

Package ‘HOIFCar’

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Type Package

Title Covariate Adjustment in RCT by Higher-Order Influence Functions

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Description Estimates treatment effects using covariate adjustment methods in Randomized Clinical Trials (RCT) motivated by higher-order influence functions (HOIF). Provides point estimates, oracle bias, variance, and approximate variance for HOIF-adjusted estimators. For methodology details, see Zhao et al. (2024) <[doi:10.48550/arXiv.2411.08491](https://doi.org/10.48550/arXiv.2411.08491)>.

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Suggests mvtnorm

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Imports brglm2, BB, parallel, doParallel, foreach, glmnet, stats, MASS

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esti_mean_treat	<i>Estimate treatment effect and the corresponding variance estimation on the treatment arm using different covariate adjustment methods.</i>
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Description

Implements a unified framework for comparing covariate adjustment method for completely randomized experiments under randomization-based framework.

Usage

```
esti_mean_treat(X, Y, A, H = NULL)
```

Arguments

X	The n by p covariates matrix.
Y	Vector of n dimensional observed response.
A	Vector of n dimensional treatment assignment.
H	The n by n hat projection matrix corresponding to X.

Value

A list with two named vectors:

point_est Point estimates for all estimators:

- unadj: Unadjusted estimator
- db: Debiased estimator (Lu et al., 2023)
- adj2c: HOIF-inspired debiased estimator (Zhao et al., 2024), the same as db
- adj2: HOIF-motivated adjusted estimator (Zhao et al., 2024)
- adj3: Bias-free adjusted estimator based on adj2
- lin: Covariate-adjusted estimator (Lin, 2013)
- lin_db: Debiased estimator with population leverage scores (Lei, 2020)

var_est Variance estimates corresponding to each estimator:

- unadj: Variance estimate for unadjusted estimator
- db: Variance estimate for debiased estimator (Lu et al., 2023)
- adj2c: Variance for adj2c, using formulas given in (Lu et al., 2023)
- adj2c_v2: Conservative variance for adj2c (Zhao et al., 2024)
- adj2: Variance for adj2, with formulas motivated by (Lu et al., 2023)
- adj2_v2: Conservative variance for adj2 (Zhao et al., 2024)
- adj3: Variance for adj3, with formulas motivated by (Lu et al., 2023)
- adj3_v2: Conservative variance for adj3 (Zhao et al., 2024)
- lin: HC3-type variance for Lin's (2013) estimator
- lin_db: HC3-type variance for Lei's (2020) estimator

References

- Lin, W. (2013). *Agnostic notes on regression adjustments to experimental data: Reexamining Freedman's critique*. *The Annals of Statistics*, Vol. 7(1), 295–318, doi:10.1214/12AOAS583.
- Lei, L. and Ding, P. (2020) *Regression adjustment in completely randomized experiments with a diverging number of covariates*. *Biometrika*, Vol. 108(4), 815–828, doi:10.1093/biomet/asaa103.
- Lu, X., Yang, F. and Wang, Y. (2023) *Debiased regression adjustment in completely randomized experiments with moderately high-dimensional covariates*. *arXiv preprint*, arXiv:2309.02073, doi:10.48550/arXiv.2309.02073.
- Zhao, S., Wang, X., Liu, L. and Zhang, X. (2024) *Covariate Adjustment in Randomized Experiments Motivated by Higher-Order Influence Functions*. *arXiv preprint*, arXiv:2411.08491, doi:10.48550/arXiv.2411.08491.

Examples

```
set.seed(100)
n <- 500
p <- n * 0.3
beta <- runif(p, -1 / sqrt(p), 1 / sqrt(p))

X <- mvtnorm::rmvt(n, sigma = diag(1, p), df = 3)
Y1 <- as.numeric(X %*% beta)
Y0 <- rep(0, n)

pi1 <- 2/3
n1 <- ceiling(n * pi1)
ind <- sample(n, size = n1)
A <- rep(0, n)
A[ind] <- 1
Y <- Y1 * A + Y0 * (1 - A)
Xc <- scale(X, scale = FALSE)
H <- Xc %*% MASS::ginv(t(Xc) %*% Xc) %*% t(Xc)

result_ls <- esti_mean_treat(X, Y, A, H)
point_est <- result_ls$point_est
var_est <- result_ls$var_est
print(paste0('True mean treat:', round(mean(Y1), digits = 3), '.'))
print('Absolute bias:')
print(abs(point_est - mean(Y1)))
print('Estimate variance:')
print(var_est)
```

Description

Implements the (HOIF-inspired) debiased estimators for average treatment effect (ATE) or treatment effect on the treatment/control arm with variance estimation using asymptotic-variance. Designed for randomized experiments with moderately high-dimensional covariates.

Usage

```
fit.adj2.adj2c.Random(Y, X, A, pi1 = NULL, target = "ATE")
```

Arguments

Y	Numeric vector of length n containing observed responses.
X	Numeric matrix (n x p) of covariates. Centering is required. Intercept term can include or not.
A	Binary vector of length n indicating treatment assignment (1 = treatment, 0 = control).
pi1	Default is NULL. The assignment probability for the randomization assignment.
target	A character string specifying the target estimand. Must be one of: - "ATE" (default): Average Treatment Effect (difference between treatment and control arms). - "EY1": Expected outcome under treatment (estimates the effect for the treated group). - "EY0": Expected outcome under control (estimates the effect for the control group).

Value

A list containing three named vectors, including point estimates and variance estimates:

tau_vec Point estimates:

- adj2: Point estimation of the HOIF-inspired debiased estimator given by Zhao et al.(2024).
- adj2c: Point estimation of the debiased estimator given by Lu et al. (2023), which is also the HOIF-inspired debiased estimator given by Zhao et al.(2024).

var_vec_v1 Variance estimates for adj2 and adj2c, with formulas inspired by Lu et al. (2023):

- adj2: Variance for adj2.
- adj2c: Variance for adj2c.

var_vec_v2 Variance estimates for adj2 and adj2c, with formulas given in Zhao et al. (2024), which is more conservative.

- adj2: Variance for adj2.
- adj2c: Variance for adj2c.

References

Lu, X., Yang, F. and Wang, Y. (2023) *Debiased regression adjustment in completely randomized experiments with moderately high-dimensional covariates*. *arXiv preprint*, arXiv:2309.02073, doi:10.48550/arXiv.2309.02073.

Zhao, S., Wang, X., Liu, L. and Zhang, X. (2024) *Covariate Adjustment in Randomized Experiments Motivated by Higher-Order Influence Functions*. *arXiv preprint*, arXiv:2411.08491, doi:10.48550/arXiv.2411.08491.

Examples

```

set.seed(100)
n <- 500
p <- n * 0.3
beta <- runif(p, -1 / sqrt(p), 1 / sqrt(p))

X <- mvtnorm::rmvt(n, sigma = diag(1, p), df = 3)
Y1 <- as.numeric(X %*% beta)
Y0 <- as.numeric(X %*% beta - 1)

pi1 <- 2/3
n1 <- ceiling(n * pi1)
ind <- sample(n, size = n1)
A <- rep(0, n)
A[ind] <- 1
Y <- Y1 * A + Y0 * (1 - A)

Xc <- cbind(1, scale(X, scale = FALSE))
result.adj2.adj2c.random.ate.ls <- fit.adj2.adj2c.Random(Y, Xc, A, target = 'ATE')
result.adj2.adj2c.random.ate.ls

result.adj2.adj2c.random.treat.ls <- fit.adj2.adj2c.Random(Y, Xc, A, target = 'EY1')
result.adj2.adj2c.random.treat.ls

result.adj2.adj2c.random.control.ls <- fit.adj2.adj2c.Random(Y, Xc, A, target = 'EY0')
result.adj2.adj2c.random.control.ls

```

fit.adj2.adj2c.Super	<i>Covariate-Adjusted Treatment Effect Estimation under the Super-Population Framework</i>
----------------------	--

Description

Implements HOIF-inspired debiased estimators for average treatment effect (ATE) or treatment effect on the treatment/control arm with variance estimation using influence function-based and asymptotic-variance. Designed for randomized experiments with moderately high-dimensional covariates.

Usage

```

fit.adj2.adj2c.Super(
  Y,
  X,
  A,
  intercept = TRUE,
  pi1 = NULL,
  target = "ATE",
  lc = FALSE
)

```

Arguments

Y	Numeric vector of length n containing observed responses.
X	Numeric matrix (n x p) of covariates. Centering is required. May include intercept column.
A	Binary vector of length n indicating treatment assignment (1 = treatment, 0 = control).
intercept	Logical. If TRUE (default), X already contains intercept. Set FALSE if X does not contain intercept.
pi1	The assignment probability for the randomization assignment. If 'NULL' (the default), the empirical assignment probability is used.
target	A character string specifying the target estimand. Must be one of: - "ATE" (default): Average Treatment Effect (difference between treatment and control arms). - "EY1": Expected outcome under treatment (estimates the effect for the treated group). - "EY0": Expected outcome under control (estimates the effect for the control group).
lc	Default is FALSE. If TRUE, then performs linear calibration to achieve efficiency gain using $\hat{\mu}_0(X_i)$ and $\hat{\mu}_1(X_i)$.

Value

A list containing three named vectors, including point estimates and variance estimates:

tau_vec Point estimates:

- adj2: Point estimation of the HOIF-inspired debiased estimator (Zhao et al., 2024).
- adj2c: Point estimation of the the HOIF-inspired debiased estimator (Zhao et al., 2024), which is also the debiased estimator given by Lu et al. (2023).

var_infl_vec Influence function-based variance estimates:

- adj2: Variance for adj2 via the sample variance of its influence function formula.
- adj2c: Variance for adj2c via the sample variance of its influence function formula.

var_rb_vec Variance estimates inspired by Bannick et al. (2025):

- adj2: Variance for adj2 following the asymptotic variance given by Bannick et al. (2025).
- adj2c: Variance for adj2c following the asymptotic variance given by Bannick et al. (2025).

References

- Bannick, M. S., Shao, J., Liu, J., Du, Y., Yi, Y. and Ye, T. (2025) *A General Form of Covariate Adjustment in Clinical Trials under Covariate-Adaptive Randomization*. *Biometrika*, Vol. xx(x), 1-xx, doi:10.1093/biomet/asaf029.
- Lu, X., Yang, F. and Wang, Y. (2023) *Debiased regression adjustment in completely randomized experiments with moderately high-dimensional covariates*. *arXiv preprint*, arXiv:2309.02073, doi:10.48550/arXiv.2309.02073.
- Zhao, S., Wang, X., Liu, L. and Zhang, X. (2024) *Covariate Adjustment in Randomized Experiments Motivated by Higher-Order Influence Functions*. *arXiv preprint*, arXiv:2411.08491, doi:10.48550/arXiv.2411.08491.

Examples

```

set.seed(120)
alpha0 <- 0.1;
n <- 400;

p0 <- ceiling(n * alpha0)
beta0_full <- 1 / (1:p0) ^ (1 / 2) * (-1) ^ c(1:p0)
beta <- beta0_full / norm(beta0_full,type='2')

Sigma_true <- matrix(0, nrow = p0, ncol = p0)
for (i in 1:p0) {
  for (j in 1:p0) {
    Sigma_true[i, j] <- 0.1 ** (abs(i - j))
  }
}

X <- mvtnorm::rmvt(n, sigma = Sigma_true, df = 3)

lp0 <- X %%% beta
delta_X <- 1 - 1/4 * X[, 2] - 1/8 * X[, 3]
lp1 <- lp0 + delta_X

Y0 <- lp0 + rnorm(n)
Y1 <- lp1 + rnorm(n)

pi1 <- 1 / 2
A <- rbinom(n, size = 1, prob = pi1)
Y <- A * Y1 + (1 - A) * Y0

Xc <- cbind(1, scale(X, scale = FALSE))
result.adj2.adj2c.sp.ate.ls <- fit.adj2.adj2c.Super(Y, Xc, A, intercept = TRUE,
                                                    target = 'ATE', lc = TRUE)

result.adj2.adj2c.sp.ate.ls
result.adj2.adj2c.sp.treat.ls <- fit.adj2.adj2c.Super(Y, Xc, A, intercept = TRUE,
                                                    target = 'EY1', lc = TRUE)

result.adj2.adj2c.sp.treat.ls
result.adj2.adj2c.sp.control.ls <- fit.adj2.adj2c.Super(Y, Xc, A, intercept = TRUE,
                                                    target = 'EY0', lc = TRUE)

result.adj2.adj2c.sp.control.ls

```

fit.JASA

*Covariate Adjustment via Jackknife Score-based Adjustment (JASA)
for Generalized Linear Working Models*

Description

Implements the Jackknife Score-Based Adjustment (JASA) method and its calibration for covariate adjustment in simple randomized experiments where covariate dimension p may be large relatively to sample size n . Handles Continuous, Binary, and Poisson outcomes.

Usage

```
fit.JASA(
  Y,
  X,
  A,
  family = "gaussian",
  pi1 = NULL,
  is.parallel = FALSE,
  core_num = 4,
  opt_obj = c("beta", "mu")[1]
)
```

Arguments

Y	Numeric vector of outcome values.
X	Matrix of centered baseline covariates (may include intercept). Dimensions: n x p.
A	Binary treatment vector (0 = control, 1 = treatment). Assignment is assumed to follow simple randomization.
family	GLM family specification: "gaussian", "binomial", or "poisson". Default: "gaussian".
pi1	The assignment probability for the simple randomization. If NULL (default), the empirical assignment probability is used.
is.parallel	Boolean for parallelization. Default: FALSE.
core_num	Number of cores for parallel computing (default is 4 if is.parallel = TRUE).
opt_obj	Ways to optimization: 'beta' (GLM coefficients) or 'mu' (expected outcomes). Default: 'beta'.

Value

List with components:

tau_vec	Named vector of average treatment effect estimates (JASA, JASA-cal)
tau0_vec	Treatment effect estimates on the control group
tau1_vec	Treatment effect estimates on the treatment group
var_tau_vec	Variance estimates for average treatment effect estimates
var_tau0_vec	Variance estimates for treatment effect estimates on the control group
var_tau1_vec	Variance estimates for treatment effect estimates on the treatment group
y_hat_mat	Matrix of predicted outcomes (columns: control, treatment) using varied Leave-One-Out strategy.
obj_value_mat	Matrix of objective values from optimization (columns: control, treatment)

Examples

```

generate_data_SR <- function(n, family, pi1, p_n_ratio = 0.05, seed = 123){
  set.seed(seed)
  alpha0 <- 0.15
  p0 <- ceiling(round(n * alpha0))
  beta0_full <- 1/(1:p0)^(1/4)*(-1)^c(1:p0)
  Sigma_true <- matrix(0, nrow = p0, ncol = p0)
  for (i in 1:p0) {
    for (j in 1:p0) {
      Sigma_true[i, j] <- 0.1 ** (abs(i - j))
    }
  }

  if(family != 'poisson'){
    X <- mvtnorm::rmvt(n, sigma = Sigma_true, df = 3)
  }else{
    X0 <- mvtnorm::rmvt(n, sigma = Sigma_true, df = 3)
    X <- pmin(pmax(X0, -3), 3)
    rm(X0)
  }

  beta <- beta0_full / norm(beta0_full,type='2')
  lp0 <- X %%% beta

  delta_X <- 1 - 1/2 * pmin(X[, 1]^2, 5) + 1/4 * X[, 1:10] %%% beta[1:10]
  lp1 <- lp0 + delta_X

  if (family == 'binomial') {
    r0 <- plogis(2 * lp0)
    r1 <- plogis(2 * lp1)
    Y1 <- rbinom(n, size=1, prob=r1)
    Y0 <- rbinom(n, size=1, prob=r0)
  }else if(family == 'poisson'){
    # quantile(lp1);quantile(lp0)
    lp1_tran <- pmin(lp1, 4)
    lp0_tran <- pmin(lp0, 4)
    r1 <- exp(lp1_tran)
    r0 <- exp(lp0_tran)

    Y1 <- rpois(n,r1)
    Y0 <- rpois(n,r0)
  }else if(family == 'gaussian'){
    r1 <- lp1;
    r0 <- lp0
    Y1 <- r1 + rnorm(n)
    Y0 <- r0 + rnorm(n)
  }
}

A <- rbinom(n, size=1, prob=pi1)
Y <- A * Y1 + (1 - A) * Y0

```

```

p <- ceiling(round(n * p_n_ratio))
if(p > ncol(X)){
  if(family != 'poisson'){
    X_noise <- rmvt(n, sigma = diag(p - ncol(X)), df = 3)
  }else{
    X0_noise <- rmvt(n, sigma = diag(p - ncol(X)), df = 3)
    X_noise <- pmin(pmax(X0_noise, -3), 3)
  }
  X_obs <- cbind(X, X_noise)
}else{
  X_obs <- X[, 1:p, drop = FALSE]
}

data_ls <- list(
  X = X_obs, Y = Y, A = A,
  Y1 = Y1, Y0 = Y0,
  r1 = r1, r0 = r0
)
return(data_ls)
}

n <- 400; pi1 <- 1/3

family <- 'gaussian'; p_n_ratio <- 0.05
data_ls <- generate_data_SR(n, family, pi1, p_n_ratio)
X <- data_ls$X;
A <- data_ls$A
Y <- data_ls$Y

## Not run:
Xc <- scale(X, scale = FALSE)
Xc_aug <- cbind(1, Xc)
result.jasa.ls <- fit.JASA(Y, Xc_aug, A, family, opt_obj = 'beta')
result.jasa.ls$tau_vec
result.jasa.ls$var_tau_vec

family <- 'poisson'; p_n_ratio <- 0.05
data_ls <- generate_data_SR(n, family, pi1, p_n_ratio)
X <- data_ls$X;
A <- data_ls$A
Y <- data_ls$Y

Xc <- scale(X, scale = FALSE)
Xc_aug <- cbind(1, Xc)
result.jasa.ls <- fit.JASA(Y, Xc_aug, A, family, opt_obj = 'mu')
result.jasa.ls$tau_vec
result.jasa.ls$var_tau_vec

family <- 'binomial'; p_n_ratio <- 0.05
data_ls <- generate_data_SR(n, family, pi1, p_n_ratio)

```

```

X <- data_ls$X;
A <- data_ls$A
Y <- data_ls$Y

Xc <- scale(X, scale = FALSE)
Xc_aug <- cbind(1, Xc)
result.jasa.ls <- fit.JASA(Y, Xc_aug, A, family, opt_obj = 'beta')
result.jasa.ls$tau_vec
result.jasa.ls$var_tau_vec

## End(Not run)

```

get_oracle_bias_var_adj2c

Estimate the oracle bias, the exact variance and approximated variance of the debiased estimator tau_adj2c inspired by HOIF (Zhao et al.(2024)).

Description

Estimate the oracle bias, the exact variance and approximated variance of the debiased estimator tau_adj2c inspired by HOIF (Zhao et al.(2024)).

Usage

```
get_oracle_bias_var_adj2c(X, Y1, n1 = NULL)
```

Arguments

X	The n by p covariates matrix.
Y1	Vector of n dimensional potential response Y(1).
n1	The number of subjects in the treatment group.

Value

A list of oracle bias and variance of the debised adjusted estimator tau_adj2c.

bias_adj2c The oracle bias of the debiased estimator tau_adj2c.

variance_exact_adj2c

The oracle exact bias of the debiased estimator tau_adj2c.

variance_approx_adj2c

The oracle approximated variance of the debiased estimator tau_adj2c which omits the term of order $o(1/n)$.

variance_unadj The oracle variance of the unadjusted estimator.

References

Zhao, S., Wang, X., Liu, L., & Zhang, X. (2024). Covariate adjustment in randomized experiments motivated by higher-order influence functions. arXiv preprint. <https://arxiv.org/abs/2411.08491>.

Examples

NULL

get_oracle_bias_var_adj_2_3	<i>Estimate the oracle bias, the exact variance and approximated variance of the debiased estimator and the bias-free estimator motivated by HOIF (Zhao et al.(2024)).</i>
-----------------------------	--

Description

Estimate the oracle bias, the exact variance and approximated variance of the debiased estimator and the bias-free estimator motivated by HOIF (Zhao et al.(2024)).

Usage

get_oracle_bias_var_adj_2_3(X, Y1, n1 = NULL)

Arguments

X	The n by p covariates matrix.
Y1	Vector of n dimensional potential response Y(1).
n1	The number of subjects in the treatment group.

Value

A list of oracle bias and variance of the adjusted estimator motivated by HOIF and the bias-free estimator.

bias_adj2	The oracle bias of the estimator tau_adj2.
variance_exact_adj2	The oracle exact variance of the estimator tau_adj2.
variance_approx_adj2	The oracle approximated variance of the estimator tau_adj2 which omits the term of order o(1/n).
variance_exact_adj3	The oracle exact variance of the bias-free estimator tau_adj3.
variance_unadj	The oracle variance of the unadjusted estimator.

References

Zhao, S., Wang, X., Liu, L., & Zhang, X. (2024). Covariate adjustment in randomized experiments motivated by higher-order influence functions. arXiv preprint. <https://arxiv.org/abs/2411.08491>

Examples

```

# Linear setting
set.seed(100)
n <- 500
p <- 50
beta <- rt(p,3)

X <- mvtnorm::rmvt(n, sigma = diag(1, p), df = 3)
Y1 <- as.numeric(X %%% beta)
pi1 <- 0.50
n1 <- ceiling(n*pi1)

result_adj_db <- get_oracle_bias_var_adj_db(X = X,Y1=Y1,n1=n1)
result_adj2c <- get_oracle_bias_var_adj2c(X = X,Y1=Y1,n1=n1)
result_adj2_3 <- get_oracle_bias_var_adj_2_3(X = X,Y1=Y1,n1=n1)
unlist(result_adj_db)
unlist(result_adj2c)
unlist(result_adj2_3)


# Nonlinear setting
n <- 500;
alpha <- 0.2;
set.seed(1000)
p <- ceiling(n*alpha)
Sigma_true <- matrix(0,nrow=p,ncol=p)
for(i in 1:p){
  for(j in 1:p){
    Sigma_true[i,j] <- 0.1** (abs(i-j))
  }
}

X <- mvtnorm::rmvt(n, sigma = Sigma_true, df = 3)
beta <- rt(p,3)
or_baseline <- sign(X %%% beta) * abs(X %%% beta)^(1/2) + sin(X %%% beta)
epsilon1 <- epsilon0 <- rt(n,3)
Y1 <- 1 + as.numeric(or_baseline) + epsilon1


pi1 <- 0.50
n1 <- ceiling(n*pi1)

result_adj_db <- get_oracle_bias_var_adj_db(X = X,Y1=Y1,n1=n1) # from LYW paper
result_adj2c <- get_oracle_bias_var_adj2c(X = X,Y1=Y1,n1=n1)
result_adj2_3 <- get_oracle_bias_var_adj_2_3(X = X,Y1=Y1,n1=n1)
unlist(result_adj_db)
unlist(result_adj2c)
unlist(result_adj2_3)

```

```
get_oracle_bias_var_adj_db
```

Estimate the oracle bias, the oracle variance of the unadjusted estimator, the adjusted estimator by Lei's (2020) and the debiased estimator tau_db by Lu et al.(2023).

Description

Estimate the oracle bias, the oracle variance of the unadjusted estimator, the adjusted estimator by Lei's (2020) and the debiased estimator tau_db by Lu et al.(2023).

Usage

```
get_oracle_bias_var_adj_db(X, Y1, n1 = NULL)
```

Arguments

X	The n by p covariates matrix.
Y1	Vector of n dimensional potential response Y(1).
n1	The number of subjects in the treatment group.

Value

A list of the oracle bias and variance of .

bias_adj	The oracle bias of the adjusted estimator tau_adj we proposed.
variance_unadj	The oracle variance of the unadjusted estimator.
variance_adj_lin	The oracle variance of Lei's (2020) debiased estimator with linear working model.
variance_db	The oracle variance of the debiased estimator tau_db by Lu et al.(2023).

References

Lihua Lei, Peng Ding. Regression adjustment in completely randomized experiments with a diverging number of covariates. *Biometrika*, 815–828, 2020.

Xin Lu, Fan Yang, and Yuhao Wang. Debiased regression adjustment in completely randomized experiments with moderately high-dimensional covariates. *arXiv preprint arXiv:2309.02073*, 2023.

Examples

```
NULL
```

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