRUE, MSM_profile = FALSE, use_parallel = TRUE)

# For 2 covariates and 3 number of transitions

# Simulate msdata_4state instead of loading from disk
msdata_4state <- simdata(seed=123, n=1000, dist="weibull", cdist="exponential",
  cparams=list(rate = 0.1), lambdas=c(0.1, 0.2, 0.3, 0.4),
  gammas=c(1.5, 2, 2.5, 2.6), beta_list=list(c(-0.05, 0.01, 0.5, 0.6),
  c(-0.03, 0.02, 0.07, 0.08), c(-0.04, 0.03, 0.04, -0.03),
  c(-0.05, 0.05, 0.6, 0.8)), cov_means=c(0, 10, 2, 3), cov_sds=c(1, 20, 5, 1.05),
  trans_list=list(c(2, 3, 4, 5), c(3, 4, 5), c(4, 5), c(5), c()),
  state_names=c("Tx", "Rec", "Death", "Reldeath", "srv"))

set.seed(123)
sub_msdata_4state <- msdata_4state[msdata_4state$id %in% sample(unique(msdata_4state$id), 10), ]
```

```

covs1 <- sub_msdata_4state[,9:10]
flassomsm_pirls(msdata = sub_msdata_4state,X=sub_msdata_4state[,c(13:32)],
  p = length(covs1),lambda_lasso = 0.5,lambda_fused = 0.6, tol_lim = 1e-4,max_iter = 10,
  trace = TRUE, MSM_profile = FALSE,use_parallel = TRUE)

# For 2 covariates and 10 number of transitions
##

```

---

highDmsm

*Multi state data with high dimensional covariates*


---

### Description

Multi state data with 3 states, 100 continuous biomarkers

### Usage

```
data(highDmsm)
```

### Format

A dataframe with 500 rows and 107 columns including all the states and covariates

**id** ID of subjects

**state1** Time in days from transplantation to state-1 or last follow up

**status1** Status of state-1

**state2** Time in days from transplantation to state-2 or last follow up

**status2** Status of state-1

**state3,status3** Time in days from transplant to the respective states along with its status

**v1,...,v100** The 100 biomarkers attached to the dataset

### Examples

```
data(highDmsm)
```

---

msdata\_3state

*Short Multi state data*


---

**Description**

Simulated multi-state data with 3 states expanded in msdata format

**Usage**

```
data(msdata_3state)
```

**Format**

A dataframe with 12 rows and 2 variables expanded in wide format for 3 orders of transitions

**id** ID of subjects

**from** From which state the individual is shifting

**to** To which state the individual is shifting

**trans** Order of transition of a particular individual at a specific time

**Tstart** Starting time of a transition

**Tstop** Stop time of a transition

**time** Total time duration of a particular transition

**status** Indicator of that particular transition

**x1,x2** 2 continuous covariates originally in the dataset

**x1.1,...,x2.3** The 2 covariates expanded in 3 orders of transitions

**Examples**

```
data(msdata_3state)
```

---

msdata\_4state

*Multi state data*


---

**Description**

Simulated multi-state data with 4 states expanded in msdata format

**Usage**

```
data(msdata_4state)
```

**Format**

A dataframe with 9198 rows and 4 variables expanded in wide format for 10 orders of transitions

**id** ID of subjects

**from** From which state the individual is shifting

**to** To which state the individual is shifting

**trans** Order of transition of a particular individual at a specific time

**Tstart** Starting time of a transition

**Tstop** Stop time of a transition

**time** Total time duration of a particular transition

**status** Indicator of that particular transition

**x1,...,x4** 4 continuous covariates originally in the dataset

**x1.1,...,x4.10** The 4 covariates expanded in 10 orders of transitions

**Examples**

```
data(msdata_4state)
```

---

```
prederr
```

```
prederr
```

---

**Description**

Evaluates the predictive performance of the multi-state model

**Usage**

```
prederr(
  msdata,
  X,
  beta_est,
  times,
  state_of_interest,
  trans_matrix,
  test_fraction = 0.2,
  quick = FALSE,
  verbose = FALSE
)
```

**Arguments**

<code>msdata</code>	is a multi-state model in extended form having columns Tstart,Tstop,trans (covariates expanded transition wise)
<code>X</code>	covariate matrix of the original covariates before expanding, (for example if the dataset initially contains 4 covariates then the matrix has to be formed with the 4 covariates only and not their expanded version )
<code>beta_est</code>	estimated beta coefficients from the fitted model
<code>times</code>	time points at which prediction error is to be calculated
<code>state_of_interest</code>	the target state for which prediction accuracy is evaluated
<code>trans_matrix</code>	transition matrix initially defined for multi-state model
<code>test_fraction</code>	fraction of subjects randomly assigned to test set
<code>quick</code>	specify whether the model will run complete code or quick mode
<code>verbose</code>	Logical indicating whether to print progress messages

**Details**

This function is designed to evaluate the predictive performance of a multi-state survival model using Brier score using subject specific covariates and their estimated coefficients from a penalized regression model. It also incorporates baseline hazards for each transition from a Cox model using `msfit()` for more accurate prediction and also computes the predicted state probabilities with `probrans()`.

**Value**

Gives a list of objects like brier score at specified time points, Integrated Brier score, predicted probabilities, their true states and the time points

**Author(s)**

Atanu Bhattacharjee,Gajendra Kumar Vishwakarma,Abhipsa Tripathy

**Examples**

```
##
set.seed(123)
data(msdata_3state)
tmat_3state <- mstate::transMat(x = list(c(2, 3), c(3), c()),
                               names = c("State1", "State2", "State3"))
beta_est1 <- c(0.13, -0.16, -0.12, -0.20, -0.15, -0.55)
prederr(msdata = msdata_3state, X = msdata_3state[, 9:10], beta_est = beta_est1,
        times = seq(0.5, 1.5, length.out = 5), state_of_interest = 2,
        trans_matrix = tmat_3state, test_fraction = 0.2, quick = TRUE, verbose = TRUE)

data(msdata_4state)
set.seed(123)
sub_msdata_4state <- msdata_4state[msdata_4state$id %in% sample(unique(msdata_4state$id), 10), ]
```

```

tmat_4state <- mstate::transMat(x = list(c(2, 3, 4,5), c(3, 4, 5), c(4,5), c(5),c()),
                                names = c("Tx", "Lrc", "Fp", "Dp", "srv"))
beta_est1 <- as.numeric (c(0.13,-0.16,-0.12,-0.20,-0.15,-0.55,-0.35,-0.28,-0.34,-0.12))
times1 <- seq(0.5, 1.5, length.out = 5)
prederr(msdata = sub_msdata_4state, X = sub_msdata_4state[,9],
        beta_est = beta_est1,times = times1,state_of_interest = 2,
        trans_matrix = tmat_4state,test_fraction = 0.2,quick = TRUE,verbose = TRUE)

##

```

---

simdata

*simdata*


---

## Description

Simulation of a multi-state model with  $n$  no. of states.

## Usage

```

simdata(
  seed = 123,
  n = 1000,
  dist = "weibull",
  cdist = "exponential",
  cparams = list(rate = 0.1),
  lambdas,
  gammas,
  beta_list,
  cov_means,
  cov_sds,
  trans_list,
  state_names
)

```

## Arguments

seed	Random seed for reproducibility
n	Number of subjects
dist	distribution to follow for baseline hazard ("exponential", "weibull", "gompertz")
cdist	distribution to follow for censoring distribution ("uniform", "exponential", "weibull")
cparams	parameter vector for censoring distribution
lambdas	scale parameter of the baseline distribution
gammas	shape parameter of the baseline distribution
beta_list	a list containing coefficients for the covariates to be generated, each value corresponds to one transition

cov_means	mean value of each of the covariates
cov_sds	standard deviation of each of the covariates
trans_list	transition matrix of the multi-state model based on number of states
state_names	states of the multi-state model

### Details

This function is used for simulating a multi-state model with  $n$  no. of states and status corresponding to each state along with a number of covariates both continuous or categorical.

### Value

a multi-state dataframe with given number of states, corresponding status and the covariate vector

### Author(s)

Atanu Bhattacharjee,Gajendra Kumar Vishwakarma,Abhipsa Tripathy

### Examples

```
##
msdata_4state <- simdata(seed=123,n=1000,dist="weibull",cdist="exponential",
  cparams=list(rate = 0.1),lambdas=c(0.1, 0.2, 0.3, 0.4),
  gammas=c(1.5, 2, 2.5, 2.6),beta_list=list(c(-0.05, 0.01, 0.5, 0.6),
  c(-0.03, 0.02, 0.07, 0.08),c(-0.04, 0.03, 0.04, -0.03),
  c(-0.05, 0.05, 0.6, 0.8)),cov_means=c(0, 10, 2, 3),cov_sds=c(1,20,5,1.05),
  trans_list=list(c(2, 3, 4, 5),c(3, 4, 5),c(4, 5), c(5), c()),
  state_names=c("Tx", "Rec", "Death", "Reldeath", "srv"))
##
```

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