Package 'lmtp'

July 18, 2020

Title Non-Parametric Causal Effects of Feasible Interventions Based on
Modified Treatment Policies

Version 0.0.5

Description Non-parametric estimators for casual effects based on longitudinal modified treatment
policies as described in Diaz, Williams, and Hoffman (<arXiv:2006.01366>), tradi-
tional point treatment,
and traditional longitudinal effects. Continuous, binary, and categorical treatments are al-
lowed as well are
censored outcomes. The treatment mechanism is estimated via a density ratio classification pro-
cedure
irrespective of treatment variable type. For both continuous and binary outcomes, additive treat-
ment effects
can be calculated and relative risks and odds ratios may be calculated for binary outcomes. Esti-
mation is enhanced
using the Super Learner from 'sl3' available for download from GitHub using 're-
motes::install_github(``tlverse/sl3@devel")'.

Depends R (>= 2.10)

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Encoding UTF-8

LazyData true

RoxygenNote 7.1.0

Imports slider, stats, nnls, cli, utils, R6, generics, origami, future
(>= 1.17.0), progressr

Suggests testthat (>= 2.1.0), covr, rmarkdown, knitr, ranger, twang

Enhances sl3 (>= 1.3.7)

NeedsCompilation no

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R **topics documented:**

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create_node_list   *Create a node list specification*

Description

Creates a node list specification that is used by the provided estimators. `create_node_list()` is
not explicitly called by the analyst, rather it is provided so the analyst can confirm how estimators
will use variables before actually performing the estimation procedure.

Usage

```
create_node_list(trt, tau, time_vary = NULL, baseline = NULL, k = Inf)
```

Arguments

trt	A vector of column names of treatment variables.
tau	The number of time points of observation, excluding the final outcome.
time_vary	A list of length tau with the column names for new time_vary to be introduced at each time point. The list should be ordered following the time ordering of the model.
baseline	An optional vector of columns names for baseline covariates to be included for adjustment at every timepoint.
k	An integer specifying how previous time points should be used for estimation at the given time point. Default is `Inf`, all time points.

Value

A list the same length of the time_vary parameter with the variables to be used for estimation at that
given time point.

Examples

```
a <- c("A_1", "A_2", "A_3", "A_4")
bs <- c("W_1", "W_2")
time_vary <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))

# assuming no Markov property
create_node_list(a, 4, time_vary, bs, k = Inf)

# assuming a Markov property
create_node_list(a, 4, time_vary, bs, k = 0)
```

---

event_locf   *Time To Event Last Outcome Carried Forward*

Description

A helper function to prepare survival data for use with LMTP estimators by imputing outcome nodes using last outcome carried forward when an observation experiences the event before the end-of-follow-up.

Usage

```
event_locf(data, outcomes)
```

Arguments

data	The dataset to modify.
outcomes	A vector of outcome nodes ordered by time.

Value

A modified dataset with future outcome nodes set to 1 if an observation experienced an event at any previous time point.

Examples

```
event_locf(sim_point_surv, c(paste0("Y.", 0:6)))
```

| lmtp_contrast | *Perform Contrasts of LMTP Fits* |

Description

Estimates contrasts of multiple LMTP fits compared to either a known reference value or a reference LMTP fit.

Usage

```
lmtp_contrast(..., ref, type = c("additive", "rr", "or"))
```

Arguments

...	One or more objects of class lmtp.
ref	A reference value or another lmtp fit to compare all other fits against.
type	The contrasts of interest. Options are "additive" (the default), "rr", and "or".

Value

A list of class `lmtp_contrast` containing the following components:

type	The type of contrast performed.
null	The null hypothesis.
vals	A dataframe containing the contrasts estimates, standard errors, and confidence intervals.
eifs	Un-centered estimated influence functions for contrasts estimated.

Examples

```
library(lmtp)
head(sim_cens)
a <- c("A1", "A2")
nodes <- list(c("L1"), c("L2"))
cens <- c("C1", "C2")
y <- "Y"
# mean population outcome
psi_null <- lmtp_tmle(sim_cens, a, y, time_vary = nodes,
                      cens = cens, shift = NULL, folds = 2)

# treatment rule, everyone is increased by 0.5
d <- function(data, x) data[[x]] + 0.5
psi_rule1 <- lmtp_tmle(sim_cens, a, y, time_vary = nodes,
                       cens = cens, shift = d, folds = 2)

# treatment rule, everyone is decreased by 0.5
```

```
d <- function(data, x) data[[x]] - 0.5
psi_rule2 <- lmtp_tmle(sim_cens, a, y, time_vary = nodes,
                       cens = cens, shift = d, folds = 2)

# Example 1.1
# Additive effect of rule 1 compared to a known constant
lmtp_contrast(psi_rule1, ref = 0.9)

# Example 1.2
# Additive effect of rule 1 compared to the population mean outcome
lmtp_contrast(psi_rule1, ref = psi_null)

# Example 1.3
# Additive effects of rule 1 and 2 compared to the population mean outcome
lmtp_contrast(psi_rule1, psi_rule2, ref = psi_null)

# Example 1.4
# Relative risk of rule 1 compared to observed exposure
lmtp_contrast(psi_rule1, ref = psi_null, type = "rr")

# Example 1.5
# Odds of rule 1 compared to observed exposure
lmtp_contrast(psi_rule1, ref = psi_null, type = "or")
```

---

lmtp_ipw   *LMTP IPW Estimator*

Description

Inverse probability of treatment weighting estimator for the effects of traditional causal effects and modified treatment policies for both point treatment and longitudinal data with binary, continuous, or time-to-event outcomes. Supports binary, categorical, and continuous exposures.

Usage

```
lmtp_ipw(
  data,
  trt,
  outcome,
  baseline = NULL,
  time_vary = NULL,
  cens = NULL,
  k = Inf,
  id = NULL,
  shift,
  learners = NULL,
  folds = 10,
  bound = 1e-05
)
```

Arguments

`data`	A data frame in wide format containing all necessary variables for the estimation problem.
`trt`	A vector containing the column names of treatment variables ordered by time.
`outcome`	The column name of the outcome variable. In the case of time-to-event analysis, a vector containing the columns names of intermediate outcome variables and the final outcome variable ordered by time. Only numeric values are allowed. If the outcome type is binary, data should be coded as 0 and 1.
`baseline`	An optional vector of columns names of baseline covariates to be included for adjustment at every timepoint.
`time_vary`	A list the same length as the number of time points of observation with the column names for new time-varying covariates introduced at each time point. The list should be ordered following the time ordering of the model.
`cens`	An optional vector of column names of censoring indicators the same length as the number of time points of observation. If missingness in the outcome is present or if time-to-event outcome, must be provided.
`k`	An integer specifying how previous time points should be used for estimation at the given time point. Default is `Inf`, all time points.
`id`	An optional column name containing cluster level identifiers.
`shift`	A two argument function that specifies how treatment variables should be shifted. See examples for how to specify shift functions for continuous, binary, and categorical exposures.
`learners`	An optional `sl3` learner stack for estimation of the exposure mechanism. If not specified, will default to using a generalized linear model.
`folds`	The number of folds to be used for cross-fitting. Minimum allowable number is two folds.
`bound`	Determines that maximum and minimum values (scaled) predictions will be bounded by. The default is 1e-5, bounding predictions by 1e-5 and 0.9999.

Value

A list of class `lmtp` containing the following components:

`estimator`	The estimator used, in this case "IPW".
`theta`	The estimated population LMTP effect.
`standard_error`	NA
`low`	NA
`high`	NA
`shift`	The shift function specifying the treatment policy of interest.
`density_ratios`	An n x Tau matrix of the estimated density ratios.
`weights_r`	A list the same length as `folds`, containing the Super Learner ensemble weights at each time-point for each fold for the propensity.

Examples

```
library(lmtp)

# Example 1.1
# Point treatment, continuous exposure, continuous outcome, no loss-to-follow-up
# Interested in the effect of a population wide decrease in A of 5 units
# The true value under this intervention is about 519.
set.seed(56)
n <- 1000
W <- rnorm(n, 10, 5)
A <- 23 + 5*W + rnorm(n)
Y <- 7.2*A + 3*W + rnorm(n)
ex1_dat <- data.frame(W, A, Y)
d <- function(data, x) data[[x]] - 5
psi1.1 <- lmtp_ipw(ex1_dat, "A", "Y", baseline = "W", shift = d, folds = 2)
psi1.1

# Example 1.2
# Point treatment, continuous exposure, continuous outcome, no loss-to-follow-up
# Interested in the effect of a modified treatment policy where A is decreased by 15
# units only among observations whose observed A was above 80.
# The true value under this intervention is about 513.
d <- function(data, x) (data[[x]] > 80)*(data[[x]] - 15) + (data[[x]] <= 80)*data[[x]]
psi1.2 <- lmtp_ipw(ex1_dat, "A", "Y", baseline = "W", shift = d, folds = 2)
psi1.2

# Example 2.1
# Longitudinal setting, time-varying continuous exposure bounded by 0,
# time-varying covariates, and a binary outcome with no loss-to-follow-up.
# Interested in the effect of a treatment policy where exposure decreases by
# one unit at every time point if an observations observed exposure is greater
# than or equal to 2. The true value under this intervention is about 0.305.
head(sim_t4)
# specifying treament variables
a <- c("A_1", "A_2", "A_3", "A_4")
# specifying time varying covariates
tv <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))
# treatment policy function to be applied at all time points
d <- function(data, trt) {
  a <- data[[trt]]
  (a - 1) * (a - 1 >= 1) + a * (a - 1 < 1)
}
progressr::with_progress({
  psi2.1 <- lmtp_ipw(sim_t4, a, "Y", time_vary = tv, shift = d, folds = 2)
})
psi2.1

# Example 2.2
# Example 2.1 assumed that the outcome (as well as the treatment variables)
# were directly affected by all other nodes in the past. In certain situtations,
# domain specific knowledge may suggest otherwise leading to a Markov processes.
```

```
# This can be controlled using the k argument.
progressr::with_progress({
  psi2.2 <- lmtp_ipw(sim_t4, a, "Y", time_vary = tv, shift = d,
                     k = 0, folds = 2)
})
psi2.2

# Example 2.3
# Using the same data as examples 2.1 and 2.2.
# Now estimating the effect of a dynamic modified treatment policy.
a <- c("A_1", "A_2", "A_3", "A_4")
time_varying <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))
# our same shift function
shift <- function(data, trt) {
  (data[[trt]] - 1) * (data[[trt]] - 1 >= 1) + data[[trt]] * (data[[trt]] - 1 < 1)
}
# creating a dynamic mtp that applies the shift function
# but also depends on history and the current time
dynamic_mtp <- function(data, trt) {
  if (trt == "A_1") {
    # if its the first time point, follow the same mtp as before
    shift(data, trt)
  } else {
    # otherwise check if the time varying covariate equals 1
    ifelse(data[[sub("A", "L", trt)]] == 1,
           shift(data, trt), # if yes continue with the policy
           data[[trt]]) # otherwise do nothing
  }
}
psi2.3 <- lmtp_ipw(sim_t4, a, "Y", time_vary = time_varying,
                   k = 0, shift = dynamic_mtp, folds = 2)
psi2.3

# Example 2.4
# Using the same data as examples 2.1, 2.2, and 2.3, but now treating the exposure
# as an ordered categorical variable. To account for the exposure being a
# factor we just need to modify the shift function (and the original data)
# so as to respect this.
for (i in a) {
  sim_t4[[i]] <- factor(sim_t4[[i]], levels = 0:5, ordered = TRUE)
}
d <- function(data, trt) {
  out <- list()
  a <- data[[trt]]
  for (i in 1:length(a)) {
    if (as.character(a[i]) %in% c("0", "1")) {
      out[[i]] <- as.character(a[i])
    } else {
      out[[i]] <- as.numeric(as.character(a[i])) - 1
    }
  }
  factor(unlist(out), levels = 0:5, ordered = TRUE)
}
```

```
progressr::with_progress({
  psi2.4 <- lmtp_ipw(sim_t4, a, "Y", time_vary = tv, shift = d, k = 0, folds = 2)
})
psi2.4

# Example 3.1
# Longitudinal setting, time-varying binary treatment, time-varying covariates
# and baseline covariates with no loss-to-follow-up. Interested in a traditional
# causal effect where treatment is set to 1 at all time points for all observations.
data("iptwExWide", package = "twang")
a <- paste0("tx", 1:3)
baseline <- c("gender", "age")
tv <- list(c("use0"), c("use1"), c("use2"))
progressr::with_progress({
  psi3.1 <-
    lmtp_ipw(iptwExWide, a, "outcome", baseline = baseline, time_vary = tv,
             shift = static_binary_on, folds = 2)
})
psi3.1

# Example 4.1
# Longitudinal setting, time-varying continuous treatment, time-varying covariates,
# binary outcome with right censoring. Interested in the mean population outcome under
# the observed exposures in a hypothetical population with no loss-to-follow-up.
head(sim_cens)
a <- c("A1", "A2")
tv <- list(c("L1"), c("L2"))
cens <- c("C1", "C2")
y <- "Y"
psi4.1 <- lmtp_ipw(sim_cens, a, y, time_vary = tv, cens = cens,
                   shift = NULL, folds = 2)
psi4.1

# Example 4.2
# Using the same data as example 4.1, but now interested in the causal effect of a
# treatment policy where exposure increased by 0.5 units at all time points. The
# true value under this intervention is about 0.88.
d <- function(data, x) data[[x]] + 0.5
psi4.2 <- lmtp_ipw(sim_cens, a, y, time_vary = tv,
                   cens = cens, shift = d, folds = 2)
psi4.2

# Example 5.1
# Time-to-event analysis with a binary time-invariant exposure. Interested in
# the effect of treatment being given to all observations on the cumulative
# incidence of our time-to-event outcome.
a <- "trt"
# for a survival problem, the outcome arugment now takes a vector of outcomes
# if an observation experiences the event prior to the end of follow-up, all future
# outcome nodes should be set to 1 (i.e., last observation carried forward).
y <- paste0("Y.", 1:6)
cens <- paste0("C.", 0:5)
baseline <- c("W1", "W2")
```

```
progressr::with_progress({
  psi5.1 <- lmtp_ipw(sim_point_surv, a, y, baseline, cens = cens,
                     shift = static_binary_on, folds = 2)
})
psi5.1
```

---

lmtp_sdr   *LMTP Sequential Doubly Robust Estimator*

Description

Sequentially doubly robust estimator for the effects of traditional causal effects and modified treat-
ment policies for both point treatment and longitudinal data with binary, continuous, or time-to-
event outcomes. Supports binary, categorical, and continuous exposures.

Usage

```
lmtp_sdr(
  data,
  trt,
  outcome,
  baseline = NULL,
  time_vary = NULL,
  cens = NULL,
  shift,
  k = Inf,
  outcome_type = c("binomial", "continuous"),
  id = NULL,
  bounds = NULL,
  learners_outcome = NULL,
  learners_trt = NULL,
  folds = 10,
  bound = 1e-05
)
```

Arguments

data	A data frame in wide format containing all necessary variables for the estimation problem.
trt	A vector containing the column names of treatment variables ordered by time.
outcome	The column name of the outcome variable. In the case of time-to-event analysis, a vector containing the columns names of intermediate outcome variables and the final outcome variable ordered by time. Only numeric values are allowed. If the outcome type is binary, data should be coded as 0 and 1.
baseline	An optional vector of columns names of baseline covariates to be included for adjustment at every timepoint.

`time_vary`	A list the same length as the number of time points of observation with the column names for new time-varying covariates introduced at each time point. The list should be ordered following the time ordering of the model.
`cens`	An optional vector of column names of censoring indicators the same length as the number of time points of observation. If missingness in the outcome is present or if time-to-event outcome, must be provided.
`shift`	A two argument function that specifies how treatment variables should be shifted. See examples for how to specify shift functions for continuous, binary, and categorical exposures.
`k`	An integer specifying how previous time points should be used for estimation at the given time point. Default is `Inf`, all time points.
`outcome_type`	Outcome variable type (i.e., continuous, binomial).
`id`	An optional column name containing cluster level identifiers.
`bounds`	An optional vector of the bounds for continuous outcomes. If `NULL`, the bounds will be taken as the minimum and maximum of the observed data. Should be left as `NULL` if the outcome type is binary.
`learners_outcome`	
	An optional sl3 learner stack for estimation of the outcome regression. If not specified, will default to using a generalized linear model.
`learners_trt`	An optional sl3 learner stack for estimation of the exposure mechanism. If not specified, will default to using a generalized linear model.
`folds`	The number of folds to be used for cross-fitting. Minimum allowable number is two folds.
`bound`	Determines that maximum and minimum values (scaled) predictions will be bounded by. The default is 1e-5, bounding predictions by 1e-5 and 0.9999.

Value

A list of class `lmtp` containing the following components:

`estimator`	The estimator used, in this case "SDR".
`theta`	The estimated population LMTP effect.
`standard_error`	The estimated standard error of the LMTP effect.
`low`	Lower bound of the 95% confidence interval of the LMTP effect.
`high`	Upper bound of the 95% confidence interval of the LMTP effect.
`eif`	The estimated, un-centered, influence function of the estimate.
`shift`	The shift function specifying the treatment policy of interest.
`outcome_reg`	An n x Tau + 1 matrix of outcome regression predictions. The mean of the first column is used for calculating theta.
`density_ratios`	An n x Tau matrix of the estimated density ratios.
`weights_m`	A list the same length as `folds`, containing the Super Learner ensemble weights at each time-point for each fold for the outcome regression.
`weights_r`	A list the same length as `folds`, containing the Super Learner ensemble weights at each time-point for each fold for the propensity.
`outcome_type`	The outcome variable type.

Examples

```
library(lmtp)
# Example 1.1
# Point treatment, continuous exposure, continuous outcome, no loss-to-follow-up
# Interested in the effect of a population wide decrease in A of 5 units
# The true value under this intervention is about 519.
set.seed(56)
n <- 1000
W <- rnorm(n, 10, 5)
A <- 23 + 5*W + rnorm(n)
Y <- 7.2*A + 3*W + rnorm(n)
ex1_dat <- data.frame(W, A, Y)
d <- function(data, x) data[[x]] - 5
psi1.1 <- lmtp_sdr(ex1_dat, "A", "Y", "W", shift = d,
                   outcome_type = "continuous", folds = 2)
psi1.1

# Example 1.2
# Point treatment, continuous exposure, continuous outcome, no loss-to-follow-up
# Interested in the effect of a modified treatment policy where A is decreased by 15
# units only among observations whose observed A was above 80.
# The true value under this intervention is about 513.
d <- function(data, x) (data[[x]] > 80)*(data[[x]] - 15) + (data[[x]] <= 80)*data[[x]]
psi1.2 <- lmtp_sdr(ex1_dat, "A", "Y", "W", shift = d,
                   outcome_type = "continuous", folds = 2)
psi1.2

# Example 2.1
# Longitudinal setting, time-varying continuous exposure bounded by 0,
# time-varying covariates, and a binary outcome with no loss-to-follow-up.
# Interested in the effect of a treatment policy where exposure decreases by
# one unit at every time point if an observations observed exposure is greater
# than or equal to 2. The true value under this intervention is about 0.305.
head(sim_t4)
# specifying treament variables
a <- c("A_1", "A_2", "A_3", "A_4")
# specifying time varying covariates
tv <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))
# treatment policy function to be applied at all time points
d <- function(data, trt) {
  a <- data[[trt]]
  (a - 1) * (a - 1 >= 1) + a * (a - 1 < 1)
}
progressr::with_progress({
  psi2.1 <- lmtp_sdr(sim_t4, a, "Y", time_vary = tv, shift = d, folds = 2)
})
psi2.1

# Example 2.2
# Example 2.1 assumed that the outcome (as well as the treatment variables)
# were directly affected by all other nodes in the past. In certain situtations,
```

```
# domain specific knowledge may suggest otherwise leading to a Markov processes.
# This can be controlled using the k argument.
progressr::with_progress({
  psi2.2 <- lmtp_sdr(sim_t4, a, "Y", time_vary = tv, shift = d,
                     k = 0, folds = 2)
})
psi2.2

# Example 2.3
# Using the same data as examples 2.1 and 2.2.
# Now estimating the effect of a dynamic modified treatment policy.
a <- c("A_1", "A_2", "A_3", "A_4")
time_varying <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))
# our same shift function
shift <- function(data, trt) {
  (data[[trt]] - 1) * (data[[trt]] - 1 >= 1) + data[[trt]] * (data[[trt]] - 1 < 1)
}
# creating a dynamic mtp that applies the shift function
# but also depends on history and the current time
dynamic_mtp <- function(data, trt) {
  if (trt == "A_1") {
    # if its the first time point, follow the same mtp as before
    shift(data, trt)
  } else {
    # otherwise check if the time varying covariate equals 1
    ifelse(data[[sub("A", "L", trt)]] == 1,
           shift(data, trt), # if yes continue with the policy
           data[[trt]]) # otherwise do nothing
  }
}
psi2.3 <- lmtp_sdr(sim_t4, a, "Y", time_vary = time_varying,
                   k = 0, shift = dynamic_mtp, folds = 2)
psi2.3

# Example 2.4
# Using the same data as examples 2.1, 2.2, and 2.3, but now treating the exposure
# as an ordered categorical variable. To account for the exposure being a
# factor we just need to modify the shift function (and the original data)
# so as to respect this.
for (i in a) {
  sim_t4[[i]] <- factor(sim_t4[[i]], levels = 0:5, ordered = TRUE)
}
d <- function(data, trt) {
  out <- list()
  a <- data[[trt]]
  for (i in 1:length(a)) {
    if (as.character(a[i]) %in% c("0", "1")) {
      out[[i]] <- as.character(a[i])
    } else {
      out[[i]] <- as.numeric(as.character(a[i])) - 1
    }
  }
  factor(unlist(out), levels = 0:5, ordered = TRUE)
```

```
}
progressr::with_progress({
  psi2.4 <- lmtp_sdr(sim_t4, a, "Y", time_vary = tv, shift = d, k = 0, folds = 2)
})
psi2.4

# Example 3.1
# Longitudinal setting, time-varying binary treatment, time-varying covariates
# and baseline covariates with no loss-to-follow-up. Interested in a traditional
# causal effect where treatment is set to 1 at all time points for all observations.
data("iptwExWide", package = "twang")
a <- paste0("tx", 1:3)
baseline <- c("gender", "age")
tv <- list(c("use0"), c("use1"), c("use2"))
progressr::with_progress({
  psi3.1 <-
    lmtp_sdr(iptwExWide, a, "outcome", baseline = baseline, time_vary = tv,
              shift = static_binary_on, outcome_type = "continuous",
              folds = 2)
})
psi3.1

# Example 4.1
# Longitudinal setting, time-varying continuous treatment, time-varying covariates,
# binary outcome with right censoring. Interested in the mean population outcome under
# the observed exposures in a hypothetical population with no loss-to-follow-up.
head(sim_cens)
a <- c("A1", "A2")
tv <- list(c("L1"), c("L2"))
cens <- c("C1", "C2")
y <- "Y"
psi4.1 <- lmtp_sdr(sim_cens, a, y, time_vary = tv, cens = cens,
                    shift = NULL, folds = 2)
psi4.1

# Example 4.2
# Using the same data as example 4.1, but now interested in the causal effect of a
# treatment policy where exposure increased by 0.5 units at all time points. The
# true value under this intervention is about 0.88.
d <- function(data, x) data[[x]] + 0.5
psi4.2 <- lmtp_sdr(sim_cens, a, y, time_vary = tv,
                    cens = cens, shift = d, folds = 2)
psi4.2

# Example 5.1
# Time-to-event analysis with a binary time-invariant exposure. Interested in
# the effect of treatment being given to all observations on the cumulative
# incidence of our time-to-event outcome.
a <- "trt"
# for a survival problem, the outcome arugment now takes a vector of outcomes
# if an observation experiences the event prior to the end of follow-up, all future
# outcome nodes should be set to 1 (i.e., last observation carried forward).
y <- paste0("Y.", 1:6)
```

```
cens <- paste0("C.", 0:5)
baseline <- c("W1", "W2")
progressr::with_progress({
  psi5.1 <- lmtp_sdr(sim_point_surv, a, y, baseline, cens = cens,
                     shift = static_binary_on, folds = 2)
})
psi5.1
```

---

lmtp_sub   *LMTP Substitution Estimator*

Description

G-computation estimator for the effects of traditional causal effects and modified treatment policies
for both point treatment and longitudinal data with binary, continuous, or time-to-event outcomes.
Supports binary, categorical, and continuous exposures.

Usage

```
lmtp_sub(
  data,
  trt,
  outcome,
  baseline = NULL,
  time_vary = NULL,
  cens = NULL,
  shift,
  k = Inf,
  outcome_type = c("binomial", "continuous"),
  id = NULL,
  bounds = NULL,
  learners = NULL,
  folds = 10,
  bound = 1e-05
)
```

Arguments

data	A data frame in wide format containing all necessary variables for the estimation problem.
trt	A vector containing the column names of treatment variables ordered by time.
outcome	The column name of the outcome variable. In the case of time-to-event analysis, a vector containing the columns names of intermediate outcome variables and the final outcome variable ordered by time. Only numeric values are allowed. If the outcome type is binary, data should be coded as 0 and 1.

baseline	An optional vector of columns names of baseline covariates to be included for adjustment at every timepoint.
time_vary	A list the same length as the number of time points of observation with the column names for new time-varying covariates introduced at each time point. The list should be ordered following the time ordering of the model.
cens	An optional vector of column names of censoring indicators the same length as the number of time points of observation. If missingness in the outcome is present or if time-to-event outcome, must be provided.
shift	A two argument function that specifies how treatment variables should be shifted. See examples for how to specify shift functions for continuous, binary, and categorical exposures.
k	An integer specifying how previous time points should be used for estimation at the given time point. Default is Inf, all time points.
outcome_type	Outcome variable type (i.e., continuous, binomial).
id	An optional column name containing cluster level identifiers.
bounds	An optional vector of the bounds for continuous outcomes. If NULL, the bounds will be taken as the minimum and maximum of the observed data. Should be left as NULL if the outcome type is binary.
learners	An optional sl3 learner stack for estimation of the outcome regression. If not specified, will default to using a generalized linear model.
folds	The number of folds to be used for cross-fitting. Minimum allowable number is two folds.
bound	Determines that maximum and minimum values (scaled) predictions will be bounded by. The default is 1e-5, bounding predictions by 1e-5 and 0.9999.

Value

A list of class lmtp containing the following components:

estimator	The estimator used, in this case "substitution".
theta	The estimated population LMTP effect.
standard_error	NA
low	NA
high	NA
shift	The shift function specifying the treatment policy of interest.
outcome_reg	An n x Tau + 1 matrix of outcome regression predictions. The mean of the first column is used for calculating theta.
weights_m	A list the same length as folds, containing the Super Learner ensemble weights at each time-point for each fold for the outcome regression.
outcome_type	The outcome variable type.

Examples

```
library(lmtp)

# Example 1.1
# Point treatment, continuous exposure, continuous outcome, no loss-to-follow-up
# Interested in the effect of a population wide decrease in A of 5 units
# The true value under this intervention is about 519.
set.seed(56)
n <- 1000
W <- rnorm(n, 10, 5)
A <- 23 + 5*W + rnorm(n)
Y <- 7.2*A + 3*W + rnorm(n)
ex1_dat <- data.frame(W, A, Y)
d <- function(data, x) data[[x]] - 5
psi1.1 <- lmtp_sub(ex1_dat, "A", "Y", "W", shift = d,
                   outcome_type = "continuous", folds = 2)
psi1.1

# Example 1.2
# Point treatment, continuous exposure, continuous outcome, no loss-to-follow-up
# Interested in the effect of a modified treatment policy where A is decreased by 15
# units only among observations whose observed A was above 80.
# The true value under this intervention is about 513.
d <- function(data, x) (data[[x]] > 80)*(data[[x]] - 15) + (data[[x]] <= 80)*data[[x]]
psi1.2 <- lmtp_sub(ex1_dat, "A", "Y", "W", shift = d,
                   outcome_type = "continuous", folds = 2)
psi1.2

# Example 2.1
# Longitudinal setting, time-varying continuous exposure bounded by 0,
# time-varying covariates, and a binary outcome with no loss-to-follow-up.
# Interested in the effect of a treatment policy where exposure decreases by
# one unit at every time point if an observations observed exposure is greater
# than or equal to 2. The true value under this intervention is about 0.305.
head(sim_t4)
# specifying treament variables
a <- c("A_1", "A_2", "A_3", "A_4")
# specifying time varying covariates
tv <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))
# treatment policy function to be applied at all time points
d <- function(data, trt) {
  a <- data[[trt]]
  (a - 1) * (a - 1 >= 1) + a * (a - 1 < 1)
}
progressr::with_progress({
  psi2.1 <- lmtp_sub(sim_t4, a, "Y", time_vary = tv, shift = d, folds = 2)
})
psi2.1

# Example 2.2
# Example 2.1 assumed that the outcome (as well as the treatment variables)
```

```
# were directly affected by all other nodes in the past. In certain situtations,
# domain specific knowledge may suggest otherwise leading to a Markov processes.
# This can be controlled using the k argument.
progressr::with_progress({
  psi2.2 <- lmtp_sub(sim_t4, a, "Y", time_vary = tv, shift = d,
                     k = 0, folds = 2)
})
psi2.2

# Example 2.3
# Using the same data as examples 2.1 and 2.2.
# Now estimating the effect of a dynamic modified treatment policy.
a <- c("A_1", "A_2", "A_3", "A_4")
time_varying <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))
# our same shift function
shift <- function(data, trt) {
  (data[[trt]] - 1) * (data[[trt]] - 1 >= 1) + data[[trt]] * (data[[trt]] - 1 < 1)
}
# creating a dynamic mtp that applies the shift function
# but also depends on history and the current time
dynamic_mtp <- function(data, trt) {
  if (trt == "A_1") {
    # if its the first time point, follow the same mtp as before
    shift(data, trt)
  } else {
    # otherwise check if the time varying covariate equals 1
    ifelse(data[[sub("A", "L", trt)]] == 1,
           shift(data, trt), # if yes continue with the policy
           data[[trt]]) # otherwise do nothing
  }
}
psi2.3 <- lmtp_sub(sim_t4, a, "Y", time_vary = time_varying,
                   k = 0, shift = dynamic_mtp, folds = 2)
psi2.3

# Example 2.4
# Using the same data as examples 2.1, 2.2, and 2.3, but now treating the exposure
# as an ordered categorical variable. To account for the exposure being a
# factor we just need to modify the shift function (and the original data)
# so as to respect this.
for (i in a) {
  sim_t4[[i]] <- factor(sim_t4[[i]], levels = 0:5, ordered = TRUE)
}
d <- function(data, trt) {
  out <- list()
  a <- data[[trt]]
  for (i in 1:length(a)) {
    if (as.character(a[i]) %in% c("0", "1")) {
      out[[i]] <- as.character(a[i])
    } else {
      out[[i]] <- as.numeric(as.character(a[i])) - 1
    }
  }
```

```
    factor(unlist(out), levels = 0:5, ordered = TRUE)
}
progressr::with_progress({
  psi2.4 <- lmtp_sub(sim_t4, a, "Y", time_vary = tv, shift = d, k = 0, folds = 2)
})
psi2.4

# Example 3.1
# Longitudinal setting, time-varying binary treatment, time-varying covariates
# and baseline covariates with no loss-to-follow-up. Interested in a traditional
# causal effect where treatment is set to 1 at all time points for all observations.
data("iptwExWide", package = "twang")
a <- paste0("tx", 1:3)
baseline <- c("gender", "age")
tv <- list(c("use0"), c("use1"), c("use2"))
progressr::with_progress({
  psi3.1 <-
    lmtp_sub(iptwExWide, a, "outcome", baseline = baseline, time_vary = tv,
             shift = static_binary_on, outcome_type = "continuous",
             folds = 2)
})
psi3.1

# Example 4.1
# Longitudinal setting, time-varying continuous treatment, time-varying covariates,
# binary outcome with right censoring. Interested in the mean population outcome under
# the observed exposures in a hypothetical population with no loss-to-follow-up.
head(sim_cens)
a <- c("A1", "A2")
tv <- list(c("L1"), c("L2"))
cens <- c("C1", "C2")
y <- "Y"
psi4.1 <- lmtp_sub(sim_cens, a, y, time_vary = tv,
                   cens = cens, shift = NULL, folds = 2)
psi4.1

# Example 4.2
# Using the same data as example 4.1, but now interested in the causal effect of a
# treatment policy where exposure increased by 0.5 units at all time points. The
# true value under this intervention is about 0.88.
d <- function(data, x) data[[x]] + 0.5
psi4.2 <- lmtp_sub(sim_cens, a, y, time_vary = tv, cens = cens, shift = d, folds = 2)
psi4.2

# Example 5.1
# Time-to-event analysis with a binary time-invariant exposure. Interested in
# the effect of treatment being given to all observations on the cumulative
# incidence of our time-to-event outcome.
a <- "trt"
# for a survival problem, the outcome arugment now takes a vector of outcomes
# if an observation experiences the event prior to the end of follow-up, all future
# outcome nodes should be set to 1 (i.e., last observation carried forward).
y <- paste0("Y.", 1:6)
```

```
cens <- paste0("C.", 0:5)
baseline <- c("W1", "W2")
progressr::with_progress({
  psi5.1 <- lmtp_sub(sim_point_surv, a, y, baseline, cens = cens,
                     shift = static_binary_on, folds = 2)
})
psi5.1
```

---

lmtp_tmle   *LMTP Targeted Maximum Likelihood Estimator*

Description

Targeted maximum likelihood estimator for the effects of traditional causal effects and modified
treatment policies for both point treatment and longitudinal data with binary, continuous, or time-
to-event outcomes. Supports binary, categorical, and continuous exposures.

Usage

```
lmtp_tmle(
  data,
  trt,
  outcome,
  baseline = NULL,
  time_vary = NULL,
  cens = NULL,
  shift,
  k = Inf,
  outcome_type = c("binomial", "continuous"),
  id = NULL,
  bounds = NULL,
  learners_outcome = NULL,
  learners_trt = NULL,
  folds = 10,
  bound = 1e-05
)
```

Arguments

data	A data frame in wide format containing all necessary variables for the estimation problem.
trt	A vector containing the column names of treatment variables ordered by time.
outcome	The column name of the outcome variable. In the case of time-to-event analysis, a vector containing the columns names of intermediate outcome variables and the final outcome variable ordered by time. Only numeric values are allowed. If the outcome type is binary, data should be coded as 0 and 1.

baseline	An optional vector of columns names of baseline covariates to be included for adjustment at every timepoint.
time_vary	A list the same length as the number of time points of observation with the column names for new time-varying covariates introduced at each time point. The list should be ordered following the time ordering of the model.
cens	An optional vector of column names of censoring indicators the same length as the number of time points of observation. If missingness in the outcome is present or if time-to-event outcome, must be provided.
shift	A two argument function that specifies how treatment variables should be shifted. See examples for how to specify shift functions for continuous, binary, and categorical exposures.
k	An integer specifying how previous time points should be used for estimation at the given time point. Default is Inf, all time points.
outcome_type	Outcome variable type (i.e., continuous, binomial).
id	An optional column name containing cluster level identifiers.
bounds	An optional vector of the bounds for continuous outcomes. If NULL, the bounds will be taken as the minimum and maximum of the observed data. Should be left as NULL if the outcome type is binary.
learners_outcome	
	An optional sl3 learner stack for estimation of the outcome regression. If not specified, will default to using a generalized linear model.
learners_trt	An optional sl3 learner stack for estimation of the exposure mechanism. If not specified, will default to using a generalized linear model.
folds	The number of folds to be used for cross-fitting. Minimum allowable number is two folds.
bound	Determines that maximum and minimum values (scaled) predictions will be bounded by. The default is 1e-5, bounding predictions by 1e-5 and 0.9999.

Value

A list of class lmtp containing the following components:

estimator	The estimator used, in this case "TMLE".
theta	The estimated population LMTP effect.
standard_error	The estimated standard error of the LMTP effect.
low	Lower bound of the 95% confidence interval of the LMTP effect.
high	Upper bound of the 95% confidence interval of the LMTP effect.
eif	The estimated, un-centered, influence function of the estimate.
shift	The shift function specifying the treatment policy of interest.
outcome_reg	An n x Tau + 1 matrix of outcome regression predictions. The mean of the first column is used for calculating theta.
density_ratios	An n x Tau matrix of the estimated density ratios.

weights_m	A list the same length as folds, containing the Super Learner ensemble weights at each time-point for each fold for the outcome regression.
weights_r	A list the same length as folds, containing the Super Learner ensemble weights at each time-point for each fold for the propensity.
outcome_type	The outcome variable type.

Examples

```
library(lmtp)

# Example 1.1
# Point treatment, continuous exposure, continuous outcome, no loss-to-follow-up
# Interested in the effect of a population wide decrease in A of 5 units
# The true value under this intervention is about 519.
set.seed(56)
n <- 1000
W <- rnorm(n, 10, 5)
A <- 23 + 5*W + rnorm(n)
Y <- 7.2*A + 3*W + rnorm(n)
ex1_dat <- data.frame(W, A, Y)
d <- function(data, x) data[[x]] - 5
psi1.1 <- lmtp_tmle(ex1_dat, "A", "Y", "W", shift = d,
                    outcome_type = "continuous", folds = 2)
psi1.1

# Example 1.2
# Point treatment, continuous exposure, continuous outcome, no loss-to-follow-up
# Interested in the effect of a modified treatment policy where A is decreased by 15
# units only among observations whose observed A was above 80.
# The true value under this intervention is about 513.
d <- function(data, x) (data[[x]] > 80)*(data[[x]] - 15) + (data[[x]] <= 80)*data[[x]]
psi1.2 <- lmtp_tmle(ex1_dat, "A", "Y", "W", shift = d,
                    outcome_type = "continuous", folds = 2)
psi1.2

# Example 2.1
# Longitudinal setting, time-varying continuous exposure bounded by 0,
# time-varying covariates, and a binary outcome with no loss-to-follow-up.
# Interested in the effect of a treatment policy where exposure decreases by
# one unit at every time point if an observations observed exposure is greater
# than or equal to 2. The true value under this intervention is about 0.305.
head(sim_t4)
# specifying treatment variables
a <- c("A_1", "A_2", "A_3", "A_4")
# specifying time varying covariates
tv <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))
# treatment policy function to be applied at all time points
d <- function(data, trt) {
  a <- data[[trt]]
  (a - 1) * (a - 1 >= 1) + a * (a - 1 < 1)
}
```

```
progressr::with_progress({
  psi2.1 <- lmtp_tmle(sim_t4, a, "Y", time_vary = tv, shift = d, folds = 2)
})
psi2.1

# Example 2.2
# Example 2.1 assumed that the outcome (as well as the treatment variables)
# were directly affected by all other nodes in the past. In certain situtations,
# domain specific knowledge may suggest otherwise leading to a Markov processes.
# This can be controlled using the k argument.
progressr::with_progress({
  psi2.2 <- lmtp_tmle(sim_t4, a, "Y", time_vary = tv, shift = d,
                      k = 0, folds = 2)
})
psi2.2

# Example 2.3
# Using the same data as examples 2.1 and 2.2.
# Now estimating the effect of a dynamic modified treatment policy.
a <- c("A_1", "A_2", "A_3", "A_4")
time_varying <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))
# our same shift function
shift <- function(data, trt) {
  (data[[trt]] - 1) * (data[[trt]] - 1 >= 1) + data[[trt]] * (data[[trt]] - 1 < 1)
}
# creating a dynamic MTP that applies the shift function
# but also depends on history and the current time
dynamic_mtp <- function(data, trt) {
  if (trt == "A_1") {
    # if its the first time point, follow the same mtp as before
    shift(data, trt)
  } else {
    # otherwise check if the time varying covariate equals 1
    ifelse(data[[sub("A", "L", trt)]] == 1,
           shift(data, trt), # if yes continue with the policy
           data[[trt]]) # otherwise do nothing
  }
}
psi2.3 <- lmtp_tmle(sim_t4, a, "Y", time_vary = time_varying,
                    k = 0, shift = dynamic_mtp, folds = 2)
psi2.3

# Example 2.4
# Using the same data as examples 2.1, 2.2, and 2.3, but now treating the exposure
# as an ordered categorical variable. To account for the exposure being a
# factor we just need to modify the shift function (and the original data)
# so as to respect this.
for (i in a) {
  sim_t4[[i]] <- factor(sim_t4[[i]], levels = 0:5, ordered = TRUE)
}
d <- function(data, trt) {
  out <- list()
  a <- data[[trt]]
```

```
  for (i in 1:length(a)) {
    if (as.character(a[i]) %in% c("0", "1")) {
      out[[i]] <- as.character(a[i])
    } else {
      out[[i]] <- as.numeric(as.character(a[i])) - 1
    }
  }
  factor(unlist(out), levels = 0:5, ordered = TRUE)
}
progressr::with_progress({
  psi2.4 <- lmtp_tmle(sim_t4, a, "Y", time_vary = tv, shift = d, k = 0, folds = 2)
})
psi2.4

# Example 3.1
# Longitudinal setting, time-varying binary treatment, time-varying covariates
# and baseline covariates with no loss-to-follow-up. Interested in a traditional
# causal effect where treatment is set to 1 at all time points for all observations.
data("iptwExWide", package = "twang")
a <- paste0("tx", 1:3)
baseline <- c("gender", "age")
tv <- list(c("use0"), c("use1"), c("use2"))
progressr::with_progress({
  psi3.1 <-
    lmtp_tmle(iptwExWide, a, "outcome", baseline = baseline, time_vary = tv,
              shift = static_binary_on, outcome_type = "continuous",
              folds = 2)
})
psi3.1

# Example 4.1
# Longitudinal setting, time-varying continuous treatment, time-varying covariates,
# binary outcome with right censoring. Interested in the mean population outcome under
# the observed exposures in a hypothetical population with no loss-to-follow-up.
head(sim_cens)
a <- c("A1", "A2")
tv <- list(c("L1"), c("L2"))
cens <- c("C1", "C2")
y <- "Y"
psi4.1 <- lmtp_tmle(sim_cens, a, y, time_vary = tv, cens = cens, shift = NULL, folds = 2)
psi4.1

# Example 4.2
# Using the same data as example 4.1, but now interested in the causal effect of a
# treatment policy where exposure increased by 0.5 units at all time points. The
# true value under this intervention is about 0.88.
d <- function(data, x) data[[x]] + 0.5
psi4.2 <- lmtp_tmle(sim_cens, a, y, time_vary = tv,
                    cens = cens, shift = d, folds = 2)
psi4.2

# Example 5.1
# Time-to-event analysis with a binary time-invariant exposure. Interested in
```

```
# the effect of treatment being given to all observations on the cumulative
# incidence of our time-to-event outcome.
a <- "trt"
# for a survival problem, the outcome arugment now takes a vector of outcomes
# if an observation experiences the event prior to the end of follow-up, all future
# outcome nodes should be set to 1 (i.e., last observation carried forward).
y <- paste0("Y.", 1:6)
cens <- paste0("C.", 0:5)
baseline <- c("W1", "W2")
progressr::with_progress({
  psi5.1 <- lmtp_tmle(sim_point_surv, a, y, baseline, cens = cens,
                      shift = static_binary_on, folds = 2)
})
psi5.1
```

---

sim_cens   *Simulated Longitudinal Data With Censoring*

Description

A dataset with a binary outcome, two time varying treatment nodes, two time varying covariates, and two censoring indicators.

Usage

```
sim_cens
```

Format

A data frame with 1000 rows and 10 variables:

L1 Time varying covariate time 1

A1 Treatment node at time 1, effected by L_1

C1 Censoring indicator that the observation is observed after time 1

L2 Time varying covariate at time 2, effected by L_1 and A_1

A2 Treatment node at time 2, effected by L_2 and A_1

C2 Censoring indicator that the observation is observed after time 2

Y Binary outcome at time 3, effected by L_2 and A_2

sim_point_surv	*Simulated Point-treatment Survival Data*

Description

A dataset with a time-to-event outcome, two baseline nodes, a binary point treatment, six past-time outcome nodes, and six censoring indicators.

Usage

```
sim_point_surv
```

Format

A data frame with 2000 rows and 16 variables:

W1 Binary baseline variable.

W2 Categorical baseline variable.

trt Binary treatment variable.

Y.0 Outcome node at time 0.

C.0 Censoring indicator that the observation is observed future time points.

Y.1 Outcome node at time 1.

C.1 Censoring indicator that the observation is observed future time points.

Y.2 Outcome node at time 2.

C.2 Censoring indicator that the observation is observed future time points.

Y.3 Outcome node at time 3.

C.3 Censoring indicator that the observation is observed future time points.

Y.4 Outcome node at time 4.

C.4 Censoring indicator that the observation is observed future time points.

Y.5 Outcome node at time 5.

C.5 Censoring indicator that the observation is observed future time points.

Y.6 Final outcome node.

---

sim_t4	*Simulated Longitudinal Data*

Description

A dataset with a binary outcome, four time varying treatment nodes, and four time varying covariates.

Usage

```
sim_t4
```

Format

A data frame with 5000 rows and 10 variables:

ID observation ID

L_1 Time varying covariate time 1

A_1 Treatment node at time 1, effected by L_1

L_2 Time varying covariate time 1, effected by L_1 and A_1

A_2 Treatment node at time 2, effected by L_2 and A_1

L_3 Time varying covariate time 1, effected by L_2 and A_2

A_3 Treatment node at time 3, effected by L_3 and A_2

L_4 Time varying covariate time 1, effected by L_3 and A_3

A_4 Treatment node at time 3, effected by L_4 and A_3

Y Binary outcome at time 5, effected by L_4 and A_4

---

static_binary_off	*Turn All Treatment Nodes Off*

Description

A pre-packaged shift function for use with provided estimators when the exposure is binary. Used to estimate the population intervention effect when all treatment variables are set to 0.

Usage

```
static_binary_off(data, trt)
```

Arguments

data	A dataframe containing the treatment variables.
trt	The name of the current treatment variable.

Value

A dataframe with all treatment nodes set to 0.

See Also

`lmtp_tmle()`, `lmtp_sdr()`, `lmtp_sub()`, `lmtp_ipw()`

Examples

```
data("iptwExWide", package = "twang")
a <- paste0("tx", 1:3)
baseline <- c("gender", "age")
tv <- list(c("use0"), c("use1"), c("use2"))
lmtp_sdr(iptwExWide, a, "outcome", baseline = baseline, time_vary = tv,
         shift = static_binary_off, outcome_type = "continuous", folds = 2)
```

---

static_binary_on   *Turn All Treatment Nodes On*

Description

A pre-packaged shift function for use with provided estimators when the exposure is binary. Used to estimate the population intervention effect when all treatment variables are set to 1.

Usage

```
static_binary_on(data, trt)
```

Arguments

data   A dataframe containing the treatment variables.

trt   The name of the current treatment variable.

Value

A dataframe with all treatment nodes set to 1.

See Also

`lmtp_tmle()`, `lmtp_sdr()`, `lmtp_sub()`, `lmtp_ipw()`

Examples

```
data("iptwExWide", package = "twang")
a <- paste0("tx", 1:3)
baseline <- c("gender", "age")
tv <- list(c("use0"), c("use1"), c("use2"))
lmtp_sdr(iptwExWide, a, "outcome", baseline = baseline, time_vary = tv,
         shift = static_binary_on, outcome_type = "continuous", folds = 2)
```

---

tidy.lmtp   *Tidy a(n) lmtp object*

Description

Tidy a(n) lmtp object

Usage

```
## S3 method for class 'lmtp'
tidy(x, ...)
```

Arguments

x	A lmtp object produced by a call to lmtp::lmtp_tmle(), lmtp::lmtp_sdr(), lmtp::lmtp_sub(), or lmtp::lmtp_ipw().
...	Unused, included for generic consistency only.

Examples

```
a <- c("A1", "A2")
nodes <- list(c("L1"), c("L2"))
cens <- c("C1", "C2")
y <- "Y"
fit <- lmtp_tmle(sim_cens, a, y, time_vary = nodes, cens = cens, shift = NULL, folds = 2)
tidy(fit)
```

Index