

Package ‘Opt5PL’

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Title Optimal Designs for the 5-Parameter Logistic Model

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Description Obtain and evaluate various optimal designs for the 3, 4, and 5-parameter logistic models. The optimal designs are obtained based on the numerical algorithm in Hyun, Wong, Yang (2018) <[doi:10.18637/jss.v083.i05](https://doi.org/10.18637/jss.v083.i05)>.

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c_weight

One iteration to run Newton Raphson to get c-optimal weights

Description

This is a sub-part of running Newton Raphson method to search c-optimal weights for the given design points. This is function provides the obtained c-optimal weights after one iteration of Newton Raphson method.

Usage

c_weight(W, T, X, d, p, order, UB, I)

Arguments

W	A numeric vector. The first K-1 weights for a given design
T	A numeric vector. Model parameter values
X	A numeric vector. K dose levels for a given design
d	Numeric. Step adjustment
p	Numeric. Define EDP
order	Numeric. The number of model parameters
UB	Numeric. The upper bound of the design points
I	A numeric matrix. Identity matrix.

c_weight_1	<i>The first derivative of the c-optimality criterion w.r.t the model parameters</i>
------------	--

Description

The first derivative of the c-optimality criterion with respect to the model parameters. This is a sub-function of c_weight to run one iteration of Newton-Raphson method.

Usage

```
c_weight_1(W, T, X, inv, p, order)
```

Arguments

W	A numeric vector. The first K-1 weights for a given design
T	A numeric vector. Model parameter values
X	A numeric vector. K dose levels for a given design
inv	A numeric matrix. Inverse of the information matrix.
p	A numeric. Define EDP
order	numeric. The number of model parameters

c_weight_2	<i>The second derivative of the c-optimality criterion with respect to the model parameters</i>
------------	---

Description

The second derivative of the c-optimality criterion with respect to the model parameters. This is a sub-function of c_weight to run one iteration of Newton-Raphson method.

Usage

```
c_weight_2(W, T, X, inv, p, order)
```

Arguments

W	A numeric vector. The first K-1 weights for a given design
T	A numeric vector. Model parameter values
X	A numeric vector. K dose levels for a given design
inv	A numeric matrix. Inverse of the information matrix.
p	A numeric. Define EDp
order	numeric. The number of model parameters

D1	<i>Computing each element of the function c_weight_1</i>
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Description

This function computes each element of the vector function c_weight_1 which is the first derivative of the c-optimality criterion with respect to the model parameters.

Usage

```
D1(T, x, x1, inv, p, order)
```

Arguments

T	A numeric vector. Model parameter values
x	A numeric. ith dose level for a given design
x1	A numeric. last dose level for a given design
inv	A numeric matrix. Inverse of the information matrix
p	A numeric. Define EDp
order	numeric. The number of model parameters

d11 *Computing each element of the function DD_weight_1*

Description

This function computes each element of the vector function DD_weight_1 which is the first derivative of the Ds-optimality criterion with respect to the model parameters.

Usage

d11(T, x, x1, inv, inv1, order)

Arguments

T	A numeric vector. Model parameter values
x	A numeric. ith dose level for a given design
x1	A numeric. last dose level for a given design
inv	A numeric matrix. Inverse of the information matrix for the 5PL model
inv1	A numeric matrix. Inverse of the information matrix for the 4PL model
order	numeric. The number of model parameters

DD1 *Computing each element of the function c_weight_2*

Description

This function computes each element of the matrix function c_weight_2 which is the second derivative of the c-optimality criterion with respect to the model parameters.

Usage

DD1(T, x1, x2, x1, inv, p, order)

Arguments

T	A numeric vector. Model parameter values
x1	A numeric. ith dose level for a given design
x2	A numeric. jth dose level for a given design
x1	A numeric. last dose level for a given design
inv	A numeric matrix. Inverse of the information matrix
p	A numeric. Define EDp
order	numeric. The number of model parameters

dd11 *Computing each element of the function DD_weight_2*

Description

This function computes each element of the matrix function DD_weight_2 which is the second derivative of the Ds-optimality criterion with respect to the model parameters.

Usage

```
dd11(T, x1, x2, x1, inv, inv1, order)
```

Arguments

T	A numeric vector. Model parameter values
x1	A numeric. ith dose level for a given design
x2	A numeric. jth dose level for a given design
x1	A numeric. last dose level for a given design
inv	A numeric matrix. Inverse of the information matrix for the 5PL model
inv1	A numeric matrix. Inverse of the information matrix for the 4PL model
order	numeric. The number of model parameters

DD_weight *One iteration to run Newton Raphson to get Ds-optimal weights*

Description

This is a sub-part of running Newton Raphson method to search Ds-optimal weights for the given design points. This is function provides the obtained Ds-optimal weights after one iteration of Newton Raphson method.

Usage

```
DD_weight(W, T, X, d, I4, I5, order)
```

Arguments

W	A numeric vector. The first K-1 weights for a given design
T	A numeric vector. Model parameter values
X	A numeric vector. K dose levels for a given design
d	Numeric. Step adjustment
I4	A numeric matrix. Information matrix for the 4PL model
I5	A numeric matrix. Information matrix for the 5PL model
order	Numeric. The number of model parameters

DD_weight_1	<i>The first derivative of the Ds-optimality criterion with respect to the model parameters</i>
-------------	---

Description

The first derivative of the Ds-optimality criterion with respect to the model parameters. This is a sub-function of D_weight to run one iteration of Newton-Raphson method.

Usage

DD_weight_1(W, T, X, inv, inv1, order)

Arguments

W	A numeric vector. The first K-1 weights for a given design
T	A numeric vector. Model parameter values for the 5PL model
X	A numeric vector. K dose levels for a given design
inv	A numeric matrix. Inverse information matrix for the 5PL model
inv1	A numeric matrix. Inverse information matrix for the 4PL model
order	numeric. The number of model parameters

DD_weight_2	<i>The second derivative of the Ds-optimality criterion with respect to the model parameters</i>
-------------	--

Description

The second derivative of the Ds-optimality criterion with respect to the model parameters. This is a sub-function of D_weight to run one iteration of Newton-Raphson method.

Usage

DD_weight_2(W, T, X, inv, inv1, order)

Arguments

W	A numeric vector. The first K-1 weights for a given design
T	A numeric vector. Model parameter values for the 5PL model
X	A numeric vector. K dose levels for a given design
inv	A numeric matrix. Inverse information matrix for the 5PL model
inv1	A numeric matrix. Inverse information matrix for the 4PL model
order	numeric. The number of model parameters

Deff

*Obtaining D-efficiency for estimating model parameters***Description**

Obtaining D-efficiency for estimating model parameters for a given design under the 3, 4, 5-parameter logistic models. For the output, the function shows three things: 1. the obtained D-optimal design for the given parameter values; 2. the D-efficiency of the given design; and 3. the number of subjects required for the given design in order to provide the same performance as the D-optimal design does.

Usage

```
Deff(weight,dose,model,P,LB,UB,grid,N_dose)
```

Arguments

weight	A numeric vector. The first K-1 weights for a given design with K design points(K dose levels). The weights represent the proportional allocations of subjects to the dose levels in a given design.
dose	A numeric vector. K dose levels for a given design.
model	Numeric. The number of parameters in the model. This is used to specify the model to check the D-efficiency.
P	A numeric vector. Solicited information on nominal values for the vector for the 5PL model. $P=(p_1, p_2, p_3, p_4, p_5)$, where p_1 is the upper limit of the response, p_2 is the slope that control the stiffness of the response curve, p_3 is the position of the transition region in dose(this is the ED50 under the 3PL and the 4PL model), p_4 is the lower limit of the response, and p_5 is the asymmetric factor. When a user computes the D-efficiency under the 3PL or 4PL model, P is the vector of model parameter values for each model with setting p_4 and p_5 differently. Details are given in the examples.
LB	Numeric. Predetermined lower bound of the dose range for the original dose level.
UB	Numeric. Predetermined lower bound of the dose range for the original dose level.
grid	Numeric. The grid density to discretize the predetermined dose interval. Default is 0.01.
N_dose	Set to TRUE if the original dose levels take negative values. Set to FALSE if the original dose levels take positive values. Default is FALSE

Author(s)

Seung Won Hyun, Weng Kee Wong, and Yarong Yang

References

Hyun, S. W., Wong, W.K., Yang, Y. Optimal designs for asymmetric sigmoidal response curves in bioassays and immunoassays. (submitted to Statistical Methods in Medical Research)

Hyun, S.W., Wong, W.K, Yang, Y. VNM: An R Package for Finding Multiple-Objective Optimal Designs for the 4-Parameter Logistic Model. (Journal of Statistical Software, 83, 1-19, 2018, doi:10.18637/jss.v083.i05.)

Examples

```
##Under the 5PL model with the parameter values
##T5=(30000,0.5,800,0.5,2) and the dose range [1.95,32000],
##find the D-efficiency of the broad range design.

##The broad range design
dose=c(1.95,7.8,31.25,125,500,2000,8000,32000)
dlength=length(dose)
weight=rep(1/dlength,dlength-1)

##Parameter values
T5=c(30000,0.5,800,0.5,2)

##Compute D-efficiency of the broad range design
Deff(weight,dose,model=5,P=T5,LB=1.95,UB=32000,grid=.01)
```

Dp	<i>Target dose, EDp</i>
----	-------------------------

Description

This finds the target dose level ED_p which is the dose producing p percentage of the difference between the maximum and the minimum responses.

Usage

```
Dp(T, p)
```

Arguments

T	A numeric vector. Model parameter values
p	A numeric. Define ED _p

DS1

*Sensitivity function of c-optimality criterion for the EDp***Description**

This evaluates the sensitivity function of the c-optimality criterion for the EDp at the given value of x.

Usage

DS1(T, x, inv, p, order)

Arguments

T	A numeric vector. Model parameter values for the 5PL model
x	A numeric. A given dose level
inv	A numeric matrix. Inverse information matrix for the 5PL model
p	A numeric. Define EDp
order	numeric. The number of model parameters

ds11

*Sensitivity function of Ds-optimality criterion***Description**

This evaluates the sensitivity function of the Ds-optimality criterion at the given value of x.

Usage

ds11(T, x, inv, inv1, order)

Arguments

T	A numeric vector. Model parameter values for the 5PL model
x	A numeric. A given dose level
inv	A numeric matrix. Inverse information matrix for the 5PL model
inv1	A numeric matrix. Inverse information matrix for the 4PL model
order	numeric. The number of model parameters

Dseff *Obtaining Ds-efficiency for estimating the asymmetric factor under the 5-parameter logistic model.*

Description

Obtaining Ds-efficiency for estimating the asymmetric factor for a given design under the 5-parameter logistic models. For the output, the function shows three things: 1. the obtained Ds-optimal design for the given parameter values; 2. the Ds-efficiency of the given design; and 3. the number of subjects required for the given design in order to provide the same performance as the Ds-optimal design does.

Usage

Dseff(weight,dose,P,LB,UB,r,epsilon,grid,N_dose)

Arguments

weight	A numeric vector. The first K-1 weights for a given design with K design points(K dose levels). The weights represent the proportional allocations of subjects to the dose levels in a given design.
dose	A numeric vector. K dose levels for a given design.
P	A numeric vector. Solicited information on nominal values for the vector for the SPL model. $P=(p_1, p_2, p_3, p_4, p_5)$, where p_1 is the upper limit of the response, p_2 is the slope that control the stiffness of the response curve, p_3 is the position of the transition region in dose, p_4 is the lower limit of the response, and p_5 is the asymmetric factor.
LB	Numeric. Predetermined lower bound of the dose range for the original dose level.
UB	Numeric. Predetermined lower bound of the dose range for the original dose level.
r	Numeric. The number of iterations to set an initial design to search the Ds-optimal design to compute the efficiency. Default is 30 and needed to be increased (for example, $r=50$) if the searched the Ds-optimal design is not a true optimal. It can be verified by the verification plot.
epsilon	Numeric. Stopping criterion for the algorithm to search the Ds-optimal design. Default is 0.001.
grid	Numeric. The grid density to discretize the predetermined dose interval. Default is 0.01.
N_dose	Set to TRUE if the original dose levels take negative values. Set to FALSE if the original dose levels take positive values. Default is FALSE

Author(s)

Seung Won Hyun, Weng Kee Wong, and Yarong Yang

References

Hyun, S. W., Wong, W.K., Yang, Y. Optimal designs for asymmetric sigmoidal response curves in bioassays and immunoassays. (submitted to Statistical Methods in Medical Research)

Hyun, S.W., Wong, W.K., Yang, Y. VNM: An R Package for Finding Multiple-Objective Optimal Designs for the 4-Parameter Logistic Model. (Journal of Statistical Software, 83, 1-19, 2018, doi:10.18637/jss.v083.i05.)

Examples

```
##Under the 5PL model with the parameter values
##T5=(30000,0.5,800,0.5,2) and the dose range [1.95,32000],
##find the Ds-efficiency of the broad range design.

##The broad range design
dose=c(1.95,7.8,31.25,125,500,2000,8000,32000)
dlength=length(dose)
weight=rep(1/dlength,dlength-1)

##Parameter values for the 5PL model
T5=c(30000,0.5,800,0.5,2)

##Ds efficiency of the broad range design
Dseff(weight,dose,P=T5,LB=1.95,UB=32000,grid=.01)
```

DsOPT

Search Ds-optimal design for estimating the asymmetric factor under the 5-parameter logistic model.

Description

Obtain Ds-optimal design (i.e., optimal dose levels and corresponding optimal weights) for estimating the asymmetric factor under the 5-parameter logistic model.

Usage

```
DsOPT(LB,UB,P,grid,r,epsilon,N_dose,log_scale)
```

Arguments

LB	Numeric. Predetermined lower bound of the dose range for the original dose level.
UB	Numeric. Predetermined lower bound of the dose range for the original dose level.

P	A numeric vector. Solicited information on nominal values for the vector for the 5PL model. $P=(p1, p2, p3, p4, p5)$, where $p1$ is the upper limit of the response, $p2$ is the slope that control the stiffness of the response curve, $p3$ is the position of the transition region in dose, $p4$ is the lower limit of the response, and $p5$ is the asymmetric factor.
grid	Numeric. The grid density to discretize the predetermined dose interval. Default is 0.01.
r	Numeric. The number of iterations to set an initial design to search the Ds-optimal design. Default is 30 and needed to be increased (for example, $r=50$) if the searched optimal design is not a true optimal. It can be verified by the verification plot.
epsilon	Numeric. Stopping criterion for the algorithm to search the Ds-optimal design. Default is 0.001.
N_dose	Set to TRUE if the original dose levels take negative values. Set to FALSE if the original dose levels take positive values. Default is FALSE
log_scale	Set to TRUE if a user wants to set the X-axis(dose level) on log scale in the verification plot of the optimal design. Otherwise, set to FALSE. Default is TRUE. Note: this need to set FALSE when the original dose levels take negative values.

Author(s)

Seung Won Hyun, Weng Kee Wong, and Yarong Yang

References

Hyun, S. W., Wong, W.K., Yang, Y. Optimal designs for asymmetric sigmoidal response curves in bioassays and immunoassays. (submitted to Statistical Methods in Medical Research)

Hyun, S.W., Wong, W.K, Yang, Y. VNM: An R Package for Finding Multiple-Objective Optimal Designs for the 4-Parameter Logistic Model. (Journal of Statistical Software, 83, 1-19, 2018, doi:10.18637/jss.v083.i05.)

Examples

```
##Find the Ds-optimal design for estimating theta_5 under the 5PL model
##with the parameter values T5=(30000,0.5,800,0.5,2) and the dose range [1.95,32000].

##Parameter values for the 5PL model
T5=c(30000,0.5,800,0.5,2)

##Find the Ds-optimal design
DsOPT(LB=1.95, UB=32000, P=T5,grid=.01,epsilon=.001)
```

D_weight	<i>One iteration to run Newton Raphson to get D-optimal weights</i>
----------	---

Description

This is a sub-part of running Newton Raphson method to search D-optimal weights for the given design points. This is function provides the obtained D-optimal weights after one iteration of Newton Raphson method.

Usage

D_weight(W, T, X, d, q)

Arguments

W	A numeric vector. The first K-1 weights for a given design
T	A numeric vector. Model parameter values
X	A numeric vector. K dose levels for a given design
d	Numeric. Step adjustment
q	A numeric vector. User select weights defined in the function RDOPT

D_weight_1	<i>The first derivative of the D-optimality criterion w.r.t the model parameters</i>
------------	--

Description

The first derivative of the D-optimality criterion with respect to the model parameters. This is a sub-function of D_weight to run one iteration of Newton-Raphson method.

Usage

D_weight_1(q, W, T1, T2, T3, X, inv1, inv2, inv3)

Arguments

q	A numeric vector. User select weights defined in the function RDOPT
W	A numeric vector. The first K-1 weights for a given design
T1	A numeric vector. Model parameter values for the 3PL model
T2	A numeric vector. Model parameter values for the 4PL model
T3	A numeric vector. Model parameter values for the 5PL model
X	A numeric vector. K dose levels for a given design
inv1	A numeric matrix. Inverse information matrix for the 3PL model
inv2	A numeric matrix. Inverse information matrix for the 4PL model
inv3	A numeric matrix. Inverse information matrix for the 5PL model

D_weight_2	<i>The second derivative of the D-optimality criterion w.r.t the model parameters</i>
------------	---

Description

The second derivative of the D-optimality criterion with respect to the model parameters. This is a sub-function of D_weight to run one iteration of Newton-Raphson method.

Usage

```
D_weight_2(q, W, T1, T2, T3, X, inv1, inv2, inv3)
```

Arguments

q	A numeric vector. User select weights defined in the function RDOPT
W	A numeric vector. The first K-1 weights for a given design
T1	A numeric vector. Model parameter values for the 3PL model
T2	A numeric vector. Model parameter values for the 4PL model
T3	A numeric vector. Model parameter values for the 5PL model
X	A numeric vector. K dose levels for a given design
inv1	A numeric matrix. Inverse information matrix for the 3PL model
inv2	A numeric matrix. Inverse information matrix for the 4PL model
inv3	A numeric matrix. Inverse information matrix for the 5PL model

EDpeff	<i>Obtaining c-efficiency for estimating the EDp under the 5-parameter logistic model.</i>
--------	--

Description

Obtaining c-efficiency for estimating the EDp for a given design under the 5-parameter logistic models. For the output, the function shows three things: 1. the obtained c-optimal design for the given parameter values; 2. the c-efficiency of the given design; and 3. the number of subjects required for the given design in order to provide the same performance as the c-optimal design does.

Usage

```
EDpeff(weight,dose,P,EDp,LB,UB,r,epsilon,grid,N_dose)
```

Arguments

weight	A numeric vector. The first K-1 weights for a given design with K design points(K dose levels). The weights represent the proportional allocations of subjects to the dose levels in a given design.
dose	A numeric vector. K dose levels for a given design.
P	A numeric vector. Solicited information on nominal values for the vector for the 5PL model. $P=(p1, p2, p3, p4, p5)$, where p1 is the upper limit of the response, p2 is the slope that control the stiffness of the response curve, p3 is the position of the transition region in dose, p4 is the lower limit of the response, and p5 is the asymmetric factor.
EDp	Numeric. An user select value to define the EDp. For example, EDp=.05 to define the ED50.
LB	Numeric. Predetermined lower bound of the dose range for the original dose level.
UB	Numeric. Predetermined lower bound of the dose range for the original dose level.
r	Numeric. The number of iterations to set an initial design to search the c-optimal design for the EDp in order to compute the efficiency. Default is 30 and needed to be increased (for example, r=50) if the searched the c-optimal design is not a true optimal. It can be verified by the verification plot.
epsilon	Numeric. Stopping criterion for the algorithm to search the c-optimal design. Default is 0.001.
grid	Numeric. The grid density to discretize the predetermined dose interval. Default is 0.01.
N_dose	Set to TRUE if the original dose levels take negative values. Set to FALSE if the original dose levels take positive values. Default is FALSE

Author(s)

Seung Won Hyun, Weng Kee Wong, and Yarong Yang

References

- Hyun, S. W., Wong, W.K., Yang, Y. Optimal designs for asymmetric sigmoidal response curves in bioassays and immunoassays. (submitted to Statistical Methods in Medical Research)
- Hyun, S.W., Wong, W.K, Yang, Y. VNM: An R Package for Finding Multiple-Objective Optimal Designs for the 4-Parameter Logistic Model. (Journal of Statistical Software, 83, 1-19, 2018, doi:10.18637/jss.v083.i05.)

Examples

```
##Under the 5PL model with the parameter values
##T5=(30000,0.5,800,0.5,2) and the dose range [1.95,32000],
##find the c-efficiency of the broad range design.
```



```

##The broad range design
dose=c(1.95,7.8,31.25,125,500,2000,8000,32000)
dlength=length(dose)
weight=rep(1/dlength,dlength-1)

##Parameter values for the 5PL model
T5=c(30000,0.5,800,0.5,2)

##Compute the c-efficiency of the broad range design
EDpeff(weight,dose,P=T5,EDp=.5,LB=1.95,UB=32000,grid=.01)

```

EDpOPT	<i>Search c-optimal designs for estimating the EDp under the 5-parameter logistic model</i>
--------	---

Description

Obtain c-optimal design (i.e., optimal dose levels and corresponding optimal weights) for estimating the EDp under the 5-parameter logistic model. The EDp is the dose level that achieve the 100p% of the difference between the maximum and the minimum responses.

Usage

```
EDpOPT(LB,UB,P,EDp,grid,r,epsilon,N_dose,log_scale)
```

Arguments

LB	Numeric. Predetermined lower bound of the dose range for the original dose level.
UB	Numeric. Predetermined lower bound of the dose range for the original dose level.
P	A numeric vector. Solicited information on nominal values for the vector for the 5PL model. $P=(p_1, p_2, p_3, p_4, p_5)$, where p_1 is the upper limit of the response, p_2 is the slope that control the stiffness of the response curve, p_3 is the position of the transition region in dose, p_4 is the lower limit of the response, and p_5 is the asymmetric factor.
EDp	Numeric. An user select value to define the EDp. For example, $EDp=.05$ to define the ED50.
grid	Numeric. The grid density to discretize the predetermined dose interval. Default is 0.01.
r	Numeric. The number of iterations to set an initial design to search the c-optimal design. Default is 30 and needed to be increased (for example, $r=50$) if the searched optimal design is not a true optimal. It can be verified by the verification plot.
epsilon	Numeric. Stopping criterion for the algorithm to search the c-optimal design. Default is 0.001.

N_dose	Set to TRUE if the original dose levels take negative values. Set to FALSE if the original dose levels take positive values. Default is FALSE
log_scale	Set to TRUE if a user wants to set the X-axis(dose level) on log scale in the verification plot of the optimal design. Otherwise, set to FALSE. Default is TRUE. Note: this need to set FALSE when the original dose levels take negative values.

Author(s)

Seung Won Hyun, Weng Kee Wong, and Yarong Yang

References

Hyun, S. W., Wong, W.K., Yang, Y. Optimal designs for asymmetric sigmoidal response curves in bioassays and immunoassays. (submitted to Statistical Methods in Medical Research)

Hyun, S.W., Wong, W.K., Yang, Y. VNM: An R Package for Finding Multiple-Objective Optimal Designs for the 4-Parameter Logistic Model. (Journal of Statistical Software, 83, 1-19, 2018, doi:10.18637/jss.v083.i05.)

Examples

```
##Search the c-optimal design for estimating the ED50 under the 5PL model

##Parameter values for the 5PL model
T5=c(30000,0.5,800,0.5,2)

##Dose range=[1.95,32000]

EDpOPT(LB=1.95,UB=32000, P=T5,EDp=.5,grid=.01, r =30,epsilon=.001)
```

f

Gradient of the mean function

Description

This gives the first derivative of the mean response function (3, 4, or 5PL) with respect to the model parameters.

Usage

```
f(T, x, order)
```

Arguments

T	A numeric vector. Model parameter values
x	A numeric. A given dose level
order	numeric. The number of model paraemters

g	<i>Partial derivative of the EDp with respect to the model parameters</i>
---	---

Description

Partial derivative of the EDp with respect to the model parameters

Usage

$g(T, p)$

Arguments

T	A numeric vector. Model parameter values
p	A numeric. Define EDp

ginv	<i>Generalized Inverse Matrix</i>
------	-----------------------------------

Description

Obtain generalized inverse of the given matrix X.

Usage

`ginv(X, tol = sqrt(.Machine$double.eps))`

Arguments

X	A numeric matrix
tol	Default

infor	<i>Obtain a information matrix at a single design point</i>
-------	---

Description

Obtain a information matrix at a single given design point x.

Usage

infor(T, x, order)

Arguments

T	A numeric vector. Model parameter values
x	numeric. A single design point(dose level)
order	numeric. The number of model paraemters

Inv	<i>Adjusting invere information matrix being not singular</i>
-----	---

Description

When the inverse matrix is a singular, it is adjusted to become nonsingular matrix.

Usage

Inv(M, I)

Arguments

M	A numeric matrix
I	Identity matrix

Minus	<i>Matrix subtraction</i>
-------	---------------------------

Description

Matrix subtraction: $M1-M2$.

Usage

Minus(M1, M2)

Arguments

M1	A numeric matrix
M2	A numeric matrix

Multiple	<i>Matrix multiplication</i>
----------	------------------------------

Description

Matrix multiplication: $M1*M2$.

Usage

Multiple(M1, M2)

Arguments

M1	A numeric matrix
M2	A numeric matrix

Plus	<i>Matrix addition</i>
------	------------------------

Description

Matrix addition: $M1+M2$.

Usage

Plus(M1, M2)

Arguments

M1	A numeric matrix
M2	A numeric matrix

RDOPT

*Search the robust D-optimal designs for estimating model parameters***Description**

Obtain robust D-optimal design (i.e., optimal dose levels and corresponding optimal weights) for estimating the model parameters that works well under the 3, 4, 5-parameter logistic models. In addition, the function can be used to obtain D-optimal design for each of the three models.

Usage

```
RDOPT(LB,UB, P3,P4,P5,q,grid,r,epsilon,N_dose,log_scale)
```

Arguments

LB	Numeric. Predetermined lower bound of the dose range for the original dose level.
UB	Numeric. Predetermined lower bound of the dose range for the original dose level.
P3	A numeric vector. Solicited information on nominal values for the vectors for the 3PL model. $P3=(p1, p2, p3)$, where $p1$ is the upper limit of the response, $p2$ is the slope that control the stiffness of the response curve, and $p3$ is the ED50.
P4	A numeric vector. Solicited information on nominal values for the vectors for the 4PL model. $P4=(p1, p2, p3, p4)$, where $p1$ is the upper limit of the response, $p2$ is the slope that control the stiffness of the response curve, $p3$ is the ED50, and $p4$ is the lower limit of the response.
P5	A numeric vector. Solicited information on nominal values for the vectors for the 5PL model. $P5=(p1, p2, p3, p4, p5)$, where $p1$ is the upper limit of the response, $p2$ is the slope that control the stiffness of the response curve, $p3$ is the position of the transition region in dose, $p4$ is the lower limit of the response, and $p5$ is the asymmetric factor. For searching the robust D-optimal design, the nominal values for P3, P4, P5 need to be specified. However, when a user searches the D-optimal design for the 3PL, 4PL, or 5PL model, only P5 needs to be specified. Details are given in the examples.
q	A numeric vector. User select weights. $q=c(q1, q2, q3)$, where $q1, q2, q3$ represent the relative importance of the 3, 4, 5PL models respectively. They are non-negative and $q1+q2 \leq 1$. For example, $q=c(0,0,1)$ is used to find D-optimal design for the 5PL model only and $q=c(1/3,1/3,1/3)$ is used to find robust D-optimal design for the three models under the assumption that the three models are equally important.
grid	Numeric. The grid density to discretize the predetermined dose interval. Default is 0.01.
r	Numeric. The number of iterations to set an initial design to search the D-optimal design. Default is 30 and needed to be increased (for example, $r=50$) if the searched optimal design is not a true optimal. It can be verified by the verification plot.

epsilon	Numeric. Stopping criterion for the algorithm to search the D-optimal design. Default is 0.001.
N_dose	Set to TRUE if the original dose levels take negative values. Set to FALSE if the original dose levels take positive values. Default is FALSE
log_scale	Set to TRUE if a user wants to set the X-axis(dose level) on log scale in the verification plot of the optimal design. Otherwise, set to FALSE. Default is TRUE. Note: this need to set FALSE when the original dose levels take negative values.

Author(s)

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References

Hyun, S. W., Wong, W.K., Yang, Y. Optimal designs for asymmetric sigmoidal response curves in bioassays and immunoassays. (submitted to Statistical Methods in Medical Research)

Hyun, S.W., Wong, W.K, Yang, Y. VNM: An R Package for Finding Multiple-Objective Optimal Designs for the 4-Parameter Logistic Model. (Journal of Statistical Software, 83, 1-19, 2018, doi:10.18637/jss.v083.i05.)

Examples

```
##1. Search the robust D-optimal design for estimating the model parameters
##under the 3,4,5PL models
```

```
##Parameter values for the 5PL model
```

```
T5=c(30000,0.5,800,0.5,2)
```

```
##Parameter values for the 4PL model
```

```
T4=c(27264.92,0.67,3340.95,-225.55)
```

```
##Parameter values for the 3PL model
```

```
T3=c(26715.52,0.70,3204.92)
```

```
##Dose range=[1.95,32000]
```

```
##Assuming the three models are equally important
```

```
RDOPT(LB=1.95,UB=32000,P3=T3,P4=T4,P5=T5,q=c(1/3,1/3,1/3))
```

```
##2. Search the D-optimal design for the 3PL model using
```

```
##the parameter values T3=(26715.52,0.70,3204.92)
```

```
##and the dose range [1.95,32000].
```

```
#Set the parameter values for the 3PL model in the form of P5
```

```
P5=c(26715.52,0.70,3204.92,0,1)
```

```
RDOPT(LB=1.95, UB=32000,P5=P5,q=c(1,0,0))
```

```
##3. Search the D-optimal design for the 4PL model using
```

```
##the parameter values T4=(27264.92,0.67,3340.95,-225.55)
```

```
##and the dose range [1.95,32000].
```

```
#Set the parameter values for the 4PL model in the form of P5.
```

```
P5=c(27264.92,0.67,3340.95,-225.55,1)
RDOPT(LB=1.95, UB=32000,P5=P5,q=c(0,1,0))
```

SDM	<i>Summation of diagonal elements in a matrix</i>
-----	---

Description

Summation of diagonal elements in a matrix M.

Usage

```
SDM(M)
```

Arguments

M	A numeric matrix
---	------------------

smalld1	<i>Sub-function of the function D_weight_1</i>
---------	--

Description

This computes the first derivative of the D-optimality criterion with respect to the model parameters for a specified model.

Usage

```
smalld1(T, x, x1, inv, order)
```

Arguments

T	A numeric vector. Model parameter values
x	A numeric. ith dose level
x1	A numeric. last dose level
inv	A numeric matrix. Inverse information matrix
order	numeric. The number of model parameters: 3, 4, 5 for the 3, 4, 5PL models respectively

smalldd1	<i>Sub-function of the function D_weight_2</i>
----------	--

Description

This computes the second derivative of the D-optimality criterion with respect to the model parameters for a specified model.

Usage

```
smalldd1(T, x1, x2, x1, inv, order)
```

Arguments

T	A numeric vector. Model parameter values
x1	A numeric. ith dose level
x2	A numeric. jth dose level
x1	A numeric. last dose level
inv	A numeric matrix. Inverse information matrix
order	numeric. The number of model parameters: 3, 4, 5 for the 3, 4, 5PL models respectively

smallds1	<i>Sensitivity function of D-optimality criterion</i>
----------	---

Description

This evaluates the sensitivity function of the D-optimality criterion at the given value of x for a specified model.

Usage

```
smallds1(T, x, inv, order)
```

Arguments

T	A numeric vector. Model parameter values
x	A numeric. A given dose level
inv	A numeric matrix. Inverse information matrix
order	numeric. The number of model parameters: 3, 4, 5 for the 3, 4, 5PL models respectively

sMultiple *Multiply a constant to a matrix*

Description

Multiply a constant to a matrix: $s \cdot M$.

Usage

sMultiple(s, M)

Arguments

s	Numeric
M	A numeric matrix

S_weight *Newton Raphson method to get optimal weights*

Description

Newton Raphson method to get optimal weights for given design points "X".

Usage

S_weight(X, T, e1, f, ...)

Arguments

X	A numeric vector. K dose levels for a given design
T	A numeric vector. Model parameter values
e1	Numeric. Threshold to stop the iteration.
f	A character. D_weight for D-optimal weight; c_weight for c-optimal weight; DD_weight for Ds-optimal weight
...	Default.

Trans	<i>Transpose of a matrix</i>
-------	------------------------------

Description

Transpose of a matrix M.

Usage

Trans(M)

Arguments

M	A numeric matrix
---	------------------

upinfor	<i>Obtain normalized Fisher information matrix</i>
---------	--

Description

Obtain normalized Fisher information matrix for the 3, 4, 5PL models.

Usage

upinfor(W, T, X, order)

Arguments

W	A numeric vector. The first K-1 weights for a given design
T	A numeric vector. Model parameter values
X	A numeric vector. K design points for a given design
order	numeric. The number of model parameters

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