

Package: tmle (via r-universe)

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Title Targeted Maximum Likelihood Estimation

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Depends glmnet, SuperLearner (>= 2.0)

Suggests dbarts (>= 0.9-18), gam (>= 1.15), ROCR (>= 1.0-7), WeightedROC

Description Targeted maximum likelihood estimation of point treatment effects (Targeted Maximum Likelihood Learning, The International Journal of Biostatistics, 2(1), 2006. This version automatically estimates the additive treatment effect among the treated (ATT) and among the controls (ATC). The `tmle()` function calculates the adjusted marginal difference in mean outcome associated with a binary point treatment, for continuous or binary outcomes. Relative risk and odds ratio estimates are also reported for binary outcomes. Missingness in the outcome is allowed, but not in treatment assignment or baseline covariate values. The population mean is calculated when there is missingness, and no variation in the treatment assignment. The `tmleMSM()` function estimates the parameters of a marginal structural model for a binary point treatment effect. Effect estimation stratified by a binary mediating variable is also available. An `ID` argument can be used to identify repeated measures. Default settings call 'SuperLearner' to estimate the Q and g portions of the likelihood, unless values or a user-supplied regression function are passed in as arguments.

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tmle-package

Targeted Maximum Likelihood Estimation with Super Learning

Description

Targeted maximum likelihood estimation of marginal treatment effect of a binary point treatment on a continuous or binary outcome, adjusting for baseline covariates (ATE: entire population, ATT: treated population, ATC: control population). Missingness in the outcome is accounted for in the estimation procedure. The population mean outcome is calculated when there is missingness and no treatment. Controlled direct effect estimation is available, and MSM parameter estimation for binary point treatment effects. Optional data-adaptive estimation of Q and g portions of the likelihood using the SuperLearner package is strongly encouraged.

Author(s)

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See Also

[tml](#), [tmlMSM](#)

calcParameters

Calculate Parameter Estimates (calcParameters)

Description

An internal function called by the `tml` function to calculate the population mean effect when there is missingness in the data, but no treatment assignment. When observations are in treatment and control groups, estimates the additive treatment effect among the entire population (ATE), among the treated (ATT), and among the controls (ATC). If the outcome is binary, also the relative risk and odds ratio parameters. P-values and 95% confidence intervals are also calculated (on the log scale for RR and OR).

Usage

```
calcParameters(Y, A, I.Z, Delta, g1W, g0W, Q, mu1, mu0, id, family,
              obsWeights, alpha.sig=0.05, ICflag=TRUE)
```

Arguments

Y	continuous or binary outcome variable
A	binary treatment indicator, 1 - treatment, 0 - control
I.Z	Indicator $Z=z$, needed for CDE estimation
Delta	indicator of missing outcome. 1 - observed, 0 - missing
g1W	censoring mechanism estimates, $P(A = 1 W) \times P(Delta = 1 A, W)$
g0W	censoring mechanism estimates, $P(A = 0 W) \times P(Delta = 1 A, W)$
Q	a 3-column matrix ($Q(A, W)$, $Q(1, W)$, $Q(0, W)$)
mu1	targeted estimate of $E(Y A = 1, W)$
mu0	targeted estimate of $E(Y A = 0, W)$
id	subject identifier
family	family specification for regressions, generally 'gaussian' for continuous outcomes, 'binomial' for binary outcomes
obsWeights	sampling weights
alpha.sig	significance level for constructing CIs. Default = 0.05
ICflag	set to FALSE to skip evaluating IC-based variance

Value

EY1	Population mean outcome estimate, variance, p-value, 95% confidence interval (missingness only, no treatment assignment), or NULL
ATE	additive treatment effect estimate, variance, p-value, 95% confidence interval, or NULL
RR	relative risk estimate, p-value, 95% confidence interval, log(RR), variance(log(RR)), or NULL
OR	odds ratio estimate, p-value, 95% confidence interval, log(OR), variance(log(OR)), or NULL

Author(s)

Susan Gruber

See Also

[tmle](#), [estimateQ](#), [estimateG](#), [tmleMSM](#), [calcSigma](#)

calcSigma	<i>Calculate Variance-Covariance Matrix for MSM Parameters (calcSigma)</i>
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Description

An internal function called by the `tmleMSM` function to calculate the variance-covariance matrix of the parameter estimates based on the influence curve of the specified MSM.

Usage

```
calcSigma(hAV, gAVW, Y, Q, mAV, covar.MSM, covar.MSMA0, covar.MSMA1, I.V,
          Delta, ub, id, family)
```

Arguments

<code>hAV</code>	values used in numerator of weights applied to the estimation procedure
<code>gAVW</code>	$P(A = a V, W, T) * P(Delta = 1 A, V, W, T)$
<code>Y</code>	continuous or binary outcome variable
<code>Q</code>	estimated $P(Y A, V, W, T, Delta = 1)$, typically targeted values Q^* are passed in
<code>mAV</code>	predicted values for $EY1$ from the MSM using the targeted estimates for psi
<code>covar.MSM</code>	covariate values used as predictors for the MSM when $A=a$
<code>covar.MSMA0</code>	covariate values used as predictors for the MSM when $A=0$
<code>covar.MSMA1</code>	covariate values used as predictors for the MSM when $A=1$
<code>I.V</code>	indicator that observation is in stratum of interest
<code>Delta</code>	indicator of missing outcome. 1 - observed, 0 - missing
<code>ub</code>	upper bound on weights
<code>id</code>	subject identifier
<code>family</code>	'gaussian' for continuous outcomes, 'binomial' for binary outcomes

Value

<code>sigma</code>	influence-curve based variance-covariance matrix. See Rosenblum&vanderLaan2010 for details.
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Author(s)

Susan Gruber

See Also

[tmle](#), [estimateQ](#), [estimateG](#), [tmleMSM](#)

estimateG

*Estimate Treatment or Missingness Mechanism***Description**

An internal function called by the `tmle` function to obtain an estimate of conditional treatment assignment probabilities $P(A = 1|W)$, and conditional probabilities for missingness, $P(Delta = 1|A, W)$. The estimate can be based on user-supplied values, a user-supplied regression formula, or a data-adaptive super learner fit. If the SuperLearner package is not available, and there are no user-specifications, estimation is carried out using main terms regression with `glm`. These main terms-based estimates may yield poor results.

Usage

```
estimateG(d, g1W, gform, SL.library, id, V, verbose, message,
outcome="A", newdata=d, discreteSL, obsWeights)
```

Arguments

<code>d</code>	dataframe with binary dependent variable in the first column, predictors in remaining columns
<code>g1W</code>	vector of values for $P(A = 1 W)$, $P(Z = 1 A, W)$, or $P(Delta = 1 Z, A, W)$
<code>gform</code>	regression formula of the form $A \sim W1$, (dependent variable is one of A, Z, D) if specified this overrides the call to SuperLearner
<code>SL.library</code>	vector of prediction algorithms used by SuperLearner, default value is (<code>'SL.glm'</code> , <code>'tmle.SL.dbarts.k.5'</code> , <code>'SL.gam'</code>)
<code>id</code>	subject identifier
<code>V</code>	Number of cross validation folds for Super Learning
<code>verbose</code>	status messages printed if set to TRUE
<code>message</code>	text specifies whether treatment or missingness mechanism is being estimated
<code>outcome</code>	A, D, Z to indicate which quantity is being estimated.
<code>newdata</code>	optional dataset to be used for prediction after fitting on d.
<code>discreteSL</code>	If true, returns discrete SL estimates, otherwise ensemble estimates. Ignored when SL is not used.
<code>obsWeights</code>	sampling weights

Value

<code>g1W</code>	a vector containing values for $P(A = 1 W)$, matrix for $P(Z = 1 A, W)$, evaluated at $A=0, A=1$, or matrix $P(Delta = 1 Z, A, W)$ evaluated at $(0,0), (0,1), (1,0), (1,1)$
<code>coef</code>	coefficients for each term in the working model used for estimation if <code>glm</code> was used
<code>type</code>	estimation procedure

Author(s)

Susan Gruber

See Also[tmle](#), [estimateQ](#), [calcParameters](#), [tmleMSM](#), [calcSigma](#)

estimateQ

*Initial Estimation of Q portion of the Likelihood***Description**

An internal function called by the `tmle` function to obtain an initial estimate of the Q portion of the likelihood based on user-supplied matrix values for predicted values of (counterfactual outcomes) $Q(\theta, W)$, $Q(1, W)$, or a user-supplied regression formula, or based on a data-adaptively selected SuperLearner fit. In the absence of user-supplied values, a user-supplied regression formula takes precedence over data-adaptive super-learning. The default is to return cross-validated predictions.

Usage

```
estimateQ(Y, Z, A, W, Delta, Q, Qbounds, Qform, maptoYstar, SL.library, cvQinit,
         family, id, V, verbose, discreteSL, obsWeights)
```

Arguments

Y	continuous or binary outcome variable
Z	optional binary indicator for intermediate covariate for controlled direct effect estimation
A	binary treatment indicator, 1 - treatment, 0 - control
W	vector, matrix, or dataframe containing baseline covariates
Delta	indicator of missing outcome. 1 - observed, 0 - missing
Q	3-column matrix ($Q(A, W)$, $Q(\theta, W)$, $Q(1, W)$)
Qbounds	Bounds on predicted values for Q, set to <code>alpha</code> for logistic fluctuation, or <code>range(Y)</code> if not user-supplied
Qform	regression formula of the form $Y \sim A + W$
maptoYstar	if TRUE indicates continuous Y values should be shifted and scaled to fall between (0,1)
SL.library	specification of prediction algorithms, default is ('SL.glm', 'SL.glmnet', 'tmle.SL.dbarts2'). In practice, including more prediction algorithms in the library improves results.
cvQinit	logical, whether or not to estimate cross-validated values for initial Q, default=TRUE
family	family specification for regressions, generally 'gaussian' for continuous outcomes, 'binomial' for binary outcomes

id	subject identifier
V	Number of cross-validation folds for Super Learning
verbose	status message printed if set to TRUE
discreteSL	If true, returns discrete SL estimates, otherwise ensemble estimates. Ignored when SL is not used.
obsWeights	sampling weights

Value

Q	$n \times 3$ matrix, columns contain the initial estimate of $[Q(A, W) = E(Y A = a, W), Q(0, W) = E(Y A = 0, W), Q(1, W) = E(Y A = 1, W)]$. For controlled direct estimation, $n \times 5$ matrix, $E(Y Z, A, W)$, evaluated at $(z, a), (0, 0), (0, 1), (1, 0), (1, 1)$ on scale of linear predictors
Qfamily	'binomial' for targeting with logistic fluctuation, 'gaussian' for linear fluctuation
coef	coefficients for each term in working model used for initial estimation of Q if glm used.
type	type of estimation procedure

Author(s)

Susan Gruber

See Also

[tmle](#), [estimateG](#), [calcParameters](#), [tmleMSM](#), [calcSigma](#)

fev

Forced Expiratory Volume (FEV) Data (fev)

Description

Sample of 654 youths, aged 3 to 19, in the area of East Boston during middle to late 1970's. Interest concerns the relationship between smoking and FEV. Since the study is necessarily observational, statistical adjustment via regression models clarifies the relationship.

Usage

```
data(fev)
```

Format

A data frame with 654 observations on the following 5 variables.

age a numeric vector
 fev a numeric vector
 ht a numeric vector
 sex a numeric vector
 smoke a numeric vector

Source

Kahn M (2005). An Exhale Problem for Teaching Statistics. The Journal of Statistical Education, 13(2).

Rosner, B. (1999), Fundamentals of Biostatistics, 5th Ed., Pacific Grove, CA: Duxbury.

 oneStepATT

Calculate Additive treatment effect among the treated (oneStepATT)

Description

An internal function called by the tmle function to calculate the additive treatment effect among the treated (ATT) using a universal least favorable submodel (on the transformed scale if outcomes are continuous). The function is called a second time with updated arguments to calculate the additive treatment effect among the controls (ATC). Missingness in the outcome data is allowed.

Usage

```
oneStepATT(Y, A, Delta, Q, g1W, pDelta1, depsilon, max_iter, gbounds, Qbounds, obsWeights)
```

Arguments

Y	continuous or binary outcome variable
A	binary treatment indicator, 1 - treatment, 0 - control
Delta	indicator of missing outcome. 1 - observed, 0 - missing
Q	a 3-column matrix ($Q(A, W)$, $Q(1, W)$, $Q(0, W)$)
g1W	treatment mechanism estimates, $P(A = 1 W)$
pDelta1	censoring mechanism estimates, a 2-column matrix [$P(Delta = 1 A = 0, W)$, $P(Delta = 1 A = 1, W)$]
depsilon	step size for delta moves, set to 0.001
max_iter	maximum number of iterations before terminating without convergence
gbounds	bounds on the propensity score for untreated subjects
Qbounds	alpha bounds on the logit scale
obsWeights	sampling weights

Value

psi	effect estimate (on the transformed scale for continuous outcomes)
IC	influence function
conv	TRUE if procedure converged, FALSE otherwise

Author(s)

Susan Gruber

See Also

[tml](#),

summary.tml

Summarization of the results of a call to the tml routine

Description

These functions are all [methods](#) for class tml, tml.list, summary.tml, summary.tml.list objects

Usage

```
## S3 method for class 'tml'
summary(object, ...)
## S3 method for class 'tml.list'
summary(object, ...)
## S3 method for class 'tml'
print(x, ...)
## S3 method for class 'tml.list'
print(x, ...)
## S3 method for class 'summary.tml'
print(x, ...)
## S3 method for class 'summary.tml.list'
print(x, ...)
```

Arguments

object	an object of class tml or tml.list.
x	an object of class tml or tml.list for summary functions, class summary.tml or summary.tml.list for print functions.
...	currently ignored.

Details

print.tml prints the estimate, variance, p-value, and 95% confidence interval only. print.summary.tml, called indirectly by entering the command summary(result) (where result has class tml), outputs additional information. Controlled direct effect estimates have class tml.list, a list of two objects of class tml. The first item corresponds to $Z = 0$, the second to $Z = 1$

Value

estimates	list of parameter estimates, pvalues, and 95% confidence intervals
Qmodel	working model used to obtain initial estimate of Q portion of the likelihood, if glm used
Qterms	terms in the model for Q

Qcoef	coefficient of each term in model for Q
gmodel	model used to estimate treatment mechanism g
gterms	terms in the treatment mechanism model
gcoef	coefficient of each term in model for treatment mechanism
gtype	description of estimation procedure for treatment mechanism, e.g. "SuperLearner"
gdiscreteSL	flag indicating whether discrete SL or ensemble SL was used for treatment mechanism estimation
g.Zmodel	model used to estimate intermediate variable assignment mechanism g.Z
g.Zterms	terms in the intermediate mechanism model
g.Zcoef	coefficient of each term in model for intermediate mechanism
g.Ztype	description of estimation procedure for intermediate variable
g.ZdiscreteSL	flag indicating whether discrete SL or ensemble SL was used for intermediate variable estimation
g.Deltamodel	model used to estimate missingness mechanism g.Delta
g.Deltaterms	terms in the missingness mechanism model
g.Deltacoef	coefficient of each term in model for missingness mechanism
g.Deltatype	description of estimation procedure for missingness
g.DeltadiscreteSL	flag indicating whether discrete SL or ensemble SL was used for missingness estimation

Author(s)

Susan Gruber

See Also[tmle](#)**Examples**

```
# generate data
set.seed(10)
n <- 500
W <- matrix(rnorm(n*3), ncol=3)
A <- rbinom(n,1, 1/(1+exp(-(.1*W[,1] - .1*W[,2] + .5*W[,3])))
Y <- A + 2*W[,1] + W[,3] + W[,2]^2 + rnorm(n)
colnames(W) <- paste("W",1:3, sep="")

result <- tmle(Y,A,W, Qform="Y~A+W1", g1W=rep(.5, n))
summary(result)
```

summary.tmleMSM

*Summarization of the results of a call to the tmleMSM function***Description**

These functions are all [methods](#) for class tmleMSM, summary.tmleMSM objects

Usage

```
## S3 method for class 'tmleMSM'
summary(object, ...)
## S3 method for class 'tmleMSM'
print(x, ...)
## S3 method for class 'summary.tmleMSM'
print(x, ...)
```

Arguments

object	an object of class tmleMSM.
x	an object of class tmleMSM for summary functions, class summary.tmleMSM for print functions.
...	currently ignored.

Details

print.tmleMSM prints the estimate, standard error, p-value, and 95% confidence interval only. print.summary.tmleMSM, called indirectly by entering the command summary(result) (where result has class tmleMSM), outputs additional information.

Value

estimates	matrix of MSM parameter estimates, standard errors, pvalues, upper and lower bounds on 95% confidence intervals
sigma	variance-covariance matrix
Qmodel	working model used to obtain initial estimate of Q portion of the likelihood, if glm used
Qterms	terms in the model for Q
Qcoef	coefficient of each term in model for Q
gmodel	model used to estimate treatment mechanism g
gterms	terms in the treatment mechanism model
gcoef	coefficient of each term in model for treatment mechanism
gtype	description of estimation procedure for treatment mechanism, e.g. "SuperLearner"
g.AVmodel	model used to estimate $h(A,V)$ (or $h(A,T)$)
g.AVterms	terms in the model for $h(A,V)$

g.AVcoef	coefficient of each term in model for h(A,V)
g.AVtype	description of estimation procedure for h(A,V)
g.Deltamodel	model used to estimate missingness mechanism g.Delta
g.Deltaterms	terms in the missingness mechanism model
g.Deltacoef	coefficient of each term in model for missingness mechanism
g.Deltatype	description of estimation procedure for missingness
psi.Qinit	MSM parameter estimates based on initial (untargeted) estimated Q

Author(s)

Susan Gruber

See Also[tmleMSM](#)

tmle	<i>Targeted Maximum Likelihood Estimation</i>
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Description

Targeted maximum likelihood estimation of parameters of a marginal structural model, and of marginal treatment effects of a binary point treatment on an outcome. In addition to the additive treatment effect, risk ratio and odds ratio estimates are reported for binary outcomes. The `tmle` function is generally called with arguments (Y, A, W) , where Y is a continuous or binary outcome variable, A is a binary treatment variable, ($A=1$ for treatment, $A=0$ for control), and W is a matrix or dataframe of baseline covariates. The population mean outcome is calculated when there is no variation in A . If values of binary mediating variable Z are supplied, estimates are returned at each level of Z . Missingness in the outcome is accounted for in the estimation procedure if missingness indicator Δ is 0 for some observations. Repeated measures can be identified using the `id` argument. Option to adjust for biased sampling using the `obsWeights` argument. Targeted bootstrap inference can be obtained in addition to IC-based inference by setting `B` to a value greater than 1 (10,000 recommended for analyses requiring high precision).

Usage

```
tmle(Y, A, W, Z=NULL, Delta = rep(1,length(Y)), Q = NULL, Q.Z1 = NULL, Qform = NULL,
     Qbounds = NULL, Q.SL.library = c("SL.glm", "tmle.SL.dbarts2", "SL.glmnet"),
     cvQinit = TRUE, g1W = NULL, gform = NULL,
     gbound = NULL, pZ1=NULL,
     g.Zform = NULL, pDelta1 = NULL, g.Deltaform = NULL,
     g.SL.library = c("SL.glm", "tmle.SL.dbarts.k.5", "SL.gam"),
     g.Delta.SL.library = c("SL.glm", "tmle.SL.dbarts.k.5", "SL.gam"),
     family = "gaussian", fluctuation = "logistic", alpha = 0.9995, id=1:length(Y),
     V.Q = 10, V.g=10, V.Delta=10, V.Z = 10,
     verbose = FALSE, Q.discreteSL=FALSE, g.discreteSL=FALSE, g.Delta.discreteSL=FALSE,
     prescreenW.g=TRUE, min.retain = 5, target.gwt = TRUE, automate=FALSE,
     obsWeights = NULL, alpha.sig = 0.05, B = 1)
```

Arguments

Y	continuous or binary outcome variable
A	binary treatment indicator, 1 - treatment, 0 - control
W	vector, matrix, or dataframe containing baseline covariates
Z	optional binary indicator for intermediate covariate for controlled direct effect estimation
Delta	indicator of missing outcome or treatment assignment. 1 - observed, 0 - missing
Q	optional $n \times 2$ matrix of initial values for Q portion of the likelihood, $(E(Y A = 0, W), E(Y A = 1, W))$
Q.Z1	optional $n \times 2$ matrix of initial values for Q portion of the likelihood, $(E(Y Z = 1, A = 0, W), E(Y Z = 1, A = 1, W))$. (When specified, values for $E(Y Z = 0, A = 0, W), E(Y Z = 0, A = 1, W)$ are passed in using the Q argument
Qform	optional regression formula for estimation of $E(Y A, W)$, suitable for call to <code>glm</code>
Qbounds	vector of upper and lower bounds on Y and predicted values for initial Q. Defaults to the range of Y, widened by 1% of the min and max values.
Q.SL.library	optional vector of prediction algorithms to use for SuperLearner estimation of initial Q
cvQinit	logical, if TRUE, estimates cross-validated predicted values, default=TRUE
g1W	optional vector of conditional treatment assignment probabilities, $P(A = 1 W)$
gform	optional regression formula of the form $A \sim W$, if specified this overrides the call to SuperLearner
gbound	value between (0,1) for truncation of predicted probabilities. See Details section for more information
pZ1	optional $n \times 2$ matrix of conditional probabilities $P(Z = 1 A = 0, W), P(Z = 1 A = 1, W)$
g.Zform	optional regression formula of the form $Z \sim A+W$, if specified this overrides the call to SuperLearner
pDelta1	optional matrix of conditional probabilities for missingness mechanism, $n \times 2$ when Z is NULL $P(Delta = 1 A = 0, W), P(Delta = 1 A = 1, W)$. $n \times 4$ otherwise, $P(Delta = 1 Z = 0, A = 0, W), P(Delta = 1 Z = 0, A = 1, W), P(Delta = 1 Z = 1, A = 0, W), P(Delta = 1 Z = 1, A = 1, W)$
g.Deltaform	optional regression formula of the form $Delta \sim A+W$, if specified this overrides the call to SuperLearner
g.SL.library	optional vector of prediction algorithms to use for SuperLearner estimation of <code>g1W</code>
g.Delta.SL.library	optional vector of prediction algorithms to use for SuperLearner estimation of <code>pDelta1</code>
family	family specification for working regression models, generally 'gaussian' for continuous outcomes (default), 'binomial' for binary outcomes
fluctuation	'logistic' (default), or 'linear'

alpha	used to keep predicted initial values bounded away from (0,1) for logistic fluctuation
id	optional subject identifier
V.Q	Number of cross-validation folds for super learner estimation of Q
V.g	Number of cross-validation folds for super learner estimation of g
V.Delta	Number of cross-validation folds for super learner estimation of missingness mechanism
V.Z	Number of cross-validation folds for super learner estimation of intermediate variable
verbose	status messages printed if set to TRUE (default=FALSE)
Q.discreteSL	if TRUE, discreteSL is used instead of ensemble SL. Ignored when SL not used to estimate Q
g.discreteSL	if TRUE, discreteSL is used instead of ensemble SL. Ignored when SL not used to estimate g W
g.Delta.discreteSL	if TRUE, discreteSL is used instead of ensemble SL. Ignored when SL not used to estimate $P(\Delta = 1 A, W)$
prescreenW.g	Option to screen covariates before estimating g in order to retain only those associated with the outcome (Recommend FALSE in low dimensional datasets)
min.retain	Minimum number of covariates to retain when prescreening covariates for g. Ignored when prescreenW.g=FALSE
target.gwt	When TRUE, move g from denominator of clever covariate to the weight when fitting epsilon
automate	When TRUE, all tuning parameters are set to their default values. Number of cross validation folds, truncation level for g, and decision to prescreen covariates for modeling g are set data-adaptively based on sample size (see details).
obsWeights	Optional observation weights to account for biased sampling
alpha.sig	significance level for constructing 1-alpha.sig confidence intervals
B	Number of bootstrap iterations. Set $B > 1$ to obtain targeted bootstrap based inference in addition to IC-based inference (see Details).

Details

gbounds Lower bound defaults to $lb = 5/\sqrt{n}/\log(n)$. For treatment effect estimates and population mean outcome the upper bound defaults to 1. For ATT and ATC, the upper bound defaults to $1 - lb$.

W may contain factors. These are converted to indicators via a call to `model.matrix`.

Controlled direct effects are estimated when binary covariate Z is non-null. The `tmle` function returns an object of class `tmle.list`, a list of two items of class `tmle`. The first corresponds to estimates obtained when Z is fixed at 0, the second corresponds to estimates obtained when Z is fixed at 1.

When `automate = TRUE` the sample size determines the number of cross validation folds, V based on the effective sample size. When Y is continuous `n.effective = n`. When Y is binary `n.effective =`

5 * size of minority class. When $n_{\text{effective}} \leq 30$ $V = n_{\text{effective}}$; When $n_{\text{effective}} \leq 500$ $V = 20$; When $500 < n \leq 1000$ $V = 10$; When $1000 < n \leq 10000$ $V = 5$; Otherwise $V = 2$. Bounds on g set to $(5/\sqrt{n})/\log(n)$, 1), except for ATT and ATE, where upper bound is 1-lower bound. `Wretain.g` set to TRUE when number of covariates $\geq n_{\text{effective}}/5$.

Set $B = 10,000$ to obtain high precision targeted bootstrap quantile-based confidence intervals and variance of bootstrap point estimates. Set $B = 1,000$ for rough approximation, and $B = 1$ for IC-based inference only.

Value

<code>estimates</code>	list with elements EY1 (population mean), ATE (additive treatment effect), ATT (additive treatment effect among the treated), ATC (additive treatment effect among the controls), RR (relative risk), OR (odds ratio). Each element in the estimates of these is itself a list containing <ul style="list-style-type: none"> • <code>psi</code> - parameter estimate • <code>pvalue</code> - two-sided p-value • <code>CI</code> - 95% confidence interval • <code>var.psi</code> - Influence-curve based variance of estimate (ATE parameter only) • <code>log.psi</code> - Parameter estimate on log scale (RR and OR parameters) • <code>var.log.psi</code> - Influence-curve based variance of estimate on log scale (RR and OR parameters) • <code>bs.var</code> - Variance of bootstrap point estimates (when $B > 1$) • <code>bs.CI.twosided</code> - Quantile-based 2-sided confidence interval bounds • <code>bs.CI.onesided.lower</code> - Quantile-based 1-sided lower confidence interval bounds • <code>bs.CI.onesided.upper</code> - Quantile-based 1-sided upper confidence interval bounds
<code>Qinit</code>	initial estimate of Q . <code>Qinit\$coef</code> are the coefficients for a <code>glm</code> model for Q , if applicable. <code>Qinit\$Q</code> is an $n \times 2$ matrix, where n is the number of observations. Columns contain predicted values for $Q(0, W)$, $Q(1, W)$ using the initial fit. <code>Qinit\$type</code> is method for estimating Q . <code>Qinit\$Rsq</code> is R_{sq} for initial estimate of Q . <code>Qinit\$Rsq.type</code> empirical or cross-validated (depends on value of <code>cvQinit</code>), R_{sq} or pseudo- R_{sq} when Y is binary.
<code>Qstar</code>	targeted estimate of Q , an $n \times 2$ matrix with predicted values for $Q(0, W)$, $Q(1, W)$ using the updated fit
<code>g</code>	treatment mechanism estimate. A list with four items: <code>g\$g1W</code> contains estimates of $P(A = 1 W)$ for each observation, <code>g\$coef</code> the coefficients for the model for g when <code>glm</code> used, <code>g\$type</code> estimation procedure, <code>g\$discreteSL</code> flag, <code>g\$AUC</code> empirical AUC if ROCR package is available
<code>g.Z</code>	intermediate covariate assignment estimate (when applicable). A list with four items: <code>g.Z\$g1W</code> an $n \times 2$ matrix containing values of $P(Z = 1 A = 1, W)$, $P(Z = 1 A = 0, W)$ for each observation, <code>g.Z\$coef</code> the coefficients for the model for g when <code>glm</code> used, <code>g.Z\$type</code> estimation procedure, <code>g.Z\$discreteSL</code> flag
<code>g.Delta</code>	missingness mechanism estimate. A list with four items: <code>g.Delta\$g1W</code> an $n \times 4$ matrix containing values of $P(\Delta = 1 Z, A, W)$ for each observation, with

	(Z=0,A=0), (Z=0,A=1), (Z=1,A=0),(Z=1,A=1). (When Z is NULL, columns 3 and 4 are duplicates of 1 and 2.) g.Delta\$coef the coefficients for the model for g when glm used, g.Delta\$type estimation procedure, g.Delta\$discreteSL flag
gbound	bounds used to truncate g
gbound.ATT	bounds used to truncated g for ATT and ATC estimation
W.retained	names of covariates used to model the components of g

Author(s)

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See Also

[summary.tmle](#), [estimateQ](#), [estimateG](#), [calcParameters](#), [oneStepATT](#), [tmleMSM](#), [calcSigma](#)

Examples

```
library(tmle)
set.seed(1)
```

```

n <- 250
W <- matrix(rnorm(n*3), ncol=3)
A <- rbinom(n,1, 1/(1+exp(-(.2*W[,1] - .1*W[,2] + .4*W[,3])))
Y <- A + 2*W[,1] + W[,3] + W[,2]^2 + rnorm(n)

# Example 1. Simplest function invocation
# SuperLearner called to estimate Q, g
# Delta defaults to 1 for all observations
## Not run:
result1 <- tmle(Y,A,W)
summary(result1)

## End(Not run)
# Example 2:
# User-supplied regression formulas to estimate Q and g
# binary outcome
n <- 250
W <- matrix(rnorm(n*3), ncol=3)
colnames(W) <- paste("W",1:3, sep="")
A <- rbinom(n,1, plogis(0.6*W[,1] +0.4*W[,2] + 0.5*W[,3]))
Y <- rbinom(n,1, plogis(A + 0.2*W[,1] + 0.1*W[,2] + 0.2*W[,3]^2 ))
result2 <- tmle(Y,A,W, family="binomial", Qform="Y~A+W1+W2+W3", gform="A~W1+W2+W3")
summary(result2)

## Not run:
# Example 3:
# Incorporate sampling weights and
# request targeted bootstrap-based inference along with IC-based results
pi <- .25 + .5*W[,1] > 0
enroll <- sample(1:n, size = n/2, p = pi)
result3 <- tmle(Y[enroll],A[enroll],W[enroll,], family="binomial", Qform="Y~A+W1+W2+W3",
gform="A~W1+W2+W3", obsWeights = 1/pi[enroll],B=1000)
summary(result3)

# Example 4: Population mean outcome
# User-supplied (misspecified) model for Q,
# Super learner called to estimate g, g.Delta
# V set to 2 for demo, not recommended at this sample size
# approx. 20
Y <- W[,1] + W[,2]^2 + rnorm(n)
Delta <- rbinom(n, 1, 1/(1+exp(-(1.7-1*W[,1])))
result4 <- tmle(Y,A=NULL,W, Delta=Delta, Qform="Y~A+W1+W2+W3", V.g=2, V.Delta=2)
print(result4)

# Example 5: Controlled direct effect
# User-supplied models for g, g.Z
# V set to 2 for demo, not recommended at this sample size
A <- rbinom(n,1,.5)
Z <- rbinom(n, 1, plogis(.5*A + .1*W[,1]))
Y <- 1 + A + 10*Z + W[,1]+ rnorm(n)

CDE <- tmle(Y,A,W, Z, gform="A~1", g.Zform = "Z ~ A + W1", V.Q=2, V.g=2)
print(CDE)

```

```
total.effect <- tmle(Y,A, W, gform="A~1")
print(total.effect)

## End(Not run)
```

tmle.SL.dbarts2	<i>Super Learner wrappers for modeling and prediction using bart in the dbarts package</i>
-----------------	--

Description

These functions are used internally, not typically called by the user

Usage

```
tmle.SL.dbarts2(Y, X, newX, family, obsWeights, id, sigest = NA, sigdf = 3,
  sigquant = 0.90, k = 2, power = 2.0, base = 0.95, binaryOffset = 0.0,
  ntree = 200, ndpost = 1000, nskip = 100, printevery = 100, keepevery = 1,
  keeptrainfits = TRUE, usequants = FALSE, numcut = 100, printcutoffs = 0,
  nthread = 1, keepcall = TRUE, verbose = FALSE, ...)
tmle.SL.dbarts.k.5(Y, X, newX, family, obsWeights, id, sigest = NA, sigdf = 3,
  sigquant = 0.90, k = 0.5, power = 2.0, base = 0.95, binaryOffset = 0.0,
  ntree = 200, ndpost = 1000, nskip = 100, printevery = 100, keepevery = 1,
  keeptrainfits = TRUE, usequants = FALSE, numcut = 100, printcutoffs = 0,
  nthread = 1, keepcall = TRUE, verbose = FALSE, ...)
## S3 method for class 'tmle.SL.dbarts2'
predict(object, newdata, family, ...)
```

Arguments

Y	Dependent variable
X	Predictor covariate matrix or data frame used as training set
newX	Predictor covariate matrix or data frame for which predictions should be made
family	Regression family, 'gaussian' or 'binomial'
obsWeights	observation-level weights
id	identifier to group observations, not used
sigest	An estimate of error variance. See bart documentation
sigdf	Degrees of freedom for error variance prior. See bart documentation
sigquant	Quantile of error variance prior. See bart documentation
k	Tuning parameter that controls smoothing. Larger values are more conservative, see Details
power	Power parameter for tree prior
base	Base parameter for tree prior

binaryOffset	Allows fits with probabilities shrunk towards values other than 0.5. See bart documentation
nree	Number of trees in the sum-of-trees formulation
ndpost	Number of posterior draws after burn in
nskip	Number of MCMC iterations treated as burn in
printevery	How often to print messages
keepevery	Every keepevery draw is kept to be returned to the user
keeptrainfits	If TRUE the draws of $f(x)$ for x corresponding to the rows of <code>x.train</code> are returned
usequants	Controls how tree decisions rules are determined. See bart documentation
numcut	Maximum number of possible values used in decision rules
printcutoffs	Number of cutoff rules to print to screen. 0 prints nothing
nthread	Integer specifying how many threads to use
keepcall	Returns the call to BART when TRUE
verbose	Ignored for now
...	Additional arguments passed on to plot or control functions
object	Object of type tmle.SL.dbarts2
newdata	Matrix or dataframe used to get predictions from the fitted model

Details

tmle.SL.dbarts2 is in the default library for estimating Q . It uses the default setting in the dbarts package, $k = 2$. tmle.SL.dbarts.k.5 is used to estimate the components of g . It sets $k = 0.5$, to avoid shrinking predicted values too far from $(0, 1)$. See bart documentation for more information.

Value

an object of type tmle.SL.dbarts2 used internally by Super Learner

Author(s)

Chris Kennedy and Susan Gruber

See Also

[SuperLearner](#)

tmleMSM

*Targeted Maximum Likelihood Estimation of Parameter of MSM***Description**

Targeted maximum likelihood estimation of the parameter of a marginal structural model (MSM) for binary point treatment effects. The `tmleMSM` function is minimally called with arguments (Y, A, W, MSM) , where Y is a continuous or binary outcome variable, A is a binary treatment variable, ($A=1$ for treatment, $A=0$ for control), and W is a matrix or dataframe of baseline covariates. MSM is a valid regression formula for regressing Y on any combination of A, V, W, T , where V defines strata and T represents the time at which repeated measures on subjects are made. Missingness in the outcome is accounted for in the estimation procedure if missingness indicator Delta is 0 for some observations. Repeated measures can be identified using the `id` argument. Observation weights (sampling weights) may optionally be provided

Usage

```
tmleMSM(Y, A, W, V, T = rep(1,length(Y)), Delta = rep(1, length(Y)), MSM,
        v = NULL, Q = NULL, Qform = NULL, Qbounds = c(-Inf, Inf),
        Q.SL.library = c("SL.glm", "tmle.SL.dbarts2", "SL.glmnet"),
        cvQinit = TRUE, hAV = NULL, hAVform = NULL, g1W = NULL,
        gform = NULL, pDelta1 = NULL, g.Deltaform = NULL,
        g.SL.library = c("SL.glm", "tmle.SL.dbarts.k.5", "SL.gam"),
        g.Delta.SL.library = c("SL.glm", "tmle.SL.dbarts.k.5", "SL.gam"),
        ub = sqrt(sum(Delta))* log(sum(Delta)) / 5, family = "gaussian",
        fluctuation = "logistic", alpha = 0.995, id = 1:length(Y),
        V.Q = 10, V.g = 10, V.Delta = 10, inference = TRUE, verbose = FALSE,
        Q.discreteSL = FALSE, g.discreteSL = FALSE, alpha.sig = 0.05, obsWeights = NULL)
```

Arguments

<code>Y</code>	continuous or binary outcome variable
<code>A</code>	binary treatment indicator, 1 - treatment, 0 - control
<code>W</code>	vector, matrix, or dataframe containing baseline covariates. Factors are not currently allowed.
<code>V</code>	vector, matrix, or dataframe of covariates used to define strata
<code>T</code>	optional time for repeated measures data
<code>Delta</code>	indicator of missing outcome or treatment assignment. 1 - observed, 0 - missing
<code>MSM</code>	MSM of interest, specified as valid right hand side of a regression formula (see examples)
<code>v</code>	optional value defining the strata of interest ($V = v$) for stratified estimation of MSM parameter
<code>Q</code>	optional $n \times 2$ matrix of initial values for Q portion of the likelihood, $(E(Y A = 0, W), E(Y A = 1, W))$

Qform	optional regression formula for estimation of $E(Y A, W)$, suitable for call to <code>glm</code>
Qbounds	vector of upper and lower bounds on Y and predicted values for initial Q
Q.SL.library	optional vector of prediction algorithms to use for SuperLearner estimation of initial Q
cvQinit	logical, if TRUE, estimates cross-validated predicted values using discrete super learning, default=TRUE
hAV	optional $n \times 2$ matrix used in numerator of weights for updating covariate and the influence curve. If unspecified, defaults to conditional probabilities $P(A = 1 V)$ or $P(A = 1 T)$, for repeated measures data. For unstabilized weights, pass in an $n \times 2$ matrix of all 1s
hAVform	optional regression formula of the form $A \sim V+T$, if specified this overrides the call to SuperLearner
g1W	optional vector of conditional treatment assignment probabilities, $P(A = 1 W)$
gform	optional regression formula of the form $A \sim W$, if specified this overrides the call to SuperLearner
pDelta1	optional $n \times 2$ matrix of conditional probabilities for missingness mechanism, $P(Delta = 1 A = 0, V, W, T)$, $P(Delta = 1 A = 1, V, W, T)$.
g.Deltaform	optional regression formula of the form $Delta \sim A+W$, if specified this overrides the call to SuperLearner
g.SL.library	optional vector of prediction algorithms to use for SuperLearner estimation of $g1W$
g.Delta.SL.library	optional vector of prediction algorithms to use for SuperLearner estimation of $pDelta1$
ub	upper bound on inverse probability weights. See Details section for more information
family	family specification for working regression models, generally 'gaussian' for continuous outcomes (default), 'binomial' for binary outcomes
fluctuation	'logistic' (default), or 'linear'
alpha	used to keep predicted initial values bounded away from (0,1) for logistic fluctuation
id	optional subject identifier
V.Q	number of cross-validation folds for Super Learner estimation of Q
V.g	number of cross-validation folds for Super Learner estimation of g
V.Delta	number of cross-validation folds for Super Learner estimation of g_Delta
inference	if TRUE, variance-covariance matrix, standard errors, pvalues, and 95% confidence intervals are calculated. Setting to FALSE saves a little time when bootstrapping.
verbose	status messages printed if set to TRUE (default=FALSE)
Q.discreteSL	If true, use discrete SL to estimate Q , otherwise ensembleSL by default. Ignored when SL is not used.

<code>g.discreteSL</code>	If true, use discrete SL to estimate each component of g , otherwise ensembleSL by default. Ignored when SL is not used.
<code>alpha.sig</code>	significance level for constructing $1-\text{alpha.sig}$ confidence intervals
<code>obsWeights</code>	optional weights for biased sampling and two-stage designs.

Details

`ub` bounds the IC by bounding the factor $h(A, V)/[g(A, V, W)P(\text{Delta} = 1|A, V, W)]$ between 0 and `ub`, default value based on sample size.

Value

<code>psi</code>	MSM parameter estimate
<code>sigma</code>	variance covariance matrix
<code>se</code>	standard errors extracted from <code>sigma</code>
<code>pvalue</code>	two-sided p-value
<code>lb</code>	lower bound on 95% confidence interval
<code>ub</code>	upper bound on 95% confidence interval
<code>epsilon</code>	fitted value of epsilon used to target initial Q
<code>psi.Qinit</code>	MSM parameter estimate based on untargeted initial Q
<code>Qstar</code>	targeted estimate of Q, an $n \times 2$ matrix with predicted values for $Q(0, W)$, $Q(1, W)$ using the updated fit
<code>Qinit</code>	initial estimate of Q. <code>Qinit\$coef</code> are the coefficients for a glm model for Q, if applicable. <code>Qinit\$Q</code> is an $n \times 2$ matrix, where n is the number of observations. Columns contain predicted values for $Q(0, W)$, $Q(1, W)$ using the initial fit. <code>Qinit\$type</code> is method for estimating Q
<code>g</code>	treatment mechanism estimate. A list with three items: <code>g\$g1W</code> contains estimates of $P(A = 1 W)$ for each observation, <code>g\$coef</code> the coefficients for the model for g when glm used, <code>g\$type</code> estimation procedure
<code>g.AV</code>	estimate for $h(A, V)$ or $h(A, T)$. A list with three items: <code>g.AV\$g1W</code> an $n \times 2$ matrix containing values of $P(A = 0 V, T)$, $P(A = 1 V, T)$ for each observation, <code>g.AV\$coef</code> the coefficients for the model for g when glm used, <code>g.AV\$type</code> estimation procedure
<code>g_Delta</code>	missingness mechanism estimate. A list with three items: <code>g_Delta\$g1W</code> an $n \times 2$ matrix containing values of $P(\text{Delta} = 1 A, V, W, T)$ for each observation, <code>g_Delta\$coef</code> the coefficients for the model for g when glm used, <code>g_Delta\$type</code> estimation procedure

Author(s)

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References

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See Also

[summary.tmleMSM](#), [estimateQ](#), [estimateG](#), [calcSigma](#), [tmle](#)

Examples

```
library(tmle)
# Example 1. Estimating MSM parameter with correctly specified regression formulas
# MSM:  $\psi_0 + \psi_1 \cdot A + \psi_2 \cdot V + \psi_3 \cdot A \cdot V$  (saturated)
# true parameter value:  $\psi = (0, 1, -2, 0.5)$ 
# generate data
set.seed(100)
n <- 1000
W <- matrix(rnorm(n*3), ncol = 3)
colnames(W) <- c("W1", "W2", "W3")
V <- rbinom(n, 1, 0.5)
A <- rbinom(n, 1, 0.5)
Y <- rbinom(n, 1, plogis(A - 2*V + 0.5*A*V))
result.ex1 <- tmleMSM(Y, A, W, V, MSM = "A*V", Qform = "Y~.", gform = "A~1",
                    hAVform = "A~1", family = "binomial")
print(result.ex1)
## Not run:

# Example 2. Biased sampling from example 1 population
# (observations having V = 1 twice as likely to be included in the dataset)
retain.ex2 <- sample(1:n, size = n/2, p = c(1/3 + 1/3*V))
wt.ex2 <- 1/(1/3 + 1/3*V)
result.ex2 <- tmleMSM(Y[retain.ex2], A[retain.ex2], W[retain.ex2,],
                    V[retain.ex2], MSM = "A*V", Qform = "Y~.", gform = "A~1",
                    hAVform = "A~1", family = "binomial",
                    obsWeight = wt.ex2[retain.ex2])
print(result.ex2)

# Example 3. Repeated measures data, two observations per id
# (e.g., crossover study design)
# MSM:  $\psi_0 + \psi_1 \cdot A + \psi_2 \cdot V + \psi_3 \cdot V^2 + \psi_4 \cdot T$ 
# true parameter value:  $\psi = (-2, 1, 0, -2, 0)$ 
# generate data in wide format (id, W1, Y(t), W2(t), V(t), A(t))
set.seed(10)
n <- 250
```



```

id <- rep(1:n)
W1 <- rbinom(n, 1, 0.5)
W2.1 <- rnorm(n)
W2.2 <- rnorm(n)
V.1 <- rnorm(n)
V.2 <- rnorm(n)
A.1 <- rbinom(n, 1, plogis(0.5 + 0.3 * W2.1))
A.2 <- 1-A.1
Y.1 <- -2 + A.1 - 2*V.1^2 + W2.1 + rnorm(n)
Y.2 <- -2 + A.2 - 2*V.2^2 + W2.2 + rnorm(n)
d <- data.frame(id, W1, W2=W2.1, W2.2, V=V.1, V.2, A=A.1, A.2, Y=Y.1, Y.2)

# change dataset from wide to long format
longd <- reshape(d,
  varying = cbind(c(3, 5, 7, 9), c(4, 6, 8, 10)),
  idvar = "id",
  direction = "long",
  timevar = "T",
  new.row.names = NULL,
  sep = "")
# misspecified model for initial Q, partial misspecification for g.
# V set to 2 for Q and g to save time, not recommended at this sample size
result.ex3 <- tmleMSM(Y = longd$Y, A = longd$A, W = longd[,c("W1", "W2")], V = longd$V,
  T = longd$T, MSM = "A + V + I(V^2) + T", Qform = "Y ~ A + V", gform = "A ~ W2",
  id = longd$id, V.Q=2, V.g=2)
print(result.ex3)

# Example 4: Introduce 20
# V set to 2 for Q and g to save time, not recommended at this sample size
Delta <- rbinom(nrow(longd), 1, 0.8)
result.ex4 <- tmleMSM(Y = longd$Y, A = longd$A, W = longd[,c("W1", "W2")], V = longd$V, T=longd$T,
  Delta = Delta, MSM = "A + V + I(V^2) + T", Qform = "Y ~ A + V", gform = "A ~ W2",
  g.Deltaform = "Delta ~ 1", id=longd$id, verbose = TRUE, V.Q=2, V.g=2)
print(result.ex4)

## End(Not run)

```

tmleNews

Show the NEWS file (tmleNews)

Description

Shows recent changes and bug fixes documented in the tmle package NEWS file.

Usage

```
tmleNews(...)
```

Arguments

... additional arguments passed to RShowDoc

Value

NONE

Author(s)

Susan Gruber

See Also

[tmle](#), [tmleMSM](#)

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