

Package ‘bayesDP’

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Bayesian discount prior function for 1 arm and 2 arm clinical trials.

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BugReports <https://github.com/donaldmusgrove/bayesDP/issues>

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alpha_discount	<i>Bayesian Discount Prior: Historical Data Weight (alpha)</i>
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Description

alpha_discount can be used to estimate the weight applied to historical data in the context of a one- or two-arm clinical trial. alpha_discount is not used internally but is given for educational purposes.

Usage

```
alpha_discount(p_hat = NULL, discount_function = "weibull", alpha_max = 1,
  weibull_scale = 0.135, weibull_shape = 3)
```

Arguments

p_hat	scalar. The posterior probability of a stochastic comparison. This value can be the output of posterior_probability or a value between 0 and 1.
discount_function	character. Specify the discount function to use. Currently supports weibull, scaledweibull, and identity. The discount function scaledweibull scales the output of the Weibull CDF to have a max value of 1. The identity discount function uses the posterior probability directly as the discount weight. Default value is "weibull".
alpha_max	scalar. Maximum weight the discount function can apply. Default is 1.
weibull_scale	scalar. Scale parameter of the Weibull discount function used to compute alpha, the weight parameter of the historical data. Default value is 0.135.

`weibull_shape` scalar. Shape parameter of the Weibull discount function used to compute alpha, the weight parameter of the historical data. Default value is 3.

Details

This function is not used internally but is given for educational purposes. Given inputs `p_hat`, `discount_function`, `alpha_max`, `weibull_shape`, and `weibull_scale` the output is the weight that would be applied to historical data in the context of a one- or two-arm clinical trial.

Value

`alpha_discount` returns an object of class "alpha_discount".

An object of class `alpha_discount` contains the following:

`alpha_hat` scalar. The historical data weight.

References

Haddad, T., Himes, A., Thompson, L., Irony, T., Nair, R. MDIC Computer Modeling and Simulation working group.(2017) Incorporation of stochastic engineering models as prior information in Bayesian medical device trials. *Journal of Biopharmaceutical Statistics*, 1-15.

Examples

```
alpha_discount(0.5)
```

```
alpha_discount(0.5, discount_function="identity")
```

 bdpbinomial

Bayesian Discount Prior: Binomial counts

Description

`bdpbinomial` is used for estimating posterior samples from a binomial outcome where an informative prior is used. The prior weight is determined using a discount function. This code is modeled after the methodologies developed in Haddad et al. (2017).

Usage

```
bdpbinomial(y_t = NULL, N_t = NULL, y0_t = NULL, N0_t = NULL,
            y_c = NULL, N_c = NULL, y0_c = NULL, N0_c = NULL,
            discount_function = "weibull", alpha_max = 1, fix_alpha = FALSE,
            a0 = 1, b0 = 1, number_mcmc = 10000, weibull_scale = 0.135,
            weibull_shape = 3, method = "fixed", compare = TRUE)
```

Arguments

<code>y_t</code>	scalar. Number of events for the current treatment group.
<code>N_t</code>	scalar. Sample size of the current treatment group.
<code>y0_t</code>	scalar. Number of events for the historical treatment group.
<code>N0_t</code>	scalar. Sample size of the historical treatment group.
<code>y_c</code>	scalar. Number of events for the current control group.
<code>N_c</code>	scalar. Sample size of the current control group.
<code>y0_c</code>	scalar. Number of events for the historical control group.
<code>N0_c</code>	scalar. Sample size of the historical control group.
<code>discount_function</code>	character. Specify the discount function to use. Currently supports <code>weibull</code> , <code>scaledweibull</code> , and <code>identity</code> . The discount function <code>scaledweibull</code> scales the output of the Weibull CDF to have a max value of 1. The <code>identity</code> discount function uses the posterior probability directly as the discount weight. Default value is <code>"weibull"</code> .
<code>alpha_max</code>	scalar. Maximum weight the discount function can apply. Default is 1. For a two-arm trial, users may specify a vector of two values where the first value is used to weight the historical treatment group and the second value is used to weight the historical control group.
<code>fix_alpha</code>	logical. Fix alpha at <code>alpha_max</code> ? Default value is <code>FALSE</code> .
<code>a0</code>	scalar. Prior value for the beta rate. Default is 1.
<code>b0</code>	scalar. Prior value for the beta rate. Default is 1.
<code>number_mcmc</code>	scalar. Number of Monte Carlo simulations. Default is 10000.
<code>weibull_scale</code>	scalar. Scale parameter of the Weibull discount function used to compute alpha, the weight parameter of the historical data. Default value is 0.135. For a two-arm trial, users may specify a vector of two values where the first value is used to estimate the weight of the historical treatment group and the second value is used to estimate the weight of the historical control group.
<code>weibull_shape</code>	scalar. Shape parameter of the Weibull discount function used to compute alpha, the weight parameter of the historical data. Default value is 3. For a two-arm trial, users may specify a vector of two values where the first value is used to estimate the weight of the historical treatment group and the second value is used to estimate the weight of the historical control group.
<code>method</code>	character. Analysis method with respect to estimation of the weight parameter alpha. Default value <code>"fixed"</code> estimates alpha once and holds it fixed throughout the analysis. Alternative method <code>"mc"</code> estimates alpha for each Monte Carlo iteration. See the <code>bdpbinomial</code> vignette <code>vignette("bdpbinomial-vignette", package="bayesDP")</code> for more details.
<code>compare</code>	logical. Should a comparison object be included in the fit? For a one-arm analysis, the comparison object is simply the posterior chain of the treatment group parameter. For a two-arm analysis, the comparison object is the posterior chain of the treatment effect that compares treatment and control. If <code>compare=TRUE</code> , the comparison object is accessible in the <code>final</code> slot, else the <code>final</code> slot is <code>NULL</code> . Default is <code>TRUE</code> .

Details

`bdpbinomial` uses a two-stage approach for determining the strength of historical data in estimation of a binomial count mean outcome. In the first stage, a Weibull distribution function is used as a *discount function* that defines the maximum strength of the historical data (via `weibull_shape`, `weibull_scale`, and `alpha_max`) and discounts based on disagreement with the current data. Disagreement between current and historical data is determined by stochastically comparing the respective posterior distributions under noninformative priors. With binomial data, the comparison is the probability (p) that the current count is less than the historical count. The comparison metric p is then input into the Weibull discount function and the final strength of the historical data is returned (`alpha`).

In the second stage, posterior estimation is performed where the discount function parameter, `alpha`, is used as a fixed value for all posterior estimation procedures.

To carry out a single arm (OPC) analysis, data for the current treatment (`y_t` and `N_t`) and historical treatment (`y0_t` and `N0_t`) must be input. The results are then based on the posterior distribution of the current data augmented by the historical data.

To carry out a two-arm (RCT) analysis, data for the current treatment and at least one of current or historical control data must be input. The results are then based on the posterior distribution of the difference between current treatment and control, augmented by available historical data.

For more details, see the `bdpbinomial` vignette:
`vignette("bdpbinomial-vignette", package="bayesDP")`

Value

`bdpbinomial` returns an object of class "bdpbinomial". The functions `summary` and `print` are used to obtain and print a summary of the results, including user inputs. The `plot` function displays visual outputs as well.

An object of class `bdpbinomial` is a list containing at least the following components:

`posterior_treatment` list. Entries contain values related to the treatment group:

- `alpha_discount` numeric. Alpha value, the weighting parameter of the historical data.
- `p_hat` numeric. The posterior probability of the stochastic comparison between the current and historical data.
- `posterior` vector. A vector of length `number_mcmc` containing posterior Monte Carlo samples of the event rate of the treatment group. If historical treatment data is present, the posterior incorporates the weighted historical data.
- `posterior_flat` vector. A vector of length `number_mcmc` containing Monte Carlo samples of the event rate of the current treatment group under a flat/non-informative prior, i.e., no incorporation of the historical data.
- `prior` vector. If historical treatment data is present, a vector of length `number_mcmc` containing Monte Carlo samples of the event rate of the historical treatment group under a flat/non-informative prior.

`posterior_control` list. Similar entries as `posterior_treatment`. Only present if a control group is specified.

`final` list. Contains the final comparison object, dependent on the analysis type:

- One-arm analysis: vector. Posterior chain of binomial proportion.

- Two-arm analysis: vector. Posterior chain of binomial proportion difference comparing treatment and control groups.

args1 list. Entries contain user inputs. In addition, the following elements are output:

- arm2 binary indicator. Used internally to indicate one-arm or two-arm analysis.
- intent character. Denotes current/historical status of treatment and control groups.

References

Haddad, T., Himes, A., Thompson, L., Irony, T., Nair, R. MDIC Computer Modeling and Simulation working group.(2017) Incorporation of stochastic engineering models as prior information in Bayesian medical device trials. *Journal of Biopharmaceutical Statistics*, 1-15.

See Also

[summary](#), [print](#), and [plot](#) for details of each of the supported methods.

Examples

```
# One-arm trial (OPC) example
fit <- bdpbinomial(y_t      = 10,
                  N_t      = 500,
                  y0_t     = 25,
                  N0_t     = 250)
```

```
summary(fit)
print(fit)
## Not run:
plot(fit)
```

```
## End(Not run)
```

```
# Two-arm (RCT) example
fit2 <- bdpbinomial(y_t = 10,
                  N_t = 500,
                  y0_t = 25,
                  N0_t = 250,
                  y_c = 8,
                  N_c = 500,
                  y0_c = 20,
                  N0_c = 250)
```

```
summary(fit2)
print(fit2)
## Not run:
plot(fit2)
```

```
## End(Not run)
```

Description

bdplm is used to estimate the treatment effect in the presence of covariates using the regression analysis implementation of the Bayesian discount prior. This function is currently a barebones implementation and does not support summary, plot, or print methods. Currently, the function only supports a two-arm clinical trial where all of current and historical treatment and current and historical control data are present.

Usage

```
bdplm(formula = formula, data = data, data0 = NULL,
      prior_treatment_effect = NULL, prior_control_effect = NULL,
      prior_treatment_sd = NULL, prior_control_sd = NULL,
      prior_covariate_effect = 0, prior_covariate_sd = 10000,
      number_mcmc_alpha = 5000, number_mcmc_sigmagrid = 5000,
      number_mcmc_sigma = 100, number_mcmc_beta = 10000,
      discount_function = "weibull", alpha_max = 1, fix_alpha = FALSE,
      weibull_scale = 0.135, weibull_shape = 3, method = "fixed")
```

Arguments

formula	an object of class "formula." See "Details" for more information, including specification of treatment data indicators.
data	a data frame containing the current data variables in the model. A column named treatment must be present; treatment must be binary and indicate treatment group vs. control group.
data0	a data frame containing the historical data variables in the model. The column labels of data and data0 must match.
prior_treatment_effect	scalar. The historical adjusted treatment effect. If left NULL, value is estimated from the historical data.
prior_control_effect	scalar. The historical adjusted control effect. If left NULL, value is estimated from the historical data.
prior_treatment_sd	scalar. The standard deviation of the historical adjusted treatment effect. If left NULL, value is estimated from the historical data.
prior_control_sd	scalar. The standard deviation of the historical adjusted control effect. If left NULL, value is estimated from the historical data.

prior_covariate_effect	vector. The prior mean(s) of the covariate effect(s). Default value is zero. If a single value is input, the the scalar is repeated to the length of the input covariates. Otherwise, care must be taken to ensure the length of the input matches the number of covariates.
prior_covariate_sd	vector. The prior standard deviation(s) of the covariate effect(s). Default value is 1e4. If a single value is input, the the scalar is repeated to the length of the input covariates. Otherwise, care must be taken to ensure the length of the input matches the number of covariates.
number_mcmc_alpha	scalar. Number of Monte Carlo simulations for estimating the historical data weight. Default is 5000.
number_mcmc_sigmagrid	scalar. Grid size for computing sigma. Default is 5000. See "Details" for more information.
number_mcmc_sigma	scalar. Number of Monte Carlo simulations for estimating sigma. Default is 1000. See "Details" for more information.
number_mcmc_beta	scalar. Number of Monte Carlo simulations for estimating beta, the vector of regression coefficients. Default is 10000.
discount_function	character. Specify the discount function to use. Currently supports weibull, scaledweibull, and identity. The discount function scaledweibull scales the output of the Weibull CDF to have a max value of 1. The identity discount function uses the posterior probability directly as the discount weight. Default value is "weibull".
alpha_max	scalar. Maximum weight the discount function can apply. Default is 1. Users may specify a vector of two values where the first value is used to weight the historical treatment group and the second value is used to weight the historical control group.
fix_alpha	logical. Fix alpha at alpha_max? Default value is FALSE.
weibull_scale	scalar. Scale parameter of the Weibull discount function used to compute alpha, the weight parameter of the historical data. Default value is 0.135. Users may specify a vector of two values where the first value is used to estimate the weight of the historical treatment group and the second value is used to estimate the weight of the historical control group.
weibull_shape	scalar. Shape parameter of the Weibull discount function used to compute alpha, the weight parameter of the historical data. Default value is 3. Users may specify a vector of two values where the first value is used to estimate the weight of the historical treatment group and the second value is used to estimate the weight of the historical control group.
method	character. Analysis method with respect to estimation of the weight paramter alpha. Default value "fixed" estimates alpha once and holds it fixed throughout the analysis. Alternative method "mc" estimates alpha for each Monte Carlo iteration. See the the bdplm vignette vignette("bdplm-vignette", package="bayesDP") for more details.

Details

bdplm uses a two-stage approach for determining the strength of historical data in estimation of an adjusted mean or covariate effect. In the first stage, a Weibull distribution function is used as a *discount function* that defines the maximum strength of the historical data (via `weibull_shape`, `weibull_scale`, and `alpha_max`) and discounts based on disagreement with the current data. Disagreement between current and historical data is determined by stochastically comparing the respective posterior distributions under noninformative priors. Here with a two-arm regression analysis, the comparison is the probability (p) that the covariate effect of an historical data indicator is significantly different from zero. The comparison metric p is then input into the Weibull discount function and the final strength of the historical data is returned (`alpha`).

In the second stage, posterior estimation is performed where the discount function parameter, `alpha`, is used to weight the historical data effects.

The formula must include an intercept and both `data` and `data0` must be present. The column names of `data` and `data0` must match. See examples below for example usage.

The underlying model results in a marginal posterior distribution for the error variance `sigma2` that does not have a known distribution. Thus, we use a grid search to draw samples of `sigma2`. First, the marginal posterior is evaluated at a grid of `number_mcmc_sigmagrid` `sigma2` values. The bounds of the grid are taken as approximately six standard deviations from an estimate of `sigma2` using the `lm` function. Next, `number_mcmc_sigma` posterior draws of `sigma2` are made by sampling with replacement from the grid with each value having the corresponding marginal posterior probability of being selected. With posterior draws of `sigma2` in hand, we can make posterior draws of the regression coefficients.

Value

bdplm returns an object of class "bdplm".

An object of class "bdplm" is a list containing at least the following components:

`posterior` data frame. The posterior draws of the covariates, the intercept, and the treatment effect. The grid of `sigma` values are included.

`alpha_discount` vector. The posterior probability of the stochastic comparison between the current and historical data for each of the treatment and control arms. If `method="mc"`, the result is a matrix of estimates, otherwise for `method="fixed"`, the result is a vector of estimates.

`estimates` list. The posterior means and standard errors of the intercept, treatment effect, covariate effect(s) and error variance.

Examples

```
# Set sample sizes
n_t <- 30      # Current treatment sample size
n_c <- 30      # Current control sample size
n_t0 <- 80     # Historical treatment sample size
n_c0 <- 80     # Historical control sample size

# Treatment group vectors for current and historical data
treatment <- c(rep(1,n_t), rep(0,n_c))
treatment0 <- c(rep(1,n_t0), rep(0,n_c0))
```

```

# Simulate a covariate effect for current and historical data
x <- rnorm(n_t+n_c, 1, 5)
x0 <- rnorm(n_t0+n_c0, 1, 5)

# Simulate outcome:
# - Intercept of 10 for current and historical data
# - Treatment effect of 34 for current data
# - Treatment effect of 30 for historical data
# - Covariate effect of 3 for current and historical data
Y <- 10 + 34*treatment + x*3 + rnorm(n_t+n_c,0,5)
Y0 <- 10 + 30*treatment0 + x0*3 + rnorm(n_t0+n_c0,0,5)

# Place data into separate treatment and control data frames and
# assign historical = 0 (current) or historical = 1 (historical)
df_ <- data.frame(Y=Y, treatment=treatment, x=x, intercept=1)
df0 <- data.frame(Y=Y0, treatment=treatment0, x=x0, intercept=1)

# Fit model using default settings
fit <- bdplm(formula=Y ~ treatment+x, data=df_, data0=df0)

# Look at estimates and discount weight
fit$estimates
fit$alpha_discount

```

bdpnormal

Bayesian Discount Prior: Gaussian mean values

Description

bdpnormal is used for estimating posterior samples from a Gaussian outcome where an informative prior is used. The prior weight is determined using a discount function. This code is modeled after the methodologies developed in Haddad et al. (2017).

Usage

```

bdpnormal(mu_t = NULL, sigma_t = NULL, N_t = NULL, mu0_t = NULL,
  sigma0_t = NULL, N0_t = NULL, mu_c = NULL, sigma_c = NULL,
  N_c = NULL, mu0_c = NULL, sigma0_c = NULL, N0_c = NULL,
  discount_function = "weibull", alpha_max = 1, fix_alpha = FALSE,
  weibull_scale = 0.135, weibull_shape = 3, number_mcmc = 10000,
  method = "fixed", compare = TRUE)

```

Arguments

mu_t	scalar. Mean of the current treatment group.
sigma_t	scalar. Standard deviation of the current treatment group.
N_t	scalar. Number of observations of the current treatment group.

<code>mu0_t</code>	scalar. Mean of the historical treatment group.
<code>sigma0_t</code>	scalar. Standard deviation of the historical treatment group.
<code>N0_t</code>	scalar. Number of observations of the historical treatment group.
<code>mu_c</code>	scalar. Mean of the current control group.
<code>sigma_c</code>	scalar. Standard deviation of the current control group.
<code>N_c</code>	scalar. Number of observations of the current control group.
<code>mu0_c</code>	scalar. Mean of the historical control group.
<code>sigma0_c</code>	scalar. Standard deviation of the historical control group.
<code>N0_c</code>	scalar. Number of observations of the historical control group.
<code>discount_function</code>	character. Specify the discount function to use. Currently supports <code>weibull</code> , <code>scaledweibull</code> , and <code>identity</code> . The discount function <code>scaledweibull</code> scales the output of the Weibull CDF to have a max value of 1. The <code>identity</code> discount function uses the posterior probability directly as the discount weight. Default value is <code>"weibull"</code> .
<code>alpha_max</code>	scalar. Maximum weight the discount function can apply. Default is 1. For a two-arm trial, users may specify a vector of two values where the first value is used to weight the historical treatment group and the second value is used to weight the historical control group.
<code>fix_alpha</code>	logical. Fix alpha at <code>alpha_max</code> ? Default value is <code>FALSE</code> .
<code>weibull_scale</code>	scalar. Scale parameter of the Weibull discount function used to compute alpha, the weight parameter of the historical data. Default value is 0.135. For a two-arm trial, users may specify a vector of two values where the first value is used to estimate the weight of the historical treatment group and the second value is used to estimate the weight of the historical control group.
<code>weibull_shape</code>	scalar. Shape parameter of the Weibull discount function used to compute alpha, the weight parameter of the historical data. Default value is 3. For a two-arm trial, users may specify a vector of two values where the first value is used to estimate the weight of the historical treatment group and the second value is used to estimate the weight of the historical control group.
<code>number_mcmc</code>	scalar. Number of Monte Carlo simulations. Default is 10000.
<code>method</code>	character. Analysis method with respect to estimation of the weight parameter alpha. Default value <code>"fixed"</code> estimates alpha once and holds it fixed throughout the analysis. Alternative method <code>"mc"</code> estimates alpha for each Monte Carlo iteration. See the <code>bdpnormal</code> vignette <code>vignette("bdpnormal-vignette", package="bayesDP")</code> for more details.
<code>compare</code>	logical. Should a comparison object be included in the fit? For a one-arm analysis, the comparison object is simply the posterior chain of the treatment group parameter. For a two-arm analysis, the comparison object is the posterior chain of the treatment effect that compares treatment and control. If <code>compare=TRUE</code> , the comparison object is accessible in the <code>final</code> slot, else the <code>final</code> slot is <code>NULL</code> . Default is <code>TRUE</code> .

Details

bdpnormal uses a two-stage approach for determining the strength of historical data in estimation of a mean outcome. In the first stage, a Weibull distribution function is used as a *discount function* that defines the maximum strength of the historical data (via `weibull_shape`, `weibull_scale`, and `alpha_max`) and discounts based on disagreement with the current data. Disagreement between current and historical data is determined by stochastically comparing the respective posterior distributions under noninformative priors. With Gaussian data, the comparison is the probability (p) that the current mean is less than the historical mean. The comparison metric p is then input into the Weibull discount function and the final strength of the historical data is returned (α).

In the second stage, posterior estimation is performed where the discount function parameter, `alpha`, is used as a fixed value for all posterior estimation procedures.

To carry out a single arm (OPC) analysis, data for the current treatment (`mu_t`, `sigma_t`, and `N_t`) and historical treatment (`mu0_t`, `sigma0_t`, and `N0_t`) must be input. The results are then based on the posterior distribution of the current data augmented by the historical data.

To carry out a two-arm (RCT) analysis, data for the current treatment and at least one of current or historical control data must be input. The results are then based on the posterior distribution of the difference between current treatment and control, augmented by available historical data.

For more details, see the `bdpnormal` vignette:
`vignette("bdpnormal-vignette", package="bayesDP")`

Value

bdpnormal returns an object of class "bdpnormal". The functions `summary` and `print` are used to obtain and print a summary of the results, including user inputs. The `plot` function displays visual outputs as well.

An object of class `bdpnormal` is a list containing at least the following components:

`posterior_treatment` list. Entries contain values related to the treatment group:

- `alpha_discount` numeric. Alpha value, the weighting parameter of the historical data.
- `p_hat` numeric. The posterior probability of the stochastic comparison between the current and historical data.
- `posterior_mu` vector. A vector of length `number_mcmc` containing the posterior mean of the treatment group. If historical treatment data is present, the posterior incorporates the weighted historical data.
- `posterior_sigma2` vector. A vector of length `number_mcmc` containing the posterior variance of the treatment group. If historical treatment data is present, the posterior incorporates the weighted historical data.
- `posterior_flat_mu` vector. A vector of length `number_mcmc` containing Monte Carlo samples of the mean of the current treatment group under a flat/non-informative prior, i.e., no incorporation of the historical data.
- `posterior_flat_sigma2` vector. A vector of length `number_mcmc` containing Monte Carlo samples of the standard deviation of the current treatment group under a flat/non-informative prior, i.e., no incorporation of the historical data.
- `prior_mu` vector. If historical treatment data is present, a vector of length `number_mcmc` containing Monte Carlo samples of the mean of the historical treatment group under a flat/non-informative prior.

- `prior_sigma2` vector. If historical treatment data is present, a vector of length `number_mcmc` containing Monte Carlo samples of the standard deviation of the historical treatment group under a flat/non-informative prior.

`posterior_control` list. Similar entries as `posterior_treatment`. Only present if a control group is specified.

`final` list. Contains the final comparison object, dependent on the analysis type:

- One-arm analysis: vector. Posterior chain of the mean.
- Two-arm analysis: vector. Posterior chain of the mean difference comparing treatment and control groups.

`args1` list. Entries contain user inputs. In addition, the following elements are output:

- `arm2` binary indicator. Used internally to indicate one-arm or two-arm analysis.
- `intent` character. Denotes current/historical status of treatment and control groups.

References

Haddad, T., Himes, A., Thompson, L., Irony, T., Nair, R. MDIC Computer Modeling and Simulation working group.(2017) Incorporation of stochastic engineering models as prior information in Bayesian medical device trials. *Journal of Biopharmaceutical Statistics*, 1-15.

See Also

[summary](#), [print](#), and [plot](#) for details of each of the supported methods.

Examples

```
# One-arm trial (OPC) example
fit <- bdpnormal(mu_t = 30, sigma_t = 10, N_t = 250,
               mu0_t = 50, sigma0_t = 5, N0_t = 250)

summary(fit)
## Not run:
plot(fit)

## End(Not run)

# Two-arm (RCT) example
fit2 <- bdpnormal(mu_t = 30, sigma_t = 10, N_t = 250,
                 mu0_t = 50, sigma0_t = 5, N0_t = 250,
                 mu_c = 25, sigma_c = 10, N_c = 250,
                 mu0_c = 50, sigma0_c = 5, N0_c = 250)

summary(fit2)
## Not run:
plot(fit2)

## End(Not run)
```

Description

bdpsurvival is used to estimate the survival probability (single arm trial; OPC) or hazard ratio (two-arm trial; RCT) for right-censored data using the survival analysis implementation of the Bayesian discount prior. This code is modeled after the methodologies developed in Haddad et al. (2017).

Usage

```
bdpsurvival(formula = formula, data = data, breaks = NULL, a0 = 0.1,
  b0 = 0.1, surv_time = NULL, discount_function = "weibull",
  alpha_max = 1, fix_alpha = FALSE, number_mcmc = 10000,
  weibull_scale = 0.135, weibull_shape = 3, method = "fixed",
  compare = TRUE)
```

Arguments

formula	an object of class "formula." Must have a survival object on the left side and exactly two inputs on the right side: treatment and historical. See "Details" for more information.
data	data frame. A data frame with columns 'time', 'status', 'treatment', and historical.' See "Details" for required structure.
breaks	vector. Breaks (interval starts) used to compose the breaks of the piecewise exponential model. Do not include zero. Default breaks are the quantiles of the input times.
a0	scalar. Prior value for the gamma shape of the piecewise exponential hazards. Default is 0.1.
b0	scalar. Prior value for the gamma rate of the piecewise exponential hazards. Default is 0.1.
surv_time	scalar. Survival time of interest for computing the probability of survival for a single arm (OPC) trial. Default is overall, i.e., current+historical, median survival time.
discount_function	character. Specify the discount function to use. Currently supports weibull, scaledweibull, and identity. The discount function scaledweibull scales the output of the Weibull CDF to have a max value of 1. The identity discount function uses the posterior probability directly as the discount weight. Default value is "weibull".
alpha_max	scalar. Maximum weight the discount function can apply. Default is 1. For a two-arm trial, users may specify a vector of two values where the first value is used to weight the historical treatment group and the second value is used to weight the historical control group.

<code>fix_alpha</code>	logical. Fix alpha at <code>alpha_max</code> ? Default value is FALSE.
<code>number_mcmc</code>	scalar. Number of Monte Carlo simulations. Default is 10000.
<code>weibull_scale</code>	scalar. Scale parameter of the Weibull discount function used to compute alpha, the weight parameter of the historical data. Default value is 0.135. For a two-arm trial, users may specify a vector of two values where the first value is used to estimate the weight of the historical treatment group and the second value is used to estimate the weight of the historical control group.
<code>weibull_shape</code>	scalar. Shape parameter of the Weibull discount function used to compute alpha, the weight parameter of the historical data. Default value is 3. For a two-arm trial, users may specify a vector of two values where the first value is used to estimate the weight of the historical treatment group and the second value is used to estimate the weight of the historical control group.
<code>method</code>	character. Analysis method with respect to estimation of the weight parameter alpha. Default value "fixed" estimates alpha once and holds it fixed throughout the analysis. Alternative method "mc" estimates alpha for each Monte Carlo iteration. See the <code>bdpsurvival</code> vignette <code>vignette("bdpsurvival-vignette", package="bayesDP")</code> for more details.
<code>compare</code>	logical. Should a comparison object be included in the fit? For a one-arm analysis, the comparison object is simply the posterior chain of the treatment group parameter. For a two-arm analysis, the comparison object is the posterior chain of the treatment effect that compares treatment and control. If <code>compare=TRUE</code> , the comparison object is accessible in the <code>final</code> slot, else the <code>final</code> slot is NULL. Default is TRUE.

Details

`bdpsurvival` uses a two-stage approach for determining the strength of historical data in estimation of a survival probability outcome. In the first stage, a Weibull distribution function is used as a *discount function* that defines the maximum strength of the historical data (via `weibull_shape`, `weibull_scale`, and `alpha_max`) and discounts based on disagreement with the current data. Disagreement between current and historical data is determined by stochastically comparing the respective posterior distributions under noninformative priors. With a single arm survival data analysis, the comparison is the probability (p) that the current survival is less than the historical survival. For a two-arm survival data, analysis the comparison is the probability that the hazard ratio comparing treatment and control is different from zero. The comparison metric p is then input into the Weibull discount function and the final strength of the historical data is returned (α).

In the second stage, posterior estimation is performed where the discount function parameter, α , is used as a fixed value for all posterior estimation procedures.

To carry out a single arm (OPC) analysis, data for the current and historical treatments are specified in a data frame. The data frame must have columns with names 'time', 'status', 'treatment', and 'historical.' Column 'time' is the survival (censor) time of the event and 'status' is the event indicator. The column 'treatment' is used to indicate which observations are in the treatment and control group. A value of 1 indicates that the observation is in the treatment group. The column 'historical' indicates whether the observation is from the historical data (1) or current data (0). The results are then based on the posterior probability of survival at `surv_time` for the current data augmented by the historical data.

Two-arm (RCT) analyses are specified similarly to a single arm trial. Again the input data frame must have columns with names 'time', 'status', 'treatment', and 'historical.' Column 'time' is the survival (censor) time of the event and 'status' is the event indicator. Now, the 'treatment' column must use 0 to indicate the control group. The current data are augmented by historical data (if present) and the results are then based on the posterior distribution of the hazard ratio between the treatment and control groups.

For more details, see the `bdpsurvival` vignette:
`vignette("bdpsurvival-vignette", package="bayesDP")`

Value

`bdpsurvival` returns an object of class "bdpsurvival". The functions `summary` and `print` are used to obtain and print a summary of the results, including user inputs. The `plot` function displays visual outputs as well.

An object of class "bdpsurvival" is a list containing at least the following components:

`posterior_treatment` list. Entries contain values related to the treatment group:

- `alpha_discount` numeric. Alpha value, the weighting parameter of the historical data.
- `p_hat` numeric. The posterior probability of the stochastic comparison between the current and historical data.
- `posterior_survival` vector. If one-arm trial, a vector of length `number_mcmc` containing the posterior probability draws of survival at `surv_time`.
- `posterior_flat_survival` vector. If one-arm trial, a vector of length `number_mcmc` containing the probability draws of survival at `surv_time` for the current treatment not augmented by historical treatment.
- `prior_survival` vector. If one-arm trial, a vector of length `number_mcmc` containing the probability draws of survival at `surv_time` for the historical treatment.
- `posterior_hazard` matrix. A matrix with `number_mcmc` rows and `length(breaks)` columns containing the posterior draws of the piecewise hazards for each interval break point.
- `posterior_flat_hazard` matrix. A matrix with `number_mcmc` rows and `length(breaks)` columns containing the draws of piecewise hazards for each interval break point for current treatment not augmented by historical treatment.
- `prior_hazard` matrix. A matrix with `number_mcmc` rows and `length(breaks)` columns containing the draws of piecewise hazards for each interval break point for historical treatment.

`posterior_control` list. If two-arm trial, contains values related to the control group analogous to the `posterior_treatment` output.

`final` list. Contains the final comparison object, dependent on the analysis type:

- One-arm analysis: vector. Posterior chain of survival probability at requested time.
- Two-arm analysis: vector. Posterior chain of log-hazard rate comparing treatment and control groups.

`args1` list. Entries contain user inputs. In addition, the following elements are output:

- `S_t`, `S_c`, `S0_t`, `S0_c` survival objects. Used internally to pass survival data between functions.
- `arm2` logical. Used internally to indicate one-arm or two-arm analysis.

References

Haddad, T., Himes, A., Thompson, L., Irony, T., Nair, R. MDIC Computer Modeling and Simulation working group.(2017) Incorporation of stochastic engineering models as prior information in Bayesian medical device trials. *Journal of Biopharmaceutical Statistics*, 1-15.

See Also

[summary](#), [print](#), and [plot](#) for details of each of the supported methods.

Examples

```
# One-arm trial (OPC) example - survival probability at 5 years
# Simulate survival data for a single arm (OPC) trial
time <- c(rexp(50, rate=1/20), rexp(50, rate=1/10))
status <- c(rexp(50, rate=1/30), rexp(50, rate=1/30))
status <- ifelse(time < status, 1, 0)

# Collect data into a data frame
example_surv_1arm <- data.frame(status = status,
                                time = time,
                                historical = c(rep(1,50),rep(0,50)),
                                treatment = 1)

fit1 <- bdpsurvival(Surv(time, status) ~ historical + treatment,
                   data = example_surv_1arm,
                   surv_time = 5)

print(fit1)
## Not run:
plot(fit1)

## End(Not run)

# Two-arm trial (OPC) example
# Simulate survival data for a two-arm trial
time <- c(rexp(50, rate=1/20), # Current treatment
          rexp(50, rate=1/10), # Current control
          rexp(50, rate=1/30), # Historical treatment
          rexp(50, rate=1/5)) # Historical control
status <- rexp(200, rate=1/40)
status <- ifelse(time < status, 1, 0)

# Collect data into a data frame
example_surv_2arm <- data.frame(status = status,
                                time = time,
                                historical = c(rep(0,100),rep(1,100)),
                                treatment = c(rep(1,50),rep(0,50),rep(1,50),rep(0,50)))

fit2 <- bdpsurvival(Surv(time, status) ~ historical + treatment,
                   data = example_surv_2arm)

summary(fit2)
```

```
### Fix alpha at 1
fit2_1 <- bdpsurvival(Surv(time, status) ~ historical + treatment,
                     data = example_surv_2arm,
                     fix_alpha = TRUE)

summary(fit2_1)
```

plot,bdpbinomial-method

bdpbinomial Object Plot

Description

plot method for class bdpbinomial.

Usage

```
## S4 method for signature 'bdpbinomial'
plot(x, type = NULL, print = TRUE)
```

Arguments

x	object of class bdpbinomial. The result of a call to the <code>bdpbinomial</code> function.
type	character. Optional. Select plot type to print. Supports the following: "discount" gives the discount function; "posteriors" gives the posterior plots of the event rates; and "density" gives the augmented posterior density plot(s). Leave NULL to display all plots in sequence.
print	logical. Optional. Produce a plot (<code>print = TRUE</code> ; default) or return a ggplot object (<code>print = FALSE</code>). When <code>print = FALSE</code> , it is possible to use ggplot2 syntax to modify the plot appearance.

Details

The plot method for bdpbinomial returns up to three plots: (1) posterior density curves; (2) posterior density of the effect of interest; and (3) the discount function. A call to plot that omits the type input returns one plot at a time and prompts the user to click the plot or press return to proceed to the next plot. Otherwise, the user can specify a plot type to display the requested plot.

plot,bdpnormal-method *bdpnormal Object Plot*

Description

plot method for class bdpnormal.

Usage

```
## S4 method for signature 'bdpnormal'  
plot(x, type = NULL, print = TRUE)
```

Arguments

x	object of class bdpnormal. The result of a call to the <code>bdpnormal</code> function.
type	character. Optional. Select plot type to print. Supports the following: "discount" gives the discount function; "posteriors" gives the posterior plots of the event rates; and "density" gives the augmented posterior density plot(s). Leave NULL to display all plots in sequence.
print	logical. Optional. Produce a plot (<code>print = TRUE</code> ; default) or return a ggplot object (<code>print = FALSE</code>). When <code>print = FALSE</code> , it is possible to use ggplot2 syntax to modify the plot appearance.

Details

The `plot` method for `bdpnormal` returns up to three plots: (1) posterior density curves; (2) posterior density of the effect of interest; and (3) the discount function. A call to `plot` that omits the `type` input returns one plot at a time and prompts the user to click the plot or press return to proceed to the next plot. Otherwise, the user can specify a plot type to display the requested plot.

plot,bdpsurvival-method
bdpsurvival Object Plot

Description

plot method for class bdpsurvival.

Usage

```
## S4 method for signature 'bdpsurvival'  
plot(x, type = NULL, print = TRUE)
```

Arguments

<code>x</code>	object of class <code>bdpsurvival</code> . The result of a call to the <code>bdpsurvival</code> function.
<code>type</code>	character. Optional. Select plot type to print. Supports the following: "discount" gives the discount function and "survival" gives the survival curves. Leave <code>NULL</code> to display all plots in sequence.
<code>print</code>	logical. Optional. Produce a plot (<code>print = TRUE</code> ; default) or return a <code>ggplot</code> object (<code>print = FALSE</code>). When <code>print = FALSE</code> , it is possible to use <code>ggplot2</code> syntax to modify the plot appearance.

Details

The `plot` method for `bdpsurvival` returns up to two plots: (1) posterior survival curves and (2) the discount function. A call to `plot` that omits the `type` input returns one plot at a time and prompts the user to click the plot or press return to proceed to the next plot. Otherwise, the user can specify a plot type to display the requested plot.

 ppexp

Compute cdf of the piecewise exponential distribution

Description

`ppexp` is used to compute the cumulative distribution function of the piecewise exponential distribution. The function is ported from R to C++ via code adapted from the `msm` package.

Usage

```
ppexp(q, x, cuts)
```

Arguments

<code>q</code>	scalar. The time point at which the cdf is to be computed.
<code>x</code>	vector or matrix. The hazard rate(s).
<code>cuts</code>	vector. Times at which the rate changes, i.e., the interval cut points. The first element of <code>cuts</code> should be 0, and <code>cuts</code> should be in increasing order. Must be the same length as <code>x</code> (vector) or have the same number of columns as <code>x</code> (matrix)

Details

The code underlying `ppexp` is written in C++ and adapted from R code used in the `msm` package.

Value

The cumulative distribution function computed at time `q`, hazard(s) `x`, and cut points `cuts`.

Examples

```
# Single vector of hazard rates. Returns a single cdf value.
q <- 12
x <- c(0.25,0.3,0.35,0.4)
cuts <- c(0,6,12,18)
pp <- ppexp(q,x,cuts)

# Matrix of multiple vectors of hazard rates. Returns 10 cdf values.
x <- matrix(rgamma(4*10, 0.1, 0.1), nrow=10)
pp <- ppexp(q,x,cuts)
```

```
print,bdpbinomial-method
      bdpbinomial Object Print
```

Description

print method for class bdpbinomial.

Usage

```
## S4 method for signature 'bdpbinomial'
print(x)
```

Arguments

x object of class bdpbinomial. The result of a call to the [bdpbinomial](#) function.

Details

Returns same output as a call to [summary](#).

```
print,bdpnormal-method
      bdpnormal Object Print
```

Description

print method for class bdpnormal.

Usage

```
## S4 method for signature 'bdpnormal'
print(x)
```

Arguments

x object of class `bdpnormal`. The result of a call to the `bdpnormal` function.

Details

Returns same output as a call to `summary`.

```
print,bdpsurvival-method
      bdpsurvival Object Print
```

Description

print method for class `bdpsurvival`.

Usage

```
## S4 method for signature 'bdpsurvival'
print(x)
```

Arguments

x object of class `bdpsurvival`. The result of a call to the `bdpsurvival` function.

Details

Displays a print of the `bdpsurvival` fit. The output is different, conditional on a one- or two-arm survival analysis.

In the case of a one-arm analysis, a brief summary is displayed, including the current data sample size, number of events, user input survival time, the augmented median survival probability, and corresponding lower and upper 95 percent interval limits.

When a control arm is present, the output is the same as a call to `summary`.

```
probability_discount    Bayesian Discount Prior: Comparison Between Current and Historical Data
```

Description

`probability_discount` can be used to estimate the posterior probability of the comparison between historical and current data in the context of a clinical trial with normal (mean) data. `probability_discount` is not used internally but is given for educational purposes.

Usage

```
probability_discount(mu = NULL, sigma = NULL, N = NULL, mu0 = NULL,
  sigma0 = NULL, N0 = NULL, number_mcmc = 10000, method = "fixed")
```

Arguments

mu	scalar. Mean of the current data.
sigma	scalar. Standard deviation of the current data.
N	scalar. Number of observations of the current data.
mu0	scalar. Mean of the historical data.
sigma0	scalar. Standard deviation of the historical data.
N0	scalar. Number of observations of the historical data.
number_mcmc	scalar. Number of Monte Carlo simulations. Default is 10000.
method	character. Analysis method. Default value "fixed" estimates the posterior probability and holds it fixed. Alternative method "mc" estimates the posterior probability for each Monte Carlo iteration. See the the bdpnormal vignette <code>vignette("bdpnormal-vignette", package="bayesDP")</code> for more details.

Details

This function is not used internally but is given for educational purposes. Given the inputs, the output is the posterior probability of the comparison between current and historical data in the context of a clinical trial with normal (mean) data.

Value

`probability_discount` returns an object of class "probability_discount".

An object of class `probability_discount` contains the following:

`p_hat` scalar. The posterior probability of the comparison historical data weight. If `method="mc"`, a vector of posterior probabilities of length `number_mcmc` is returned.

References

Haddad, T., Himes, A., Thompson, L., Irony, T., Nair, R. MDIC Computer Modeling and Simulation working group.(2017) Incorporation of stochastic engineering models as prior information in Bayesian medical device trials. *Journal of Biopharmaceutical Statistics*, 1-15.

Examples

```
probability_discount(mu = 0, sigma = 1, N = 100,
  mu0 = 0.1, sigma0 = 1, N0 = 100)
```

summary,bdpbinomial-method

bdpbinomial Object Summary

Description

summary method for class bdpbinomial.

Usage

```
## S4 method for signature 'bdpbinomial'
summary(object)
```

Arguments

object object of class bdpbinomial. The result of a call to the [bdpbinomial](#) function.

Details

Displays a summary of the bdpbinomial fit including the input data, the stochastic comparison between current and historical data, and the resulting historical data weight (alpha). If historical data is missing then no stochastic comparison nor weight are displayed.

In the case of a one-arm analysis, the displayed 95 percent CI contains the lower and upper limits of the augmented event rate of the current data. The displayed probability of success is the event rate of the current data augmented by the historical data.

When a control arm is present, a two-arm analysis is carried out. Now, the displayed 95 percent CI contains the lower and upper limits of the difference between the treatment and control arms with the historical data augmented to current data, if present. The displayed posterior sample estimates are the event rates of the treatment and control arms, each of which are augmented when historical data are present.

summary,bdpnormal-method

bdpnormal Object Summary

Description

summary method for class bdpnormal.

Usage

```
## S4 method for signature 'bdpnormal'
summary(object)
```


Arguments

object object of class `bdpnormal`. The result of a call to the `bdpnormal` function.

Details

Displays a summary of the `bdpnormal` fit including the input data, the stochastic comparison between current and historical data, and the resulting historical data weight (α). If historical data is missing then no stochastic comparison nor weight are displayed.

In the case of a one-arm analysis, the displayed 95 percent CI contains the lower and upper limits of the augmented mean value of the current data. The displayed mean of treatment group is the mean of the current data augmented by the historical data.

When a control arm is present, a two-arm analysis is carried out. Now, the displayed 95 percent CI contains the lower and upper limits of the difference between the treatment and control arms with the historical data augmented to current data, if present. The displayed posterior sample estimates are the mean of the treatment and control arms, each of which are augmented when historical data are present.

summary,bdpsurvival-method

bdpsurvival Object Summary

Description

summary method for class `bdpsurvival`.

Usage

```
## S4 method for signature 'bdpsurvival'
summary(object)
```

Arguments

object an object of class `bdpsurvival`, a result of a call to `bdpsurvival`.

Details

Displays a summary of the `bdpsurvival` fit. The output is different, conditional on a one- or two-arm survival analysis.

In the case of a one-arm analysis, the stochastic comparison between current and historical data and the resulting historical data weight (α) are displayed, followed by a survival table containing augmented posterior estimates of the survival probability at each time point for the current data.

When a control arm is present, a two-arm analysis is carried out. A two-arm survival analysis is similar to a cox proportional hazards analysis, and the displayed summary reflects this. First, the stochastic comparison between current and historical data and the resulting historical data weight (α) are displayed, when historical data is present for the respective arm. The displayed coef value is the log-hazard between the augmented treatment and control arms ($\log(\text{treatment}) - \log(\text{control})$). The lower and upper 95 percent interval limits correspond to the coef value.

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