

Package ‘lntp’

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

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Description Non-parametric estimators for casual effects based on longitudinal modified treatment policies as described in Diaz, Williams, Hoffman, and Schenck <[doi:10.1080/01621459.2021.1955691](https://doi.org/10.1080/01621459.2021.1955691)>, traditional point treatment, and traditional longitudinal effects. Continuous, binary, and categorical treatments are allowed as well as censored outcomes. The treatment mechanism is estimated via a density ratio classification procedure irrespective of treatment variable type. For both continuous and binary outcomes, additive treatment effects can be calculated and relative risks and odds ratios may be calculated for binary outcomes.

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create_node_list	<i>Create a node list specification</i>
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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

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

Value

A list of lists. Each sub-list is the same length of the `time_vary` parameter with the variables to be used for estimation at that given time point for either the treatment mechanism or outcome regression.

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, paste0("Y.", 1:6))
```

lmtptest	<i>Perform Contrasts of LMTP Fits</i>
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Description

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

Usage

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

Arguments

...	One or more objects of class lmtptest.
ref	A reference value or another lmtptest 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 lmtptest 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

```
a <- c("A1", "A2")
nodes <- list(c("L1"), c("L2"))
cens <- c("C1", "C2")
y <- "Y"

# mean population outcome
psi_null <- lmtptest(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 <- lmtptest(sim_cens, a, y, time_vary = nodes,
                    cens = cens, shift = d, folds = 2, intervention_type = "mtp")

# treatment rule, everyone is decreased by 0.5
d <- function(data, x) data[[x]] - 0.5
```

```

psi_rule2 <- lmtipw(sim_cens, a, y, time_vary = nodes,
                   cens = cens, shift = d, folds = 2, intervention_type = "mtp")

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

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

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

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

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

```

lmtipw

LMTIPW 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

```

lmtipw(
  data,
  trt,
  outcome,
  baseline = NULL,
  time_vary = NULL,
  cens = NULL,
  shift = NULL,
  shifted = NULL,
  intervention_type = c("static", "dynamic", "mtp"),
  outcome_type = c("binomial", "continuous", "survival"),
  k = Inf,
  id = NULL,
  learners = "SL.glm",

```

```

    folds = 10,
    weights = NULL,
    .bound = 1e-05,
    .trim = 0.999,
    .SL_folds = 10
  )

```

Arguments

<code>data</code>	A data frame in wide format containing all necessary variables for the estimation problem.
<code>trt</code>	A vector containing the column names of treatment variables ordered by time.
<code>outcome</code>	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.
<code>baseline</code>	An optional vector containing the column names of baseline covariates to be included for adjustment at every time point.
<code>time_vary</code>	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.
<code>cens</code>	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.
<code>shift</code>	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.
<code>shifted</code>	An optional data frame, the same as in <code>data</code> , but modified according to the treatment policy of interest. If specified, <code>shift</code> is ignored.
<code>intervention_type</code>	The intervention type, should be one of "static", "dynamic", "mtp".
<code>outcome_type</code>	Outcome variable type (i.e., continuous, binomial, survival).
<code>k</code>	An integer specifying how previous time points should be used for estimation at the given time point. Default is <code>Inf</code> , all time points.
<code>id</code>	An optional column name containing cluster level identifiers.
<code>learners</code>	A vector of SuperLearner algorithms for estimation of the exposure mechanism. Default is "SL.glm", a main effects GLM.
<code>folds</code>	The number of folds to be used for cross-fitting. Minimum allowable number is two folds.
<code>weights</code>	An optional vector of length <code>n</code> containing sampling weights.
<code>.bound</code>	Determines that maximum and minimum values (scaled) predictions will be bounded by. The default is <code>1e-5</code> , bounding predictions by <code>1e-5</code> and <code>0.9999</code> .
<code>.trim</code>	Determines the amount the density ratios should be trimmed. The default is <code>0.999</code> , trimming the density ratios greater than the <code>0.999</code> percentile to the <code>0.999</code> percentile. A value of <code>1</code> indicates no trimming.

.SL_folds Integer. Controls the number of splits to be used for fitting the Super Learner. The default is 10.

Value

A list of class lmtip 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

```
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)

# Example 1.1
# 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.
policy <- function(data, x) {
  (data[[x]] > 80)*(data[[x]] - 15) + (data[[x]] <= 80)*data[[x]]
}

lmtip_ipw(
  ex1_dat, "A", "Y", "W",
  shift = policy, outcome_type = "continuous",
  folds = 2, intervention_type = "mtp"
)

# 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)
```

```

A <- c("A_1", "A_2", "A_3", "A_4")
L <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))

policy <- function(data, trt) {
  a <- data[[trt]]
  (a - 1) * (a - 1 >= 1) + a * (a - 1 < 1)
}

# BONUS: progressr progress bars!
progressr::handlers(global = TRUE)

lmtp_ipw(
  sim_t4, A, "Y", time_vary = L,
  shift = policy, folds = 2, intervention_type = "mtp"
)

# Example 2.2
# The previous example assumed that the outcome (as well as the treatment variables)
# were directly affected by all other nodes in the past. In certain situations,
# domain specific knowledge may suggest otherwise.
# This can be controlled using the k argument.
lmtp_ipw(
  sim_t4, A, "Y", time_vary = L,
  shift = policy, k = 0, folds = 2,
  intervention_type = "mtp"
)

# Example 2.3
# Using the same data as examples 2.1 and 2.2.
# Now estimating the effect of a dynamic modified treatment policy.
# creating a dynamic mtp that applies the shift function
# but also depends on history and the current time
policy <- function(data, trt) {
  mtp <- function(data, trt) {
    (data[[trt]] - 1) * (data[[trt]] - 1 >= 1) + data[[trt]] * (data[[trt]] - 1 < 1)
  }

  # if its the first time point, follow the same mtp as before
  if (trt == "A_1") return(mtp(data, trt))

  # otherwise check if the time varying covariate equals 1
  ifelse(
    data[[sub("A", "L", trt)]] == 1,
    mtp(data, trt), # if yes continue with the policy
    data[[trt]]    # otherwise do nothing
  )
}

lmtp_ipw(
  sim_t4, A, "Y", time_vary = L,
  k = 0, shift = policy, folds = 2
)

```

```

# 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.
tmp <- sim_t4
for (i in A) {
  tmp[[i]] <- factor(tmp[[i]], levels = 0:5, ordered = TRUE)
}

policy <- 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)
}

lmtipw(
  tmp, A, "Y", time_vary = L, shift = policy,
  k = 0, folds = 2, intervention_type = "mtp"
)

# 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.
if (require("twang")) {
  data("iptwExWide", package = "twang")

  A <- paste0("tx", 1:3)
  W <- c("gender", "age")
  L <- list(c("use0"), c("use1"), c("use2"))

  lmtipw(
    iptwExWide, A, "outcome", baseline = W, time_vary = L,
    shift = static_binary_on, outcome_type = "continuous",
    intervention_type = "static", folds = 2
  )
}

# 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")

```

```

L <- list(c("L1"), c("L2"))
C <- c("C1", "C2")
Y <- "Y"

lmtpr_ipw(sim_cens, A, Y, time_vary = L, cens = C, shift = NULL, folds = 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 the outcome.
# For a survival problem, the outcome argument 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).
A <- "trt"
Y <- paste0("Y.", 1:6)
C <- paste0("C.", 0:5)
W <- c("W1", "W2")

lmtpr_ipw(sim_point_surv, A, Y, W, cens = C, folds = 2,
          shift = static_binary_on, outcome_type = "survival")

```

lmtpr_sdr

LMTP Sequential Doubly Robust Estimator

Description

Sequentially doubly robust 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

```

lmtpr_sdr(
  data,
  trt,
  outcome,
  baseline = NULL,
  time_vary = NULL,
  cens = NULL,
  shift = NULL,
  shifted = NULL,
  k = Inf,
  intervention_type = c("static", "dynamic", "mtp"),
  outcome_type = c("binomial", "continuous", "survival"),
  id = NULL,
  bounds = NULL,
  learners_outcome = "SL.glm",
  learners_trt = "SL.glm",

```

```

    folds = 10,
    weights = NULL,
    .bound = 1e-05,
    .trim = 0.999,
    .SL_folds = 10
  )

```

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 containing the column names of baseline covariates to be included for adjustment at every time point.
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.
shifted	An optional data frame, the same as in data, but modified according to the treatment policy of interest. If specified, shift is ignored.
k	An integer specifying how previous time points should be used for estimation at the given time point. Default is Inf, all time points.
intervention_type	The intervention type, should be one of "static", "dynamic", "mtp".
outcome_type	Outcome variable type (i.e., continuous, binomial, survival).
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	A vector of SuperLearner algorithms for estimation of the outcome regression. Default is "SL.glm", a main effects GLM.
learners_trt	A vector of SuperLearner algorithms for estimation of the exposure mechanism. Default is "SL.glm", a main effects GLM.
folds	The number of folds to be used for cross-fitting. Minimum allowable number is two folds.

weights	An optional vector of length n containing sampling weights.
.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.
.trim	Determines the amount the density ratios should be trimmed. The default is 0.999, trimming the density ratios greater than the 0.999 percentile to the 0.999 percentile. A value of 1 indicates no trimming.
.SL_folds	Integer. Controls the number of splits to be used for fitting the Super Learner. The default is 10.

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

```

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)

# Example 1.1
# 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.
policy <- function(data, x) {
  (data[[x]] > 80)*(data[[x]] - 15) + (data[[x]] <= 80)*data[[x]]
}

```

```

}

lmtpr_sdr(
  ex1_dat, "A", "Y", "W", shift = policy,
  outcome_type = "continuous",
  folds = 2, intervention_type = "mtp"
)

# 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)

A <- c("A_1", "A_2", "A_3", "A_4")
L <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))

policy <- function(data, trt) {
  a <- data[[trt]]
  (a - 1) * (a - 1 >= 1) + a * (a - 1 < 1)
}

# BONUS: progressr progress bars!
progressr::handlers(global = TRUE)

lmtpr_sdr(
  sim_t4, A, "Y", time_vary = L, shift = policy,
  folds = 2, intervention_type = "mtp"
)

# Example 2.2
# The previous example assumed that the outcome (as well as the treatment variables)
# were directly affected by all other nodes in the past. In certain situations,
# domain specific knowledge may suggest otherwise.
# This can be controlled using the k argument.
lmtpr_sdr(
  sim_t4, A, "Y", time_vary = L,
  shift = policy, k = 0, folds = 2,
  intervention_type = "mtp"
)

# Example 2.3
# Using the same data as examples 2.1 and 2.2.
# Now estimating the effect of a dynamic modified treatment policy.
# creating a dynamic mtp that applies the shift function
# but also depends on history and the current time
policy <- function(data, trt) {
  mtp <- function(data, trt) {
    (data[[trt]] - 1) * (data[[trt]] - 1 >= 1) + data[[trt]] * (data[[trt]] - 1 < 1)
  }
}

```

```

# if its the first time point, follow the same mtp as before
if (trt == "A_1") return(mtp(data, trt))

# otherwise check if the time varying covariate equals 1
ifelse(
  data[[sub("A", "L", trt)]] == 1,
  mtp(data, trt), # if yes continue with the policy
  data[[trt]]     # otherwise do nothing
)
}

lmtpr_sdr(sim_t4, A, "Y", time_vary = L, k = 0, shift = policy, folds = 2)

# 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.
tmp <- sim_t4
for (i in A) {
  tmp[[i]] <- factor(tmp[[i]], levels = 0:5, ordered = TRUE)
}

policy <- 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)
}

lmtpr_sdr(
  tmp, A, "Y", time_vary = L, shift = policy,
  k = 0, folds = 2, intervention_type = "mtp"
)

# 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.
if (require("twang")) {
  data("iptwExWide", package = "twang")

  A <- paste0("tx", 1:3)
  W <- c("gender", "age")
  L <- list(c("use0"), c("use1"), c("use2"))

  lmtpr_sdr(

```

```

      iptwExWide, A, "outcome", baseline = W, time_vary = L,
      shift = static_binary_on, outcome_type = "continuous",
      intervention_type = "static", folds = 2
    )
  }

# 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")
L <- list(c("L1"), c("L2"))
C <- c("C1", "C2")
Y <- "Y"

lmtsub(sim_cens, A, Y, time_vary = L, cens = C, shift = NULL, folds = 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 the outcome.
# For a survival problem, the outcome argument 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).
A <- "trt"
Y <- paste0("Y.", 1:6)
C <- paste0("C.", 0:5)
W <- c("W1", "W2")

lmtsub(
  sim_point_surv, A, Y, W, cens = C, folds = 2,
  shift = static_binary_on, outcome_type = "survival"
)

```

lmtsub

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

```
lmtsub(
  data,
```

```

  trt,
  outcome,
  baseline = NULL,
  time_vary = NULL,
  cens = NULL,
  shift = NULL,
  shifted = NULL,
  k = Inf,
  outcome_type = c("binomial", "continuous", "survival"),
  id = NULL,
  bounds = NULL,
  learners = "SL.glm",
  folds = 10,
  weights = NULL,
  .bound = 1e-05,
  .SL_folds = 10
)

```

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 containing the column names of baseline covariates to be included for adjustment at every time point.
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.
shifted	An optional data frame, the same as in data, but modified according to the treatment policy of interest. If specified, shift is ignored.
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, survival).
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	A vector of SuperLearner algorithms for estimation of the outcome regression. Default is "SL.glm", a main effects GLM.
folds	The number of folds to be used for cross-fitting. Minimum allowable number is two folds.
weights	An optional vector of length n containing sampling weights.
.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.
.SL_folds	Integer. Controls the number of splits to be used for fitting the Super Learner. The default is 10.

Value

A list of class lmtpl 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

```

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)

# Example 1.1
# 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.
policy <- function(data, x) {
  (data[[x]] > 80)*(data[[x]] - 15) + (data[[x]] <= 80)*data[[x]]
}

```

```

}

lmtplib(ex1_dat, "A", "Y", "W", shift = policy,
        outcome_type = "continuous", folds = 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)

A <- c("A_1", "A_2", "A_3", "A_4")
L <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))

policy <- function(data, trt) {
  a <- data[[trt]]
  (a - 1) * (a - 1 >= 1) + a * (a - 1 < 1)
}

# BONUS: progressr progress bars!
progressr::handlers(global = TRUE)

lmtplib(sim_t4, A, "Y", time_vary = L, shift = policy, folds = 2)

# Example 2.2
# The previous example assumed that the outcome (as well as the treatment variables)
# were directly affected by all other nodes in the past. In certain situations,
# domain specific knowledge may suggest otherwise.
# This can be controlled using the k argument.
lmtplib(sim_t4, A, "Y", time_vary = L, shift = policy, k = 0, folds = 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.

# creating a dynamic mtp that applies the shift function
# but also depends on history and the current time
policy <- function(data, trt) {
  mtp <- function(data, trt) {
    (data[[trt]] - 1) * (data[[trt]] - 1 >= 1) + data[[trt]] * (data[[trt]] - 1 < 1)
  }

  # if its the first time point, follow the same mtp as before
  if (trt == "A_1") return(mtp(data, trt))

  # otherwise check if the time varying covariate equals 1
  ifelse(
    data[[sub("A", "L", trt)]] == 1,
    mtp(data, trt), # if yes continue with the policy
    data[[trt]]    # otherwise do nothing
  )
}

```

```

}

lmt_sub(sim_t4, A, "Y", time_vary = L, k = 0, shift = policy, folds = 2)

# 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.
tmp <- sim_t4
for (i in A) {
  tmp[[i]] <- factor(tmp[[i]], levels = 0:5, ordered = TRUE)
}

policy <- 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)
}

lmt_sub(tmp, A, "Y", time_vary = L, shift = policy, k = 0, folds = 2)

# 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.
if (require("twang")) {
  data("iptwExWide", package = "twang")

  A <- paste0("tx", 1:3)
  W <- c("gender", "age")
  L <- list(c("use0"), c("use1"), c("use2"))

  lmt_sub(iptwExWide, A, "outcome", baseline = W, time_vary = L,
         shift = static_binary_on, outcome_type = "continuous")
}

# 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")
L <- list(c("L1"), c("L2"))
C <- c("C1", "C2")

```

```

Y <- "Y"

lmtm_sub(sim_cens, A, Y, time_vary = L, cens = C, shift = NULL, folds = 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 the outcome.
# For a survival problem, the outcome argument 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).
A <- "trt"
Y <- paste0("Y.", 1:6)
C <- paste0("C.", 0:5)
W <- c("W1", "W2")

lmtm_sub(sim_point_surv, A, Y, W, cens = C, folds = 2,
         shift = static_binary_on, outcome_type = "survival")

```

lmtm_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

```

lmtm_tmle(
  data,
  trt,
  outcome,
  baseline = NULL,
  time_vary = NULL,
  cens = NULL,
  shift = NULL,
  shifted = NULL,
  k = Inf,
  intervention_type = c("static", "dynamic", "mtp"),
  outcome_type = c("binomial", "continuous", "survival"),
  id = NULL,
  bounds = NULL,
  learners_outcome = "SL.glm",
  learners_trt = "SL.glm",
  folds = 10,

```

```

weights = NULL,
.bound = 1e-05,
.trim = 0.999,
.SL_folds = 10
)

```

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 containing the column names of baseline covariates to be included for adjustment at every time point.
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.
shifted	An optional data frame, the same as in data, but modified according to the treatment policy of interest. If specified, shift is ignored.
k	An integer specifying how previous time points should be used for estimation at the given time point. Default is Inf, all time points.
intervention_type	The intervention type, should be one of "static", "dynamic", "mtp".
outcome_type	Outcome variable type (i.e., continuous, binomial, survival).
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	A vector of SuperLearner algorithms for estimation of the outcome regression. Default is "SL.glm", a main effects GLM.
learners_trt	A vector of SuperLearner algorithms for estimation of the exposure mechanism. Default is "SL.glm", a main effects GLM.
folds	The number of folds to be used for cross-fitting. Minimum allowable number is two folds.

weights	An optional vector of length n containing sampling weights.
.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.
.trim	Determines the amount the density ratios should be trimmed. The default is 0.999, trimming the density ratios greater than the 0.999 percentile to the 0.999 percentile. A value of 1 indicates no trimming.
.SL_folds	Integer. Controls the number of splits to be used for fitting the Super Learner. The default is 10.

Value

A list of class lmtpl 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

```
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)

# Example 1.1
# 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.
policy <- function(data, x) {
  (data[[x]] > 80)*(data[[x]] - 15) + (data[[x]] <= 80)*data[[x]]
}
```

```

}

lmtpl_tmle(
  ex1_dat, "A", "Y", "W", shift = policy,
  outcome_type = "continuous",
  folds = 2, intervention_type = "mtp"
)

# 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)

A <- c("A_1", "A_2", "A_3", "A_4")
L <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))
policy <- function(data, trt) {
  a <- data[[trt]]
  (a - 1) * (a - 1 >= 1) + a * (a - 1 < 1)
}

# BONUS: progressr progress bars!
progressr::handlers(global = TRUE)

lmtpl_tmle(
  sim_t4, A, "Y", time_vary = L, shift = policy,
  folds = 2, intervention_type = "mtp"
)

# Example 2.2
# The previous example assumed that the outcome (as well as the treatment variables)
# were directly affected by all other nodes in the past. In certain situations,
# domain specific knowledge may suggest otherwise.
# This can be controlled using the k argument.
lmtpl_tmle(
  sim_t4, A, "Y", time_vary = L, shift = policy,
  k = 0, folds = 2, intervention_type = "mtp"
)

# Example 2.3
# Using the same data as examples 2.1 and 2.2.
# Now estimating the effect of a dynamic modified treatment policy.
# creating a dynamic mtp that applies the shift function
# but also depends on history and the current time
policy <- function(data, trt) {
  mtp <- function(data, trt) {
    (data[[trt]] - 1) * (data[[trt]] - 1 >= 1) + data[[trt]] * (data[[trt]] - 1 < 1)
  }

  # if its the first time point, follow the same mtp as before
  if (trt == "A_1") return(mtp(data, trt))

```

```

# otherwise check if the time varying covariate equals 1
ifelse(
  data[[sub("A", "L", trt)]] == 1,
  mtp(data, trt), # if yes continue with the policy
  data[[trt]]     # otherwise do nothing
)
}

lmtp_tmle(sim_t4, A, "Y", time_vary = L,
          k = 0, shift = policy, folds = 2)

# 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.
tmp <- sim_t4
for (i in A) {
  tmp[[i]] <- factor(tmp[[i]], levels = 0:5, ordered = TRUE)
}

policy <- 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)
}

lmtp_tmle(tmp, A, "Y", time_vary = L, shift = policy,
          k = 0, folds = 2, intervention_type = "mtp")

# 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.
if (require("twang")) {
  data("iptwExWide", package = "twang")

  A <- paste0("tx", 1:3)
  W <- c("gender", "age")
  L <- list(c("use0"), c("use1"), c("use2"))

  lmtp_tmle(iptwExWide, A, "outcome", baseline = W, time_vary = L,
            shift = static_binary_on, outcome_type = "continuous",
            intervention_type = "static", folds = 2)
}

```

```

# 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")
L <- list(c("L1"), c("L2"))
C <- c("C1", "C2")
Y <- "Y"

lmtm(sim_cens, A, Y, time_vary = L, cens = C, shift = NULL, folds = 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 the outcome.
# For a survival problem, the outcome argument 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).
A <- "trt"
Y <- paste0("Y.", 1:6)
C <- paste0("C.", 0:5)
W <- c("W1", "W2")

lmtm(sim_point_surv, A, Y, W, cens = C, folds = 2,
      shift = static_binary_on, outcome_type = "survival")

```

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.
- 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

`sim_timevary_surv`*Simulated Time-varying Survival Data*

Description

A dataset with a time-to-event outcome, one baseline nodes, two time-varying covariates, a binary time-varying treatment, two outcome nodes, and two censoring indicators. Data-generating mechanism taken from Lendle, Schwab, Petersen, and van der Laan (<https://www.jstatsoft.org/article/view/v081i01>).

Usage`sim_timevary_surv`

Format

A data frame with 500 rows and 11 variables:

L0.a Continuous baseline variable.

L0.b Time varying covariate at baseline.

L0.c Time varying covariate at baseline.

A0 Treatment variable at baseline

C0 Censoring indicator that the observation is observed future time points.

L1.a Time varying covariate at time 1.

L1.b Time varying covariate at time 1.

Y1 Outcome node at time 1.

A1 Treatment variable at time 1.

C1 Censoring indicator that the observation is observed future time points.

Y2 Final outcome node.

static_binary_off	<i>Turn All Treatment Nodes Off</i>
-------------------	-------------------------------------

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

[lmp_tmle\(\)](#), [lmp_sdr\(\)](#), [lmp_sub\(\)](#), [lmp_ipw\(\)](#)

Examples

```

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

```

static_binary_on	<i>Turn All Treatment Nodes On</i>
------------------	------------------------------------

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

[lmtpr_tmle\(\)](#), [lmtpr_sdr\(\)](#), [lmtpr_sub\(\)](#), [lmtpr_ipw\(\)](#)

Examples

```

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

```

tidy.lmtp	<i>Tidy a(n) lmtp object</i>
-----------	------------------------------

Description

Tidy a(n) lmtp object

Usage

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

Arguments

x	A lmtp object produced by a call to <code>lmtp_tmle()</code> , <code>lmtp_sdr()</code> , <code>lmtp_sub()</code> , or <code>lmtp_ipw()</code> .
...	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)
```

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