Package: psborrow (via r-universe)

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Title Bayesian Dynamic Borrowing with Propensity Score

Version 0.2.1

Description A tool which aims to help evaluate the effect of external
borrowing using an integrated approach described in Lewis et
al., (2019) <doi:10.1080/19466315.2018.1497533> that combines
propensity score and Bayesian dynamic borrowing methods.

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futile.logger, methods

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VignetteBuilder R.rsp

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'simu_cov.R' 'match_cov.R' 'simu_time.R' 'run_mcmc.R'
'get_summary.R' 'utils.R'

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Description

S4 Class for specifying prior distributions and predictors for MCMC methods

---

apply_mcmc   *Fit Dynamic Borrowing MCMC Model*

Description

Fit a dynamic borrowing Weibull survival model to the given dataset and extract the posterior samples using MCMC. See the user guide for more information on the model formulation. See run_mcmc() for more information on the available parameters for tuning the MCMC sampling process

Usage

```
apply_mcmc(dt, formula_cov, ...)

extract_samples(object)

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

Arguments

dt	A data.frame containing data required for modelling. See details
formula_cov	A one sided formula specifying which non-treatment covariates should be included into the model. See details
...	Additional arguments passed onto run_mcmc(). Only exception being the path argument which is not supported by this function
object	A apply_mcmc object created by apply_mcmc()

Details

`apply_mcmc():`

The `dt` data.frame must contain 1 row per subject with the following variables:

- **time** - A continuous non-zero number specifying the time that the subject had an event at
- **cnsr** - A column of 0/1's where 1 indicates that the event was censored/right truncated
- **ext** - A column of 0/1's where 1 indicates that the subject was part of the external control
- **trt** - A column of 0/1's where 1 indicates that the subject was receiving the experimental treatment

The `dt` data.frame may also contain any additional covariates to be used in the Weibull model as specified by `formula_cov`. In order to fit a valid model `formula_cov` must contain the intercept term. The formula will be automatically adjusted to include the treatment term and as such should not be included here, if you want to include a treatment interaction term this should be done by using `~ trt:covariate` and NOT via `~ trt*covariate`.

`extract_samples():`

This function can be used to extract the samples generated by `apply_mcmc()`

`summary():`

This function provides summary statistics about the samples generated by `apply_mcmc()`

Extracted Samples:

The extracted samples can be roughly defined as follows (see the user guide for full details):

- `HR_cc_hc` - The hazard ratio between the concurrent control arm and the historical control arm. This can be be thought of as the ratio of the scale parameter between the baseline trial distribution and the baseline external control distribution. This is equivalent to `exp(alpha[2] - alpha[1])`
- `HR_trt_cc` - The hazard ratio between the treatment arm and the concurrent control arm. This is equivalent to `exp(beta_trt)`
- `alpha[1]` - The shape parameter for the trial's baseline distribution
- `alpha[2]` - The shape parameter for the historical control's baseline distribution
- `beta_trt` - The log-hazard ratio for the treatment effect. This is equivalent to `log(HR_trt_cc)`
- `beta_<var>` - The log-hazard ratio for any other covariate provided to the model via `formula_cov`
- `r0` - The scale parameter for the baseline distribution of both the trial and the historical control
- `tau/sigma` - The precision/variance for `alpha[1]` i.e. controls how much information is borrowed from the historical control arm

---

`c,.covClass-method`   *Concatenate multiple* `.covClass`s *classes*

Description

Concatenate multiple `.covClass`s classes

Usage

```
## S4 method for signature '.covClass'
c(x, ...)
```

Arguments

x	A .covClasss class with covariate information generated in [set_cov](#)
...	Other .covClasss classes with covariate information generated in [set_cov](#)

Value

A vector of .covClasss classes

Examples

```
# combine two sets of covariates
covset1 = set_cov(n_cat = 2, n_cont = 0, mu_int = 0, mu_ext = 0, var = 1)
covset2 = set_cov(n_cat = 0, n_cont = 1, mu_int = 62, mu_ext = 65, var = 11)
cov_list = c(covset1, covset2)
```

---

c,.priorClass-method   *Concatenate multiple* .priorClasss *class*

Description

Concatenate multiple .priorClasss class

Usage

```
## S4 method for signature '.priorClass'
c(x, ...)
```

Arguments

x	A .priorClasss class with prior distribution information generated in [set_prior](#)
...	A .priorClasss class with prior distribution information generated in [set_prior](#)

Value

A vector of .priorClasss classes

---

fix_col_names   *Fix Column Names*

Description

Utility function to make the mcmc column names more human friendly

Usage

```
fix_col_names(x, column_names)
```

Arguments

x	a mcmc results object created by add_mcmc()
column_names	The names to change the beta columns to

---

get_summary   *Generate summary statistics of a simulation scenario*

Description

Generate summary statistics of a simulation scenario

Usage

```
get_summary(dt)
```

Arguments

dt	a data.frame containing summary statistics for the posterior samples from each simulation

Value

a data.frame containing the mean and sd of posterior HR between treatment and control arm, the posterior mean and sd of HR between internal control and external control arm, reject rate, variance, bias and mse of the simulation set

---

is_psborrow_dev *Check if user is in psborrow development environment*

Description

Simple function which leverages the DESCRIPTION file to check if the user is in a development environment for psborrow.

Usage

```
is_psborrow_dev()
```

Value

TRUE/FALSE flag (TRUE = in development environment)

---

match_cov *Match*

Description

Match

Usage

```
match_cov(dt, match)
```

Arguments

dt   a list of `matrix`

match   A vector of covariates name to match on

Value

a list of `matrix` containing matched cohort information

Examples

```
# match internal and external trial data using different covariates
smp = set_n(ssC = 140, ssE = 275, ssExt = 100)
covset1 = set_cov(n_cat = 2, n_cont = 0, mu_int = 0, mu_ext = 0, var = 1)
covset2 = set_cov(n_cat = 0, n_cont = 1, mu_int = 62, mu_ext = 65, var = 11)
cObj = c(covset1, covset2)
sample_cov <-
  simu_cov(ssObj = smp, covObj = cObj, HR = 1, driftHR = 1.2, nsim = 2)

# match on covariates 1 and 2
```

```
match_cov(dt = sample_cov, match = c("cov1", "cov2"))

# match on all 3 covariates
match_cov(dt = sample_cov, match = c("cov1", "cov2", "cov3"))
```

---

plot_bias   *Plot bias*

Description

Plot bias for each prior distribution according to selected simulation parameters

Usage

```
plot_bias(dt, HR = 1, driftHR = 1, pred = "none")
```

Arguments

dt	a data.frame containing summary statistics for the posterior samples from each simulation generated with get_summary.
HR	pre-specified HR between treatment and control arm in the internal trial for which the bias should be plotted. Must be within unique(dt$HR).
driftHR	pre-specified HR between external control arm and internal control arm for which the bias should be plotted. Must be within unique(dt$driftHR).
pred	predictors to use when fitting exponential distribution in MCMC for which the bias should be plotted. Must be within unique(dt$pred).

Value

a bar plot of class ggplot containing the bias for each prior distribution.

---

plot_hr   *Plot mean posterior hazard ratio between treatment and control*

Description

Plot mean posterior hazard ratio between treatment and control

Usage

```
plot_hr(dt, HR = 0.67, driftHR = 1, pred = "none")
```

Arguments

dt	a `data.frame` containing summary statistics for the posterior samples from each simulation generated with `get_summary`.
HR	pre-specified HR between treatment and control arm in the internal trial for which the mean posterior hazard ratio should be plotted. Must be within `unique(dt$HR)`.
driftHR	pre-specified HR between external control arm and internal control arm for which the mean posterior hazard ratio should be plotted. Must be within `unique(dt$driftHR)`.
pred	predictors to use when fitting exponential distribution in MCMC for which the mean posterior hazard ratio should be plotted. Must be within `unique(dt$pred)`.

Value

a plot of class `ggplot` containing the mean posterior hazard ratio for each prior distribution.

---

plot_mse   *Plot mean squared error (MSE)*

Description

Plot mean squared error (MSE) for each prior distribution according to selected simulation parameters

Usage

```
plot_mse(dt, HR = 1, driftHR = 1, pred = "none")
```

Arguments

dt	a `data.frame` containing summary statistics for the posterior samples from each simulation generated with `get_summary`.
HR	pre-specified HR between treatment and control arm in the internal trial for which the MSE should be plotted. Must be within `unique(dt$HR)`.
driftHR	pre-specified HR between external control arm and internal control arm for which the MSE should be plotted. Must be within `unique(dt$driftHR)`.
pred	predictors to use when fitting exponential distribution in MCMC for which the MSE should be plotted. Must be within `unique(dt$pred)`.

Value

a bar plot of class `ggplot` containing the MSE for each prior distribution.

---

plot_power   *Plot power*

Description

Plot power for each prior distribution according to selected simulation parameters

Usage

```
plot_power(dt, HR = 0.67, driftHR = 1, pred = "none")
```

Arguments

dt	a data.frame containing summary statistics for the posterior samples from each simulation generated with get_summary.
HR	pre-specified HR between treatment and control arm in the internal trial for which the power should be plotted. Must be within unique(dt$HR).
driftHR	pre-specified HR between external control arm and internal control arm for which the power should be plotted. Must be within unique(dt$driftHR).
pred	predictors to use when fitting exponential distribution in MCMC for which the power should be plotted. Must be within unique(dt$pred).

Value

a bar plot of class ggplot containing the power for each prior distribution.

---

plot_type1error   *Plot type 1 error*

Description

Plot type 1 error for each prior distribution according to selected simulation parameters

Usage

```
plot_type1error(dt, driftHR = 1, pred = "none")
```

Arguments

dt	a data.frame containing summary statistics for the posterior samples from each simulation generated with get_summary(). Must contain simulations for HR = 1.0.
driftHR	the driftHR between the external and internal control arms for which the type 1 error should be plotted. Must be within unique(dt$driftHR).
pred	the predictors used when fitting the exponential distribution in MCMC for which the type 1 error should be plotted. Must be within unique(dt$pred).

Value

a bar plot of class ggplot containing type 1 error proportions for each prior distribution.

---

ps_message   *Conditional Message*

Description

Simple wrapper function around message() that will supress printing messages if the option psborrow.quiet is set to TRUE i.e.

```
options("psborrow.quiet" = TRUE)
```

Usage

```
ps_message(...)
```

Arguments

...   Values passed onto message()

---

rej_est   *Generate summary statistics for the MCMC chains*

Description

Generate summary statistics for the MCMC chains

Usage

```
rej_est(samples)
```

Arguments

samples   an object of class mcmc.list

Value

a vector containing the mean, median, sd, reject rate for the MCMC chains

---

run_mcmc   *Run MCMC for multiple scenarios with provided data*

Description

Run MCMC for multiple scenarios with provided data

Usage

```
run_mcmc(dt, priorObj, n.chains, n.adapt, n.burn, n.iter, seed, path)
```

Arguments

dt	a list of `matrix` containing simulated time-to-events information
priorObj	an object of class `.priorClass` generated in [`set_prior`](#)
n.chains	number of parallel chains for the model
n.adapt	number of iterations for adaptation
n.burn	number of iterations discarded as burn-in
n.iter	number of iterations to monitor
seed	the seed of random number generator. Default is the first element of .Random.seed
path	file name for saving the output including folder path

Value

a `data.frame` containing summary statistics of the posterior distribution for each simulation

Examples

```
# examples in vignette
```

---

run_mcmc_p   *Run MCMC for multiple scenarios with provided data with parallel
                                  processing*

Description

Run MCMC for multiple scenarios with provided data with parallel processing

Usage

```
run_mcmc_p(
  dt,
  priorObj,
  n.chains,
  n.adapt,
  n.burn,
  n.iter,
  seed,
  path,
  n.cores = 2
)
```

Arguments

dt	a list of `matrix` containing simulated time-to-events information
priorObj	an object of class `.priorClass` generated in set_prior
n.chains	number of parallel chains for the model
n.adapt	number of iterations for adaptation
n.burn	number of iterations discarded as burn-in
n.iter	number of iterations to monitor
seed	the seed of random number generator. Default is the first element of .Random.seed
path	file name for saving the output including folder path
n.cores	number of processes to parallelize over (default = 2)

Value

a `data.frame` containing summary statistics of the posterior distribution for each simulation

Examples

```
# similar to run_mcmc
```

---

set_clin	*Specify parameters for enrollment time, drop-out pattern and analysis start time*

Description

This function allows user to specify the enrollment and drop-out rate, and the type of clinical cut-off Date. Both enrollment times and drop-out times follow piece-wise exponential distribution.

Usage

```
set_clin(gamma, e_itv, CCOD, CCOD_t, etaC, etaE, d_itv)
```

Arguments

gamma   A vector of rate of enrollment per unit of time

e_itv   A vector of duration of time periods for recruitment with rates specified in
               gamma. Note that the length of e_itv should be same length as gamma or 1
               less.

CCOD   Type of analysis start time. Analysis starts at CCOD_t months after the first
               or last patient's enrollment if CCOD = "fixed-first" or CCOD = "fixed-last"
               respectively. Analysis starts when CCOD_t events have been observed if CCOD =
               "event"

CCOD_t   Time difference between analysis start and first patient's enrollment if CCOD =
               "fixed-first". Time difference between analysis start and last patient's en-
               rollment if CCOD = "fixed-last". Number of events observed when analysis
               starts if CCOD = "event". Patients enrolled after the analysis start time are ex-
               cluded from the analysis

etaC   A vector for dropout rate per unit time for control arm

etaE   A vector for dropout rate per unit time for experimental arm. If left NULL, it uses
               the same dropout rate as eta.

d_itv   A vector of duration of time periods for dropping out the study with rates spec-
               ified in etaC and etaE. Note that the length of d_itv should be same length as
               etaC or 1 less.

Value

A .clinClass class containing information on enrollment time, drop-out pattern and analysis start
time

Examples

```
# set the operational parameter values for the trial
# analysis starts at64 time units after first patient in
set_clin(gamma = 10, e_itv = 4, etaC = 0.003,  CCOD = "fixed-first", CCOD_t = 64)

# analysis starts at 12 time units after last patient in
set_clin(gamma = 2, e_itv = 18, etaC = 0.005,  CCOD = "fixed-last", CCOD_t = 12)
```

---

set_cov   *Set up covariates*

Description

This function saves the mean, variance and covariance among covariates. For technical details, see the vignette.

Usage

```
set_cov(n_cat, n_cont, mu_int, mu_ext, var, cov, prob_int, prob_ext)
```

Arguments

n_cat	Number of binary variable. See details
n_cont	Number of continuous variable
mu_int	Mean of covariates in the internal trial. All the covariates are simulated from a multivariate normal distribution. If left NULL, it uses default value 0 for all covariates. If provided one value, this value is used for all covariates
mu_ext	Mean of covariates in the external trial. If left NULL, it uses the same mean as mu_int
var	Variance of covariates. If left NULL, it uses default value 0 for all covariates. If provided one value, it uses this value for all covariates
cov	Covariance between each pair of covariates. Covariance needs to be provided in a certain order and users are encouraged to read the example provided in the vignette. If left NULL, it uses default value 0 for all covariates. If provided one value, it uses this value for every pair of covariates
prob_int	Probability of binary covariate equalling 1 in the internal trial. If left NULL, it uses default value 0.5 for all covariates. If provided one value, it uses this value for all covariates
prob_ext	Probability of binary covariate equalling 1 in the external trial. If left NULL, it uses the same probability as prob_int

Details

Categorical variables are created by sampling a continuous variable from the multivariate normal distribution (thus respecting the correlation to other covariates specified by cov) and then applying a cut point derived from the prob_int or prob_ext quantile of said distribution i.e. for a univariate variable it would be derived as:

```
binvar <- as.numeric(rnorm(n, mu, sqrt(var)) < qnorm(prob, mu, sqrt(var)))
```

Please note that this means that the value of mu_int & mu_ext has no impact on categorical covariates and thus can be set to any value.

As an example of how this process works assume n_cat=3 and n_cont=2. First 5 variables are sampled from the multivariate normal distribution as specified by mu_int/mu_ext, var & cov. Then, the first 3 of these variables are converted to binary based on the probabilities specified by prob_int and prob_ext. This means that that the 2 continuous variables will take their mean and sd from the last 2 entries in the vectors mu_int/mu_ext and var.

Value

A .covClass class containing covariate information

---

set_event   *Set up time-to-events*

Description

Defines the model formula and distribution to be used when simulating time-to-events. Please see the user-guide for the model formulations

Usage

```
set_event(event, lambdaC, beta, shape, t_itv, change, keep)
```

Arguments

event	Distribution of time-to-events: event = "pwexp" for piece-wise exponential distribution. event = "weibull" for Weibull distribution
lambdaC	Baseline hazard rate of internal control arm. Specify a vector for piece-wise hazard with duration specified in t_itv if event = "pwexp"
beta	covariates' coefficients (i.e. log hazard ratios). Must be equal in length to the number of covariates created by simu_cov() (or less if restricted by keep) plus the number of covariates defined by change.
shape	the shape parameter of Weibull distribution if event = "weibull". NULL if event = "pwexp"
t_itv	a vector indicating interval lengths where the exponential rates provided in lambdaC apply. Note that the length of t_itv is at least 1 less than that of lambdaC and that the final value rate in lambdaC applies after time sum(t_itv). NULL if event = "weibull"
change	A list of additional derivered covariates to be used in simulating time-to-events. See details
keep	A character vector specifying which of the original covariates (i.e. those not derived via the change argument) should be included into the model to simulate time-to-events. If left unspecified all covariates will be included.

Details

The change argument is used to specify additional derived covariates to be used when simulating time-to-events. For example, let's say have 3 covariates cov1, cov2 & cov3 but that we also wish to include a new covariate that is an interaction between cov1 and cov2 as well as another covariate that is equal to the sum of cov2 and cov3; we could implement this as follows:

```
set_event(
    event = "weibull",
    shape = 0.9,
    lambdaC = 0.0135,
    beta = c(5, 3, 1, 7, 9),
    change = list(
        c("cov1", "*", "cov2"),
        c("cov2", "+", "cov3")
    )
)
```

Note that in the above example 5 values have been specified to beta, 3 for the original three covariates and 2 for the two additional derived covariates included via change.

Variables derived via change are automatically included in the model regardless of whether they are listed in keep or not. Likewise, these covariates are derived separately and not via a standard R formula, that is to say including an interaction term does not automatically include the individual fixed effects.

Value

a .eventClass class containing time-to-events information

a matrix containing simulated time-to-events information

Examples

```
# time-to-event follows a Weibull distribution
set_event(event = "weibull", shape = 0.9, lambdaC = 0.0135)

# time-to-event follows a piece-wise exponential distribution
set_event(event = "pwexp", t_itv = 1, lambdaC = c(0.1, 0.02))
```

---

set_n *Simulate external trial indicator and treatment arm indicator*

Description

This function conducts validity check and generates a matrix with two binary variables indicating

1. if the observation belongs to the external trial
2. if the observation belongs to the treatment arm.

Usage

```
set_n(ssC, ssE, ssExt)
```

Arguments

ssC	Number of observations in the internal control arm. Default is 100
ssE	Number of observations in the internal experiment arm. Default is the same number of observations as ssC
ssExt	Number of observations in the external control arm. Default is the same number of observations as ssC

Value

A matrix containing external trial indicator and treatment indicator

---

set_prior	*Specify prior distributions and predictors for MCMC methods*

Description

Specify prior distributions and predictors for MCMC methods

Usage

```
set_prior(pred, prior, r0, alpha, sigma)
```

Arguments

pred	Predictors to include in the weibull distribution. No covariates except for treatment indicator is included if pred = NULL. Only propensity score generated using a logistic regression model on all covariates and treatment indicator are included if pred = ps. All covariates and treatment indicator are included if pred = all
prior	Prior distribution for the precision parameter that controls the degree of borrowing. Half-cauchy distribution if prior = "cauchy". No external data is included in the data if prior = "no_ext". External control arm is assumed to have the same baseline hazards as internal control arm if prior = "full_ext". Other options include "gamma" and "unif"
r0	Initial values for the shape of the weibull distribution for time-to-events
alpha	Initial values for log of baseline hazard rate for external and internal control arms. Length of alpha should be 1 if prior = "full_ext" or prior = "no_ext", and equal to 2 otherwise
sigma	Initial values for precision parameter if prior = "cauchy". If left NULL, default value 0.03 is used

Value

a .priorClass class containing survival data and prior information

Examples

```
# hierachical Bayesian model with precision parameter follows a half-cauchy distribution
set_prior(pred = "none", prior = "cauchy", r0 = 1, alpha = c(0, 0), sigma = 0.03)

# hierachical Bayesian model with precision parameter follows a gamma distribution
set_prior(pred = "none", prior = "gamma", r0 = 1, alpha = c(0, 0))

# conventional Bayesian model to not borrow from external control arm
set_prior(pred = "none", prior = "no_ext", alpha = 0)

# conventional Bayesian model to fully borrow from external control arm
set_prior(pred = "none", prior = "full_ext", alpha = 0)
```

---

simu_cov *Simulate covariates*

Description

This function generates continuous and binary covariates through simulating from a multivariate normal distribution. Outcomes are further converted to binary variables using quantiles of the normal distribution calculated from the probability provided. Then the covariates are added to the external trial and treatment arm indicators.

Usage

```
simu_cov(ssObj, covObj, driftHR, HR, nsim, seed, path)
```

Arguments

ssObj	an object of class .covClass generated in [set_n](#)
covObj	an object of class .covClass generated in [set_cov](#)
driftHR	hazard ratio of external control and internal control arms
HR	a list of hazard ratio of treatment and control arms
nsim	number of simulation. Default is 5
seed	the seed of R's random number generator. Default is the first element of .Random.seed
path	file name for saving the output including folder path

Value

a list of matrix containing simulated covariates information

Examples

```
# simulate patient-level data with 1 continuous covariate
sample = set_n(ssC = 10, ssE = 20, ssExt = 40)
cov1 = set_cov(n_cat = 0, n_cont = 1, mu_int = 0, mu_ext = 0, var = 1)
simu_cov(ssObj = sample, covObj = cov1, HR = 0.5, driftHR = 1, nsim = 2)

# simulate patient-level data with 1 binary and 2 continuous covariate
cov2 = set_cov(n_cat = 1, n_cont = 2, mu_int = 0, mu_ext = 0, var = 1,
               cov = 0.3, prob_int = 0.2, prob_ext = 0.3)
simu_cov(ssObj = sample, covObj = cov2, HR = 0.5, driftHR = 1, nsim = 2)
```

---

simu_time   *Simulate time-to-events for multiple scenarios*

Description

Simulate time-to-events for multiple scenarios

Usage

```
simu_time(dt, eventObj, clinInt, clinExt, seed, path)
```

Arguments

dt	a list of matrix generated in simu_cov containing simulated covariates information
eventObj	an object of class .eventClass generated in set_event including event information
clinInt	an object of class .clinClass generated in set_clin including internal trial information
clinExt	an object of class .clinClass generated in set_clin including external trial information
seed	the seed of R's random number generator. Default is the first element of .Random.seed
path	file name for saving the output including folder path

Value

a list of matrix containing simulated time-to-events information

Examples

```
# simulate patient-level data without covariates
# simulate survival time following weibull distribution

# simulate trial indicator and set hazard ratios
sample = set_n(ssC = 10, ssE = 20, ssExt = 40)
sample_hr <- simu_cov(ssObj = sample, HR = 1, driftHR=c(1,1.2), nsim = 10)

# enrollment pattern, drop-out, analysis start time
c_int = set_clin(gamma = 2, e_itv = 10, etaC = 0.5,  CCOD = "fixed-first", CCOD_t = 64)
c_ext = c_int

# simulate time-to-event with a weibull distribution
evt1 <- set_event(event = "weibull", shape = 0.8, lambdaC = 0.01)
simu_time(dt = sample_hr, eventObj = evt1, clinInt = c_int, clinExt = c_ext)

# simulate time-to-event with an exponential distribution
evt2 <- set_event(event = "pwexp", t_itv = 1, lambdaC = c(0.1, 0.02))
simu_time(dt = sample_hr, eventObj = evt2, clinInt = c_int, clinExt = c_int)
```

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