

Package ‘cdtmbnma’

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Type Package

Title Component, Dose, and Time Network Meta-Analysis with
Dose-Dependent Interactions

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Description Bayesian component model-based network meta-analysis for treatment combinations with explicit component dose-response and dose-dependent interaction surfaces. The main interface fits single-timepoint arm-level networks with continuous or binary outcomes, any number of components, additive, bilinear, or saturating pairwise interactions, study-level random effects, and prediction at unobserved dose combinations. A stage-one longitudinal interface fits a two-component exponential time-course model with a bilinear interaction on the asymptote. Estimation uses 'Stan' through 'cmdstanr' or 'rstan'. Methods are described in Welton et al. (2009) <doi:10.1093/aje/kwp014>, Mawdsley et al. (2016) <doi:10.1002/psp4.12091>, Wicha et al. (2017) <doi:10.1038/s41467-017-01929-y>, and Pedder et al. (2019) <doi:10.1002/jrsm.1351>.

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Depends R (>= 4.1.0)

Imports posterior, stats, graphics, grDevices, utils

Suggests cmdstanr, rstan, testthat (>= 3.0.0), knitr, rmarkdown, loo

Additional_repositories <https://stan-dev.r-universe.dev>

SystemRequirements A working Stan backend through cmdstanr/CmdStan or rstan.

VignetteBuilder knitr

RoxygenNote 7.3.2

Config/testthat/edition 3

NeedsCompilation no

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Contents

cdtmbnma-package	2
antihtn_factorial_template	3
cdtmbnma	3
cdt_data	4
cdt_extdata	5
cdt_fit	6
cdt_priors	7
cdt_time_data	8
cdt_time_fit	8
cdt_time_priors	9
coef.cdtmbnma	10
coef.cdt_timefit	10
copd_bgf_template	11
plot.cdtmbnma	11
predict.cdtmbnma	12
predict.cdt_timefit	12
sacval_example	13
summary.cdtmbnma	13
summary.cdt_timefit	14
Index	15

cdtmbnma-package	<i>Component, Dose, and Time Network Meta-Analysis</i>
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Description

Bayesian component model-based network meta-analysis for treatment combinations with explicit component dose-response and dose-dependent interaction surfaces. The main model supports single-timepoint arm-level networks with continuous or binary outcomes. A stage-one interface supports a two-component exponential time-course model for repeated arm means.

Details

The single-timepoint workflow is `cdt_data()` followed by `cdt_fit()`, or the one-call wrapper `cdtmbnma()`. Estimation uses Stan through either **cmdstanr** or **rstan**. Fitted objects have `summary()`, `coef()`, `plot()`, and `predict()` methods.

Interaction surfaces

none Additive component effects.

bilinear One parameter per component pair; the interaction grows with the product of normalised component doses.

gpdi A saturating general pharmacodynamic interaction surface.

Author(s)

Tyler Pitre

antihtn_factorial_template

Amlodipine-Anchored Hypertension Factorial Extraction Template

Description

Reads the package's antihypertensive factorial extraction form or data dictionary.

Usage

```
antihtn_factorial_template(type = c("extraction", "dictionary"))
```

Arguments

type Either "extraction" or "dictionary".

Value

A data frame.

cdtmbnma

One-Call Component Dose-Response Network Meta-Analysis

Description

Convenience wrapper that builds the design with `cdt_data()` and fits it with `cdt_fit()`.

Usage

```
cdtmbnma(data, study, components, outcome = c("continuous", "binary"),
  y = NULL, se = NULL, sd = NULL, n = NULL,
  events = NULL, n_binary = NULL, ref = NULL,
  dstar = NULL, interactions = NULL,
  interaction = c("bilinear", "none", "gpdi"),
  priors = cdt_priors(), newdata = NULL, backend = "auto", chains = 4,
  iter_warmup = 1000, iter_sampling = 1000, adapt_delta = 0.95,
  seed = 1, refresh = 0, ...)
```

Arguments

data, study, components, outcome, y, se, sd, n, events, n_binary, ref, dstar, interactions

Passed to cdt_data().

interaction, priors, newdata, backend, chains, iter_warmup, iter_sampling, adapt_delta, seed, refresh, ...

Passed to cdt_fit().

Value

An object of class cdtmbnma.

Examples

```
# Fitting needs a Stan backend, and the Stan model is compiled on first use.
if (requireNamespace("rstan", quietly = TRUE)) {
  fit <- cdtmbnma(sacval_example(), study = "study",
    components = c("d_sac", "d_val"), outcome = "continuous",
    y = "y", se = "se", backend = "rstan",
    chains = 2, iter_warmup = 500, iter_sampling = 500)
  summary(fit)
}
```

cdt_data

Assemble a Component Dose-Response Network

Description

Turns an arm-level data frame into the design consumed by cdt_fit(). Every component named in components must have a dose column, and zero means the component is absent from that arm.

Usage

```
cdt_data(data, study, components, outcome = c("continuous", "binary"),
  y = NULL, se = NULL, sd = NULL, n = NULL,
  events = NULL, n_binary = NULL, ref = NULL,
  dstar = NULL, interactions = NULL)
```

Arguments

data	A data frame with one row per study arm.
study	Name of the column identifying the study.
components	Character vector of component dose column names. A value of zero marks the component absent.
outcome	Either "continuous" or "binary".

y	For a continuous outcome, the arm mean column.
se	For a continuous outcome, the arm standard error column. Supply this or both sd and n.
sd, n	For a continuous outcome, columns of arm standard deviation and sample size.
events, n_binary	For a binary outcome, event-count and sample-size columns.
ref	Optional column flagging exactly one within-study reference arm per study.
dstar	Optional named numeric vector of dose-normalisation references for the bilinear surface.
interactions	NULL, or a list of length-2 character vectors naming component pairs to model.

Value

An object of class `cdt_data`.

Examples

```
df <- data.frame(study = c("s1", "s1", "s1"), A = c(0, 1, 1),
                 B = c(0, 0, 1), y = c(0, -1, -2), se = c(1, 1, 1))
d <- cdt_data(df, study = "study", components = c("A", "B"),
             outcome = "continuous", y = "y", se = "se")
d
```

cdt_extdata	<i>Read an Installed Package Data File</i>
-------------	--

Description

Reads a CSV file installed with the package.

Usage

```
cdt_extdata(name)
```

Arguments

name Filename under `inst/extdata`.

Value

A data frame.

cdt_fit

*Fit a Component Dose-Response Network Meta-Analysis***Description**

Compiles the Stan model on first use and samples the posterior.

Usage

```
cdt_fit(data, interaction = c("bilinear", "none", "gpdi"),
        priors = cdt_priors(), newdata = NULL, backend = "auto", chains = 4,
        iter_warmup = 1000, iter_sampling = 1000, adapt_delta = 0.95,
        seed = 1, refresh = 0, ...)
```

Arguments

data	A cdt_data object.
interaction	Interaction surface: "bilinear", "none", or "gpdi".
priors	A named list from cdt_priors().
newdata	Optional data frame of component-dose combinations for Stan generated-quantities predictions.
backend	One of "auto", "cmdstanr", or "rstan".
chains, iter_warmup, iter_sampling	Sampler settings.
adapt_delta	Target acceptance probability passed to the Stan backend.
seed	Random seed.
refresh	Console refresh interval.
...	Passed to the backend sampler.

Details

The additive model uses `interaction = "none"`. The bilinear model uses one interaction parameter per co-occurring component pair. The "gpdi" model uses a saturating surface adapted from the general pharmacodynamic interaction model.

Value

An object of class `cdtmbnma`.

Examples

```
sv <- sacval_example()
d <- cdt_data(sv, "study", c("d_sac", "d_val"), outcome = "continuous",
             y = "y", se = "se", dstar = c(d_sac = 200, d_val = 320))

# Fitting needs a Stan backend, and the Stan model is compiled on first use.
if (requireNamespace("rstan", quietly = TRUE)) {
  fit <- cdt_fit(d, interaction = "bilinear", backend = "rstan",
               chains = 2, iter_warmup = 500, iter_sampling = 500)
  summary(fit)
}
```

cdt_priors

*Prior Settings for Single-Timepoint Models***Description**

Creates prior hyperparameters for `cdt_fit()`.

Usage

```
cdt_priors(emax_sd = 10, logED50_mean = log(50), logED50_sd = 1,
          int_sd = 5, ref_sd = 10, omega_sd = 2)
```

Arguments

<code>emax_sd</code>	Prior standard deviation for component Emax values.
<code>logED50_mean</code> , <code>logED50_sd</code>	Prior mean and standard deviation for log half-maximal dose values.
<code>int_sd</code>	Prior standard deviation for interaction parameters.
<code>ref_sd</code>	Prior standard deviation for per-study reference levels.
<code>omega_sd</code>	Half-normal prior scale for the random-effect standard deviation.

Value

A named list of prior hyperparameters.

cdt_time_data	<i>Assemble a Two-Component Longitudinal Component-Dose Network</i>
---------------	---

Description

Builds data for the two-component exponential time-course model.

Usage

```
cdt_time_data(data, study, arm, time, components, y, se = NULL,
              sd = NULL, n = NULL, ref = NULL, dstar = NULL)
```

Arguments

data	A long data frame with one row per study-arm-time observation.
study	Name of the study column.
arm	Name of the arm column.
time	Name of the follow-up time column.
components	Character vector naming exactly two component dose columns.
y, se	Outcome mean and standard error columns.
sd, n	Optional standard deviation and sample-size columns used to derive se.
ref	Optional column flagging the reference arm.
dstar	Optional named numeric vector of two dose-normalisation references.

Value

An object of class `cdt_time_data`.

cdt_time_fit	<i>Fit the Two-Component Component-Dose-Time Model</i>
--------------	--

Description

Fits the stage-one longitudinal Stan model with an exponential time-course.

Usage

```
cdt_time_fit(data, priors = cdt_time_priors(), newdata = NULL,
             backend = "auto", chains = 4, iter_warmup = 1000,
             iter_sampling = 1000, adapt_delta = 0.95, seed = 1,
             refresh = 0, ...)
```

Arguments

data	A cdt_time_data object.
priors	A named list from cdt_time_priors().
newdata	Optional data frame of two-component dose combinations.
backend	One of "auto", "cmdstanr", or "rstan".
chains, iter_warmup, iter_sampling	Sampler settings.
adapt_delta	Target acceptance probability.
seed	Random seed.
refresh	Console refresh interval.
...	Passed to the backend sampler.

Value

An object of class cdt_timefit.

cdt_time_priors	<i>Prior Settings for the Two-Component Time-Course Model</i>
-----------------	---

Description

Creates prior hyperparameters for cdt_time_fit().

Usage

```
cdt_time_priors(ref_E_sd = 5, ref_lograte_mean = -3,
  ref_lograte_sd = 1, emax_sd = 10, logED50_mean = 0,
  logED50_sd = 1, eta_sd = 5, rate_sd = 1,
  omega_E_sd = 2, omega_k_sd = 0.5)
```

Arguments

ref_E_sd	Prior standard deviation for study-specific reference asymptotes.
ref_lograte_mean, ref_lograte_sd	Prior mean and standard deviation for study-specific reference log rates.
emax_sd	Prior standard deviation for component Emax values.
logED50_mean, logED50_sd	Prior mean and standard deviation for log half-maximal dose values.
eta_sd	Prior standard deviation for the bilinear interaction.
rate_sd	Prior standard deviation for component log-rate dose effects.
omega_E_sd, omega_k_sd	Half-normal prior scales for random-effect standard deviations.

Value

A named list of prior hyperparameters.

coef.cdtmbnma	<i>Extract Component Coefficients</i>
---------------	---------------------------------------

Description

Extracts component dose-response coefficient summaries.

Usage

```
## S3 method for class 'cdtmbnma'
coef(object, ...)
```

Arguments

object	A fitted cdtmbnma object.
...	Unused.

Value

A data frame with posterior summaries for component Emax and ED50 values.

coef.cdt_timefit	<i>Extract Long-Term Coefficients from a Time-Course Fit</i>
------------------	--

Description

Extracts long-term component coefficient summaries.

Usage

```
## S3 method for class 'cdt_timefit'
coef(object, ...)
```

Arguments

object	A fitted cdt_timefit object.
...	Unused.

Value

A data frame with Emax and ED50 summaries for the two components.

copd_bgf_template	<i>COPD BGF Triple-Therapy Extraction Template</i>
-------------------	--

Description

Reads the package's COPD BGF extraction form or data dictionary.

Usage

```
copd_bgf_template(type = c("extraction", "dictionary"))
```

Arguments

type Either "extraction" or "dictionary".

Value

A data frame.

plot.cdtmbnma	<i>Plot Component Dose-Response Curves</i>
---------------	--

Description

Draws marginal component dose-response curves with posterior credible bands.

Usage

```
## S3 method for class 'cdtmbnma'
plot(x, ngrid = 60, probs = c(0.025, 0.975), ...)
```

Arguments

x A fitted cdtmbnma object.
 ngrid Number of dose points per curve.
 probs Two quantiles for the credible band.
 ... Passed to plot().

Value

Invisibly, a list of plotted grids.

predict.cdtmbnma	<i>Predict Relative Effects at Component-Dose Combinations</i>
------------------	--

Description

Computes posterior relative effects against the all-zero reference at arbitrary component-dose combinations.

Usage

```
## S3 method for class 'cdtmbnma'
predict(object, newdata, probs = c(0.025, 0.975), ...)
```

Arguments

object	A fitted cdtmbnma object.
newdata	Data frame carrying the component dose columns used in fitting.
probs	Quantiles for credible intervals.
...	Unused.

Value

A data frame with doses, posterior mean, posterior standard deviation, and requested quantiles.

predict.cdt_timefit	<i>Predict Long-Term Effects from a Time-Course Fit</i>
---------------------	---

Description

Computes long-term asymptotic relative effects for the stage-one longitudinal model.

Usage

```
## S3 method for class 'cdt_timefit'
predict(object, newdata, probs = c(0.025, 0.975), ...)
```

Arguments

object	A fitted cdt_timefit object.
newdata	Data frame carrying the two component-dose columns used in fitting.
probs	Quantiles for credible intervals.
...	Unused.

Value

A data frame with doses, posterior mean, posterior standard deviation, and requested quantiles.

sacval_example

*Sacubitril and Valsartan Blood-Pressure Dose Plane***Description**

Reads the package's sacubitril/valsartan example data.

Usage

```
sacval_example()
```

Value

A data frame with columns study, arm, d_sac, d_val, n, y, sd, se, and sd_source.

Examples

```
head(sacval_example())
```

summary.cdtmbnma

*Summarise a cdtmbnma Fit***Description**

Summarises the structural parameters of a cdtmbnma fit.

Usage

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

Arguments

object	A fitted cdtmbnma object.
...	Unused.

Value

A data frame of posterior summaries and convergence diagnostics.

summary.cdt_timefit	<i>Summarise a Two-Component Time-Course Fit</i>
---------------------	--

Description

Summarises key structural parameters in a cdt_timefit object.

Usage

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

Arguments

object	A fitted cdt_timefit object.
...	Unused.

Value

A data frame of posterior summaries and convergence diagnostics.

Index

*** package**

cdtmbnma-package, [2](#)

antihtn_factorial_template, [3](#)

cdt_data, [4](#)

cdt_extdata, [5](#)

cdt_fit, [6](#)

cdt_priors, [7](#)

cdt_time_data, [8](#)

cdt_time_fit, [8](#)

cdt_time_priors, [9](#)

cdtmbnma, [3](#)

cdtmbnma-package, [2](#)

coef.cdt_timefit, [10](#)

coef.cdtmbnma, [10](#)

copd_bgf_template, [11](#)

plot.cdtmbnma, [11](#)

predict.cdt_timefit, [12](#)

predict.cdtmbnma, [12](#)

sacval_example, [13](#)

summary.cdt_timefit, [14](#)

summary.cdtmbnma, [13](#)