# Package 'graposas'

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**Type** Package

**Title** Graphical Approach Optimal Sample Size

**Version** 1.0.0

**Date** 2023-07-30

**Description** Graphical approach provides a useful framework for multiplicity adjustment in clinical trials with multiple endpoints. This package includes statistical methods to optimize sample size over initial weight and transition probability in a graphical approach under a common setting, which is to use marginal power for each endpoint in a trial design.
See Zhang, F. and Gou, J. (2023). Sample size optimization for clinical trials using graphical approaches for multiplicity adjustment, Technical Report.

**License** GPL-3

**Encoding** UTF-8

**Depends** R (>= 4.2.0)

**Imports** GA (>= 3.0.0), graphics (>= 4.2.0), mvtnorm (>= 1.1.0), stats (>= 4.0.0)

**RoxygenNote** 7.2.3

**NeedsCompilation** no

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**Repository** CRAN

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## Contents

szgaGA *Sample size optimization using graphical approach in clinical trial design with three hypotheses*

## Description

This function computes the optimal design using graphical approach along with the minimum sample size when three hypotheses are considered in a clinical trial.

## Usage

```
szgaGA(
  alpha,
  betaVec,
  deltaVec,
  cVec,
  rhoMat,
  lower = c(1, rep(1e-06, 2), rep(1e-06, 3)),
  upper = c(10000, rep(1 - 1e-06, 2), rep(1 - 1e-06, 3)),
  gaIter = c(20, 20),
  penPara = 0.1,
  seed = 2022
)
```

## Arguments

| | |
|---|---|
| alpha | a value of overall type I error rate |
| betaVec | a vector of one minus marginal powers for testing H1, H2 and H3, respectively |
| deltaVec | a vector of effect sizes for testing H1, H2 and H3, respectively |
| cVec | a vector of coefficients. When testing continuous endpoints, these coefficients are exactly one. When testing binary endpoints, the values are roughly one but not exactly one |
| rhoMat | a matrix of the correlation coefficients among three hypotheses |
| lower | a vector of lower limit of sample size n, initial weights w1 and w2, and transition probabilities g12, g23 and g31 |
| upper | a vector of upper limit of sample size n, initial weights w1 and w2, and transition probabilities g12, g23 and g31 |
| gaIter | a vector of two numbers. The first one is the parameter maxiter of the ga function, and the second one is the parameter run of the ga function |
| penPara | a number of penalization parameter for optimization to balance the sample size requirement and the power requirement |
| seed | a number of the seed of the random number generator |

## Details

R package GA is used for Genetic Algorithms.

## Value

a vector of six numbers: the optimal sample size n, initial weights w1 and w2, and transition probabilities g12, g23 and g31

## Author(s)

Jiangtao Gou

## References

Zhang, F. and Gou, J. (2023). Sample size optimization for clinical trials using graphical approaches for multiplicity adjustment, Technical Report. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311.

## Examples

```
start <- Sys.time()
szgaGA(alpha = 0.025, betaVec = c(0.15, 0.20, 0.10),
       deltaVec = c(0.1111952, 0.1037179, 0.1182625),
       cVec = c(1.003086, 1.002686, 1.00349),
       rhoMat = matrix(c(1,0.5,0.8, 0.5,1,0.6, 0.8,0.6,1), nrow = 3, byrow = TRUE),
       lower = c(750, rep(0.01, 2), rep(0.01, 3)),
       upper = c(850, rep(0.99, 2), rep(0.99, 3)),
       gaIter = c(10, 5),
       penPara = 0.015,
       seed = 234)
end <- Sys.time()
data.frame(time = end - start)
```

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# szgaGAw *Sample size optimization using graphical approach in clinical trial design with three hypotheses when the transition matrix is pre-specified*

---

## Description

This function computes the optimal design using graphical approach along with the minimum sample size when three hypotheses are considered in a clinical trial. The transition matrix is prespecified and fixed.

## Usage

```
szgaGAw(
  alpha,
  betaVec,
  deltaVec,
  cVec,
  rhoMat,
  transMat,
  lower = c(1, rep(1e-06, 2)),
  upper = c(10000, rep(1 - 1e-06, 2)),
  gaIter = c(20, 20),
  penPara = 0.1,
  seed = 2022
)
```

## Arguments

| | |
|---|---|
| alpha | a value of overall type I error rate |
| betaVec | a vector of one minus marginal powers for testing H1, H2 and H3, respectively |
| deltaVec | a vector of effect sizes for testing H1, H2 and H3, respectively |
| cVec | a vector of coefficients. When testing continuous endpoints, these coefficients are exactly one. When testing binary endpoints, the values are roughly one but not exactly one |
| rhoMat | a matrix of the correlation coefficients among three hypotheses |
| transMat | a matrix of the fixed transition probabilities among three hypotheses |
| lower | a vector of lower limit of sample size n, and initial weights w1 and w2, where w3 is computed by 1 - w1 - w2 |
| upper | a vector of upper limit of sample size n, and initial weights w1 and w2, where w3 is computed by 1 - w1 - w2 |
| gaIter | a vector of two numbers. The first one is the parameter maxiter of the ga function, and the second one is the parameter run of the ga function |
| penPara | a number of penalization parameter for optimization to balance the sample size requirement and the power requirement |
| seed | a number of the seed of the random number generator |

## Details

R package GA is used for Genetic Algorithms.

## Value

a vector of three numbers: the optimal sample size n, and initial weights w1 and w2

## Author(s)

Jiangtao Gou

## References

Zhang, F. and Gou, J. (2023). Sample size optimization for clinical trials using graphical approaches for multiplicity adjustment, Technical Report. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311.

## Examples

```
start <- Sys.time()
szgaGAw(alpha = 0.025, betaVec = c(0.15, 0.20, 0.10),
        deltaVec = c(0.1111952, 0.1037179, 0.1335865),
        cVec = c(1.003086, 1.002686, 1.004451),
        rhoMat = matrix(c(1,0.5,0.8, 0.5,1,0.6, 0.8,0.6,1), nrow = 3, byrow = TRUE),
        transMat = matrix(c(0,0.50,0.50, 0.5,0,0.5, 0.5,0.5,0), nrow = 3, byrow = TRUE),
        lower = c(700, rep(0.05, 2)),
        upper = c(900, rep(0.95, 2)),
        gaIter = c(10, 5),
        penPara = 0.0135,
        seed = 234)
end <- Sys.time()
data.frame(time = end - start)
```

---

# szgaViz *Sample size optimization using graphical approach in clinical trial design with two hypotheses*

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## Description

This function computes the optimal design using graphical approach along with the minimum sample size when two hypotheses are considered in a clinical trial.

## Usage

```
szgaViz(
  alpha,
  beta1,
  beta2,
  deltaVec,
  cVec,
  rho,
  wunit,
  initIntvl,
  visualization = TRUE
)
```

## Arguments

| | |
|---|---|
| alpha | a value of overall type I error rate |
| beta1 | a value of one minus marginal powers for testing H1 |
| beta2 | a value of one minus marginal powers for testing H2 |
| deltaVec | a vector of effect sizes for testing H1 nd H2, respectively |
| cVec | a vector of coefficients. When testing continuous endpoints, these coefficients are exactly one. When testing binary endpoints, the values are roughly one but not exactly one |
| rho | a value of correlation coefficients between two hypotheses |
| wunit | a value of initial weight on H1 for grid search and visualization |
| initIntvl | a vector of lower and upper limits for searching optimal sample size |
| visualization | a logical value, indicating whether a visualization is needed |

## Value

a vector of three numbers: the optimal weight on H1 w1, and optimal sample size n1 (based on H1) and n2 (based on H2), where n1 and n2 should be roughly the same

## Author(s)

Jiangtao Gou

Fengqing (Zoe) Zhang

## References

Zhang, F. and Gou, J. (2023). Sample size optimization for clinical trials using graphical approaches for multiplicity adjustment, Technical Report. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311.

## Examples

```
szgaViz(alpha = 0.05, beta1 = 0.20, beta2 = 0.20,
         deltaVec = c(0.3,0.3), cVec = c(1,1), rho = 0.0,
         wunit= 0.01, initIntvl = c(1,1000),
         visualization = FALSE)
```

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