

# Package ‘adaptTest’

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**Type** Package

**Title** Adaptive two-stage tests

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**Description** The functions defined in this program serve for implementing adaptive two-stage tests. Currently, four tests are included: Bauer and Koehne (1994), Lehmacher and Wassmer (1999), Vandemeulebroecke (2006), and the horizontal conditional error function. User-defined tests can also be implemented. Reference: Vandemeulebroecke, An investigation of two-stage tests, Statistica Sinica 2006.

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adaptTest-package	<i>Adaptive two-stage tests</i>
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## Description

The functions defined in this program serve for implementing adaptive two-stage tests.

## Details

Package:	adaptTest
Type:	Package
Version:	1.0
Date:	2009-10-14
License:	GPL (version 2 or later)
LazyLoad:	yes

An adaptive two-stage test can be considered as a family of decreasing functions  $f[c](p_1)$  in the unit square. Each of these functions is a conditional error function, specifying the type I error conditional on the p-value  $p_1$  of the first stage. For example,  $f[c](p_1) = \min(1, c/p_1)$  corresponds to Fisher's combination test (Bauer and Koehne, 1994). Based on this function family, the test can be put into practice by specifying the desired overall level  $\alpha$ , stopping bounds  $\alpha_1 \leq \alpha_0$  and a parameter  $\alpha_2$ . After computing  $p_1$ , the test stops with or without rejection of the null hypothesis if  $p_1 \leq \alpha_1$  or  $p_1 > \alpha_0$ , respectively. Otherwise, the null hypothesis is rejected if and only if  $p_2 \leq f[c](p_1)$  holds for the p-value  $p_2$  of the second stage, where  $c$  is such that the local level of this latter test is  $\alpha_2$  (e.g.,  $c = c(\alpha_2) = \exp(-\chi_{4,\alpha_2}^2/2)$  for Fisher's combination test).

This package provides functions for handling conditional error functions, performing calculations among the different parameters ( $\alpha$ ,  $\alpha_0$ ,  $\alpha_1$ ,  $\alpha_2$  and  $c$ ) and computing overall p-values, in addition to graphical visualization routines. Currently, four predefined tests are included: Bauer and Koehne (1994), Lehman and Wassmer (1999), Vandemeulebroecke (2006), and the horizontal conditional error function. User-defined tests can also be implemented.

This package contains the following functions:

- Key functions are [CEF](#), [plotCEF](#), [tsT](#), [ovP](#).
- Further functions are [a1Table](#), [getpar](#), [parconv](#), [pathCEF](#), [plotBounds](#), [eq](#), [ne](#), [ge](#), [gt](#), [le](#), [lt](#).

The functions [a1Table](#), [getpar](#), [parconv](#) and [tsT](#) can handle the four predefined tests mentioned above. The functions [CEF](#), [plotCEF](#), [pathCEF](#) and [ovP](#) can also handle these, and user-defined tests in addition. The functions [plotBounds](#), [eq](#), [ne](#), [ge](#), [gt](#), [le](#) and [lt](#) do not directly handle tests.

## Note

Note that a family of conditional error functions can be parameterized in two alternative ways: more "traditionally" by some parameter  $c$  that, in turn, depends on the local level  $\alpha_2$  of the test after the second stage, or - perhaps more conveniently - by  $\alpha_2$  itself.

In this implementation, early stopping bounds are *not* part of the conditional error function. Rather, they are specified separately and "imposed" on it.

I want to thank Niklas Hack for technical support.

## Author(s)

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## References

Bauer, P., Koehne, K. (1994). Evaluation of experiments with adaptive interim analyses. *Biometrics* 50, 1029-1041.

Brannath, W., Posch, M., Bauer, P. (2002). Recursive combination tests. *J. Amer. Statist. Assoc.* 97, 236-244.

Lehmacher, W., Wassmer, G. (1999). Adaptive sample size calculations in group sequential trials. *Biometrics* 55, 1286-1290.

Vandemeulebroecke, M. (2006). An investigation of two-stage tests. *Statistica Sinica* 16, 933-951.

Vandemeulebroecke, M. (2006). *A general approach to two-stage tests*. Doctoral thesis, Otto-von-Guericke-Universitaet Magdeburg, <http://www.dissertation.de>.

Vandemeulebroecke, M. (2008). Group sequential and adaptive designs - a review of basic concepts and points of discussion. *Biometrical Journal* 50, 541-557.

## See Also

[CEF](#), [tsT](#)

## Examples

```
## Example from Bauer and Koehne (1994)
alpha <- 0.1
alpha2 <- 0.1
alpha0 <- 0.5
alpha1 <- tsT(typ="b", a=alpha, a0=alpha0, a2=alpha2)
plotCEF(typ="b", a2=alpha2, add=FALSE)
plotBounds(alpha1, alpha0)
CEF(typ="b", a2=alpha2)
```

---

a1Table *Function to produce tables of alpha1*

---

### Description

This function produces tables of  $\alpha_1$  for a grid of different choices of  $\alpha$  and  $\alpha_0$ .

### Usage

```
a1Table(typ, a = NA, a0 = NA, Pocock = FALSE, round = FALSE)
```

### Arguments

typ	type of test: "b" for Bauer and Koehne (1994), "l" for Lehmacher and Wassmer (1999), "v" for Vandemeulebroecke (2006) and "h" for the horizontal conditional error function
a	vector of different choices of $\alpha$ , the overall test level
a0	vector of different choices of $\alpha_0$ , the futility stopping bound
Pocock	logical determining whether the "Pocock-type" should be calculated or the full level should be applied after the second stage (see details; default: full level after second stage).
round	rounding specification, logical or integer (see details; default: no rounding)

### Details

This function produces tables of  $\alpha_1$  on a grid spanned by the vectors *a* and *a0* (i.e.,  $\alpha$  and  $\alpha_0$ ). This is done either for the "Pocock-type" (i.e., under the condition  $\alpha_1 = \alpha_2$ ; Pocock = TRUE) or using the full level after the second stage ( $\alpha = \alpha_2$ ; Pocock = FALSE (the default)). The function a1Table can be a convenient shortcut for a repeated use of `tST`; see this latter function for further details.

The result is rounded to round digits after the comma (round = TRUE rounds to 1 digit; round = FALSE and round = 0 prevent rounding).

### Value

a1Table returns a matrix of  $\alpha_1$  values, with the corresponding  $\alpha$  and  $\alpha_0$  values being displayed as dimnames.

### Author(s)

Marc Vandemeulebroecke

## References

- Bauer, P., Koehne, K. (1994). Evaluation of experiments with adaptive interim analyses. *Biometrics* 50, 1029-1041.
- Lehmacher, W., Wassmer, G. (1999). Adaptive sample size calculations in group sequential trials. *Biometrics* 55, 1286-1290.
- Vandemeulebroecke, M. (2006). An investigation of two-stage tests. *Statistica Sinica* 16, 933-951.

## See Also

[adaptTest](#) package description, [tsT](#)

## Examples

```
## Produce basic reference tables for the test by Vandemeulebroecke (2006)
alpha <- c(0.1, 0.05, 0.025, 0.01)
alpha0 <- 1:10/10
a1Table(typ="v", a=alpha, a0=alpha0, Pocock=FALSE)
a1Table(typ="v", a=alpha, a0=alpha0, Pocock=TRUE)
```

---

CEF

*Function to specify a conditional error function*

---

## Description

This function returns a conditional error function.

## Usage

```
CEF(typ = NA, fun = NA, dis = NA, a2 = NA, c = NA, p1 = NA, p2 = p1)
```

## Arguments

typ	type of test: "b" for Bauer and Koehne (1994), "l" for Lehmacher and Wassmer (1999), "v" for Vandemeulebroecke (2006) and "h" for the horizontal conditional error function
c	the parameter $c$
a2	$\alpha_2$ , the local level of the test after the second stage
p1	the p-value $p_1$ of the test after the first stage
p2	the p-value $p_2$ of the test after the second stage, defaults to p1
fun	a conditional error function
dis	a distortion method for a supplied conditional error function (see details): "p1" for power lines, "vt" for vertical translation

## Details

There are two alternative ways of specifying the desired conditional error function:

- through a type `typ`, and either a parameter (either `a2` or `c`) or a point (`p1`, `p2`), OR
- through an initial conditional error function `fun`, and possibly a distortion method `dis` together with either the parameter `a2` or a point (`p1`, `p2`)

Most people will only need the first of these two ways; the second leads to user-defined non-standard tests.

If `typ` is specified, a parameter `a2` or `c` or the point (`p1`, `p2`) must be provided. In this case, CEF returns the conditional error function of the chosen type with the given parameter or running through the given point.

If `typ` is not specified, a conditional error function (i.e., a nonincreasing function defined on  $[0,1]$  with values in  $[0,1]$ ) `fun` must be provided. If no distortion method is selected (`dis` = NA), `fun` is returned unchanged. Otherwise, the function is distorted using the chosen distortion method, either to match a desired second stage level `a2` or to run through a specified point (`p1`, `p2`) (one of which must be provided). Currently, two distortion methods are implemented:

- `dis` = "p1", Power lines: For an initial function  $f$ , define  $f[r](x) = (f(x^r))^{1/r}$ ,  $r > 0$ . Note that if  $f$  is a conditional error function of type "b" (Bauer and Koehne, 1994), so is  $f[r]$ .
- `dis` = "p1", Vertical translation: The initial function is shifted vertically.

See [parconv](#) for more information on the two alternative parameterizations by  $\alpha_2$  and  $c$ .

## Value

These functions return a conditional error *function* (see details).

## Note

Provide either `typ` or `fun`, not both! If `typ` is provided, then also specify `a2`, `c`, or `p1` (and possibly `p2`). If `fun` is provided, then also specify `dis` and `a2`, or `dis` and `p1` (and possibly `p2`), or none of these.

Warning: Values of `a2` close to 0 or 1 may not work for `dis` = "p1".

Note that in this implementation of adaptive two-stage tests, early stopping bounds are *not* part of the conditional error function. Rather, they are specified separately (see also [tsT](#)).

## Author(s)

Marc Vandemeulebroecke

## References

- Bauer, P., Koehne, K. (1994). Evaluation of experiments with adaptive interim analyses. *Biometrics* 50, 1029-1041.
- Lehmacher, W., Wassmer, G. (1999). Adaptive sample size calculations in group sequential trials. *Biometrics* 55, 1286-1290.
- Vandemeulebroecke, M. (2006). An investigation of two-stage tests. *Statistica Sinica* 16, 933-951.

**See Also**

[adaptTest](#) package description, [parconv](#), [plotCEF](#), [tsT](#)

**Examples**

```
## Plot two conditional error functions of the Lehmacher-Wassmer (1999) type:
## one to the local level alpha2=0.1, and one that runs through (p1,p2)=(0.3,0.7)
foo1 <- CEF(typ="l", a2=0.1)
foo2 <- CEF(typ="l", p1=0.3, p2=0.7)
plot(foo1, xlim=0:1)
plot(foo2, add=TRUE)

## A different way of doing the same
plotCEF(typ="l", a2=0.1, add=FALSE)
plotCEF(typ="l", p1=0.3, p2=0.7, plt.pt=FALSE)
```

---

getpar	<i>Function to calculate the parameter that specifies the conditional error function running through a given point</i>
--------	--

---

**Description**

This function calculates the parameter that specifies the conditional error function running through a given point  $(p_1, p_2)$ , based on a chosen family of conditional error functions.

**Usage**

```
getpar(typ, p1 = NA, p2 = p1, c = FALSE)
```

**Arguments**

typ	type of test: "b" for Bauer and Koehne (1994), "l" for Lehmacher and Wassmer (1999), "v" for Vandemeulebroecke (2006) and "h" for the horizontal conditional error function
p1	the p-value $p_1$ of the test after the first stage
p2	the p-value $p_2$ of the test after the second stage, defaults to p1
c	logical determining whether the parameter $\alpha_2$ or the parameter $c$ is returned ( $\alpha_2$ is the default).

**Details**

See [parconv](#) for more information on the two alternative parameterizations by  $\alpha_2$  and  $c$ .

**Value**

getpar returns the parameter (either  $\alpha_2$  or  $c$ , depending on the chosen parameterization) that specifies the conditional error function running through  $(p_1, p_2)$ .

**Author(s)**

Marc Vandemeulebroecke

**References**

Bauer, P., Koehne, K. (1994). Evaluation of experiments with adaptive interim analyses. *Biometrics* 50, 1029-1041.

Lehmacher, W., Wassmer, G. (1999). Adaptive sample size calculations in group sequential trials. *Biometrics* 55, 1286-1290.

Vandemeulebroecke, M. (2006). An investigation of two-stage tests. *Statistica Sinica* 16, 933-951.

**See Also**

[adaptTest](#) package description, [parconv](#), [CEF](#)

**Examples**

```
## Plot the conditional error function of the Lehmacher-Wassmer (1999) type that runs through (p1,p2)=(0.3,0.7)
alpha2 <- getpar(typ="1", p1=0.3, p2=0.7)
plotCEF(typ="1", a2=alpha2, add=FALSE)

## Other ways of doing the same as above
plotCEF(typ="1", p1=0.3, p2=0.7, add=FALSE)
plot(CEF(typ="1", p1=0.3, p2=0.7), xlim=0:1)
```

---

OrderComparisons

*Functions to perform simple order comparisons*

---

**Description**

These functions perform simple order comparisons for two arguments, dealing with the machine inaccuracy for floating point arithmetics.

**Usage**

```
eq(x, y, tol = .Machine$double.eps^0.5)
ne(x, y, tol = .Machine$double.eps^0.5)
ge(x, y, tol = .Machine$double.eps^0.5)
gt(x, y, tol = .Machine$double.eps^0.5)
le(x, y, tol = .Machine$double.eps^0.5)
lt(x, y, tol = .Machine$double.eps^0.5)
```

**Arguments**

x	first argument (must be a numeric scalar)
y	second argument (must be a numeric scalar)
tol	comparison tolerance; differences smaller than tol are not considered.



**Details**

When comparing two numeric scalars (e.g., for equality), machine inaccuracy can be the source of obviously erroneous results. These functions perform binary order comparisons that are tolerant towards machine inaccuracy, as an alternative to the standard comparators `==`, `!=`, `>=`, `>`, `<=` and `<`.

**Value**

The functions return a logical TRUE if their condition holds, and a logical FALSE otherwise.

`eq(x, y)` checks whether `x` is equal to `y`

`ne(x, y)` checks whether `x` is not equal to `y`

`ge(x, y)` checks whether `x` is greater than or equal to `y`

`gt(x, y)` checks whether `x` is greater than `y`

`le(x, y)` checks whether `x` is less than or equal to `y`

`lt(x, y)` checks whether `x` is less than `y`

**Note**

These functions cannot be used in a vectorized fashion.

**Author(s)**

Marc Vandemeulebroecke

**See Also**

[identical](#), [all.equal](#)

**Examples**

```
v <- seq(0.7, 0.8, by=0.1)
v[2]==0.8
eq(v[2], 0.8)
```

---

ovP

*Function to compute and visualize overall p-values*

---

**Description**

This function computes and plots overall p-values for adaptive two-stage tests.

**Usage**

```
ovP(typ = NA, fun = NA, dis = NA, p1 = 1:49/50, p2 = p1,
     a1 = 0, a0 = 1, grid = FALSE, plt = FALSE,
     invisible = FALSE, wire = FALSE, round = FALSE)
```

### Arguments

<code>typ</code>	type of test: "b" for Bauer and Koehne (1994), "l" for Lehmacher and Wassmer (1999), "v" for Vandemeulebroecke (2006) and "h" for the horizontal conditional error function
<code>fun</code>	a conditional error function
<code>dis</code>	a distortion method for a supplied conditional error function (see details): "p1" for power lines, "vt" for vertical translation
<code>p1</code>	the p-value $p_1$ of the test after the first stage, or a vector of such p-values
<code>p2</code>	the p-value $p_2$ of the test after the second stage, or a vector of such p-values; defaults to p1
<code>a1</code>	$\alpha_1$ , the efficacy stopping bound and local level of the test after the first stage (default: no stopping for efficacy)
<code>a0</code>	$\alpha_0$ , the futility stopping bound (default: no stopping for futility)
<code>grid</code>	logical determining whether a grid should be spanned by p1 and p2 (default: no grid is spanned)
<code>plt</code>	logical determining whether the overall p-values should be plotted or not (default: not)
<code>invisible</code>	logical determining whether the printing of the overall p-values should be suppressed or not (default: not)
<code>wire</code>	logical determining whether the overall p-values should be plotted in wireframe-style or in cloud-style (default: cloud-style)
<code>round</code>	rounding specification, logical or integer (see details; default: no rounding)

### Details

The overall p-value for an adaptive two-stage test is computed as  $p_1$  if  $p_1 \leq \alpha_1$  or  $p_1 > \alpha_0$ , and as

$$\alpha_1 + \int_{\alpha_1}^{\alpha_0} ce f_{(p_1, p_2)}(x) dx$$

otherwise, where  $ce f_{(p_1, p_2)}$  is the conditional error function (of a specified family) running through the observed pair of p-values  $(p_1, p_2)$ .

There are two alternative ways of specifying the family of conditional error functions (i.e., the test): through a type `typ`, or through an initial conditional error function `fun` and a distortion method `dis`; see [CEF](#) for details.

If `p1` and `p2` are of length 1, a single overall p-value is computed (and not plotted). Otherwise, the behavior of `ovP` depends on `grid`:

- If `grid = FALSE`, overall p-values are computed (and not plotted) for the elementwise pairs of `p1` and `p2`. Here, `p1` and `p2` must be of the same length.
- If `grid = TRUE`, a grid is spanned by `p1` and `p2`, and p-values are computed (and possibly plotted) over this grid. Here, `p1` and `p2` may be of different length. Plotting is triggered by `plt = TRUE`, and the style of the plot (wireframe or cloud) is determined by `wire`. `invisible = TRUE` suppresses the printing of the p-values.

The p-values are rounded to `round` digits after the comma (`round = TRUE` rounds to 1 digit; `round = FALSE` and `round = 0` prevent rounding). The plot always shows unrounded values.

**Value**

A p-value, a vector of p-values or a matrix of p-values.

**Note**

Provide either `typ` or `fun`, not both! If `fun` is provided, then also specify `dis`.

**Author(s)**

Marc Vandemeulebroecke

**References**

Bauer, P., Koehne, K. (1994). Evaluation of experiments with adaptive interim analyses. *Biometrics* 50, 1029-1041.

Brannath, W., Posch, M., Bauer, P. (2002). Recursive combination tests. *J. Amer. Statist. Assoc.* 97, 236-244.

Lehmacher, W., Wassmer, G. (1999). Adaptive sample size calculations in group sequential trials. *Biometrics* 55, 1286-1290.

Vandemeulebroecke, M. (2006). An investigation of two-stage tests. *Statistica Sinica* 16, 933-951.

**See Also**

[adaptTest](#) package description, [CEF](#)

**Examples**

```
## Visualize a Lehmacher Wassmer (1999) test to the overall level 0.1
## and compute and visualize the overall p-value for an observed (p1,p2)=(0.3,0.7)
alpha <- .1
alpha0 <- .5
alpha1 <- .05
plotBounds(a1=alpha1, a0=alpha0, add=FALSE)
plotCEF(typ="l", a2=tsT(typ="l", a=alpha, a0=alpha0, a1=alpha1))
plotCEF(typ="l", p1=.3, p2=.7)
ovP(typ="l", p1=.3, p2=.7, a1=alpha1, a0=alpha0)
# The overall p-value is the area left of alpha1, plus the area below the
# conditional error function running though (0.3,0.7) between alpha1 and alpha0.

## Investigate the p-values of the Lehmacher Wassmer (1999) test from above
ovP(typ="l", a1=alpha1, a0=alpha0, grid=TRUE, p1=1:9/10, round=3)
ovP(typ="l", a1=alpha1, a0=alpha0, grid=TRUE, plt=TRUE, invisible=TRUE, wire=TRUE)
```

---

parconv	<i>Function to convert between two different parameterizations of a family of conditional error functions</i>
---------	---

---

### Description

This function converts between two different parameterizations of a family of conditional error functions: a (more ‘traditional’) parameter  $c$ , and a (more convenient) parameter  $\alpha_2$  specifying the local level of the test after the second stage.

### Usage

```
parconv(typ, a2 = NA, c = NA)
```

### Arguments

typ	type of test: "b" for Bauer and Koehne (1994), "l" for Lehmacher and Wassmer (1999), "v" for Vandemeulebroecke (2006) and "h" for the horizontal conditional error function
a2	$\alpha_2$ , the local level of the test after the second stage (see details)
c	the parameter $c$ (see details)

### Details

Traditionally, a family of conditional error functions is often parameterized by some parameter  $c$  that, in turn, depends on the local level  $\alpha_2$  of the test after the second stage. However, it can be convenient to parameterize the family directly by  $\alpha_2$ . The function `parconv` converts one parameter into the other: provide one, and it returns the other.

Essentially, the relation between the two parameterizations is implemented as:

- $c = \exp(-\chi_{4, \alpha_2}^2/2)$  for Fisher’s combination test (Bauer and Koehne, 1994)
- $c = \Phi^{-1}(1 - \alpha_2)$  for the inverse normal method (Lehmacher and Wassmer, 1999)
- $\alpha_2 = (\Gamma(1 + 1/r))^2/\Gamma(1 + 2/r)$  for Vandemeulebroecke (2006)
- $c = \alpha_2$  for the family of horizontal conditional error functions

### Value

`parconv` returns  $\alpha_2$  corresponding to the supplied  $c$ , or  $c$  corresponding to the supplied  $\alpha_2$ .

### Note

Provide either `a2` or `c`, not both!

$\alpha_2$  is the local level of the test after the second stage, and it equals the integral under the corresponding conditional error function:

$$\alpha_2 = \int_0^1 cef_{\alpha_2}(p_1) dp_1,$$

where  $cef_{\alpha_2}$  is the conditional error function (of a specified family) with parameter  $\alpha_2$ .

Note that in this implementation of adaptive two-stage tests, early stopping bounds are *not* part of the conditional error function. Rather, they are specified separately (see also [tsT](#)).

$\alpha_2$  can take any value in  $[0, 1]$ ;  $c$  can take values in

- $[0, 1]$  for Fisher's combination test (Bauer and Koehne, 1994)
- $(-\infty, \infty)$  for the inverse normal method (Lehmacher and Wassmer, 1999)
- $[0, \infty)$  for Vandemeulebroecke (2006)
- $[0, 1]$  for the family of horizontal conditional error functions

### Author(s)

Marc Vandemeulebroecke

### References

Bauer, P., Koehne, K. (1994). Evaluation of experiments with adaptive interim analyses. *Biometrics* 50, 1029-1041.

Lehmacher, W., Wassmer, G. (1999). Adaptive sample size calculations in group sequential trials. *Biometrics* 55, 1286-1290.

Vandemeulebroecke, M. (2006). An investigation of two-stage tests. *Statistica Sinica* 16, 933-951.

### See Also

[adaptTest](#) package description, [getpar](#), [CEF](#)

### Examples

```
## Obtain the parameter c for Fisher's combination test, using the local level 0.05 for the test after the second
parconv(typ="b", a2=0.05)
```

---

pathCEF

*Function to plot several conditional error functions running through a "path" of given points*

---

### Description

This function plots several conditional error functions of the same family such that each one runs through one of several given points.

### Usage

```
pathCEF(typ = NA, fun = NA, dis = NA, p1 = 1:49/50, p2 = p1,
        x = 0:200/200, plt.pt = FALSE, plt.ptann = FALSE, xlab = NA, ylab = NA, ...)
```

**Arguments**

typ	type of test: "b" for Bauer and Koehne (1994), "l" for Lehmacher and Wassmer (1999), "v" for Vandemeulebroecke (2006) and "h" for the horizontal conditional error function
fun	a conditional error function
dis	a distortion method for a supplied conditional error function (see details): "p1" for power lines, "vt" for vertical translation
p1	a vector (at least of length 2) of p-values $p_1$ of the test after the first stage
p2	a vector (at least of length 2) of p-values $p_2$ of the test after the second stage, defaults to p1; must be of same length as p1
x	vector on which the conditional error functions are plotted (should be relatively dense in [0,1])
plt.pt	logical determining whether the points that the conditional error functions are made to run through should be plotted or not (default: not)
plt.ptann	logical determining whether the points that the conditional error functions are made to run through should be annotated or not (default: not)
xlab	a label for the x axis (default: no label)
ylab	a label for the y axis (default: no label)
...	arguments to be passed on to the underlying plot and points functions (e.g., graphical parameters)

**Details**

It can be instructive to plot not only one conditional error function, but to visualize a whole family. This can easily be done with pathCEF. The function is used in a similar way as plotCEF, but p1 and p2 are now vectors (of the same length, at least of length 2). Conditional error functions are plotted that run through the specified elementwise points (p1 , p2) (which by default lie on the main diagonal).

Internally, pathCEF uses plotCEF to plot the individual conditional error functions; see this latter function for further details.

**Value**

The function pathCEF is invoked for its plotting effect; it returns no meaningful value.

**Note**

Provide either typ or fun, not both! If fun is provided, then also specify dis.

Unlike plotCEF, it is not possible with pathCEF to specify the conditional error functions by the parameter  $\alpha_2$  or the parameter  $c$ .

plt.ptann is not considered if plt.pt = FALSE.

**Author(s)**

Marc Vandemeulebroecke

## References

- Bauer, P., Koehne, K. (1994). Evaluation of experiments with adaptive interim analyses. *Biometrics* 50, 1029-1041.
- Lehmacher, W., Wassmer, G. (1999). Adaptive sample size calculations in group sequential trials. *Biometrics* 55, 1286-1290.
- Vandemeulebroecke, M. (2006). An investigation of two-stage tests. *Statistica Sinica* 16, 933-951.

## See Also

[adaptTest](#) package description, [CEF](#), [plotCEF](#), [tsT](#)

## Examples

```
## Compare the tests by Bauer and Koehne (1994), Lehmacher and Wassmer (1999) and Vandemeulebroecke (2006)
oldmfcol <- par(mfcol=c(1,3))
pathCEF(typ="b", main="BK 94")
pathCEF(typ="l", main="LW 99")
pathCEF(typ="v", main="V 06")
par(oldmfcol)
```

---

plotBounds

*Function to plot the stopping bounds of an adaptive two-stage test*

---

## Description

This function plots the stopping bounds of an adaptive two-stage test.

## Usage

```
plotBounds(a1 = 0, a0 = 1, add = TRUE, xlab = NA, ylab = NA, ...)
```

## Arguments

- |      |  |
|------|--|
| a1   | $\alpha_1$ , the efficacy stopping bound and local level of the test after the first stage (default: no stopping for efficacy) |
| a0   | $\alpha_0$ , the futility stopping bound (default: no stopping for futility)   |
| add  | logical determining whether the bounds should be added to an existing plot (default) or a new plot should be opened            |
| xlab | a label for the x axis (default: no label)   |
| ylab | a label for the y axis (default: no label)   |
| ...  | arguments to be passed on to the underlying lines functions (e.g., graphical parameters)                                       |

**Details**

This function plots the stopping bounds  $\alpha_1$  and  $\alpha_0$  of an adaptive two-stage test, either onto an existing plot or into a new plot.

**Value**

The function `plotBounds` is invoked for its plotting effect; it returns no meaningful value.

**Note**

Note that in this implementation of adaptive two-stage tests, early stopping bounds are *not* part of the conditional error function. Rather, they are specified separately (see also [tsT](#)).

**Author(s)**

Marc Vandemeulebroecke

**See Also**

[adaptTest](#) package description, [plotCEF](#)

**Examples**

```
## Example from Bauer and Koehne (1994): full level after final stage, alpha0 = 0.5
alpha <- 0.1
alpha2 <- 0.1
alpha0 <- 0.5
alpha1 <- tsT(typ="b", a=alpha, a0=alpha0, a2=alpha2)
plotCEF(typ="b", a2=alpha2, add=FALSE)
plotBounds(alpha1, alpha0)
```

---

plotCEF

*Function to plot a conditional error function*

---

**Description**

This function plots a conditional error function.

**Usage**

```
plotCEF(typ = NA, fun = NA, dis = NA, a2 = NA, c = NA, p1 = NA, p2 = p1,
        x = 0:200/200, add = TRUE, xlim = c(0, 1), ylim = c(0, 1),
        plt.pt = TRUE, plt.ptann = TRUE, xlab = NA, ylab = NA, ...)
```



**Arguments**

typ	type of test: "b" for Bauer and Koehne (1994), "l" for Lehmacher and Wassmer (1999), "v" for Vandemeulebroecke (2006) and "h" for the horizontal conditional error function
fun	a conditional error function
dis	a distortion method for a supplied conditional error function (see details): "p1" for power lines, "vt" for vertical translation
a2	$\alpha_2$ , the local level of the test after the second stage
c	the parameter $c$
p1	the p-value $p_1$ of the test after the first stage
p2	the p-value $p_2$ of the test after the second stage, defaults to p1
x	vector on which the conditional error function is plotted (should be relatively dense in [0,1])
add	logical determining whether the bounds should be added to an existing plot (default) or a new plot should be opened
xlim	the x limits of the plot (default: $c(0, 1)$ ; other choices can be used to "zoom in")
ylim	the y limits of the plot (default: $c(0, 1)$ ; other choices can be used to "zoom in")
plt.pt	logical determining whether the point that the conditional error function is made to run through should be plotted or not (default: yes)
plt.ptann	logical determining whether the point that the conditional error function is made to run through should be annotated or not (default: yes)
xlab	a label for the x axis (default: no label)
ylab	a label for the y axis (default: no label)
...	arguments to be passed on to the underlying plot and points functions (e.g., graphical parameters)

**Details**

There are two alternative ways of specifying the desired conditional error function:

- through a type `typ`, and either a parameter (either `a2` or `c`) or a point (`p1`, `p2`), OR
- through an initial conditional error function `fun`, and possibly a distortion method `dis` together with either the parameter `a2` or a point (`p1`, `p2`)

Most people will only need the first of these two ways; the second leads to user-defined non-standard tests.

If `typ` is specified, a parameter `a2` or `c` or the point (`p1`, `p2`) must be provided. In this case, `plotCEF` plots the conditional error function of the chosen type with the given parameter or running through the given point.

If `typ` is not specified, a conditional error function (i.e., a nonincreasing function defined on  $[0,1]$  with values in  $[0,1]$ ) `fun` must be provided. If no distortion method is selected (`dis = NA`), `fun` is

plotted unchanged. Otherwise, the function is distorted using the chosen distortion method, either to match a desired second stage level  $a_2$  or to run through a specified point  $(p_1, p_2)$  (one of which must be provided). Currently, two distortion methods are implemented:

- `dis = "p1"`, Power lines: For an initial function `fun`, define  $f[r](x) = (f(x^r))^{1/r}$ ,  $r > 0$ . Note that if `fun` is a conditional error function of type "b" (Bauer and Koehne, 1994), so is `f[r]`.
- `dis = "p1"`, Vertical translation: The initial function `fun` is shifted vertically.

See [parconv](#) for more information on the two alternative parameterizations by  $\alpha_2$  and  $c$ .

Internally, `plotCEF` uses [CEF](#) to compute the conditional error function that is to be plotted.

### Value

The function `plotCEF` is invoked for its plotting effect; it returns no meaningful value.

### Note

Provide either `typ` or `fun`, not both! If `typ` is provided, then also specify  $a_2$ ,  $c$ , or  $p_1$  (and possibly  $p_2$ ). If `fun` is provided, then also specify `dis` and  $a_2$ , or `dis` and  $p_1$  (and possibly  $p_2$ ), or none of these.

Warning: Values of  $a_2$  close to 0 or 1 may not work for `dis = "p1"`.

`plt.pt` and `plt.ptann` are not considered if  $p_1 = \text{NA}$ . `plt.ptann` is not considered if `plt.pt = FALSE`.

Note that in this implementation of adaptive two-stage tests, early stopping bounds are *not* part of the conditional error function. Rather, they are specified separately (see also [tsT](#)).

### Author(s)

Marc Vandemeulebroecke

### References

Bauer, P., Koehne, K. (1994). Evaluation of experiments with adaptive interim analyses. *Biometrics* 50, 1029-1041.

Lehmacher, W., Wassmer, G. (1999). Adaptive sample size calculations in group sequential trials. *Biometrics* 55, 1286-1290.

Vandemeulebroecke, M. (2006). An investigation of two-stage tests. *Statistica Sinica* 16, 933-951.

### See Also

[adaptTest](#) package description, [parconv](#), [CEF](#), [tsT](#)

## Examples

```
## Plot two conditional error functions of the Lehmacher-Wassmer (1999) type:
## one to the local level alpha2=0.1, and one that runs through (p1,p2)=(0.3,0.7)
plotCEF(typ="l", a2=0.1, add=FALSE)
plotCEF(typ="l", p1=0.3, p2=0.7)

## Plot an explicitly defined conditional error function, and distort it
plotCEF(fun=function(x) ifelse(x<.5,(1-x)^2, (1-x)/2), add=FALSE)
plotCEF(fun=function(x) ifelse(x<.5,(1-x)^2, (1-x)/2), dis="pl", a2=.5)
foo <- CEF(fun=function(x) ifelse(x<.5,(1-x)^2, (1-x)/2), dis="pl", a2=.5)
plotCEF(fun=foo, col="red")
```

tsT

*Function to implement an adaptive two-stage test*

## Description

There are four key quantities for the specification of an adaptive two-stage test: the overall test level  $\alpha$ , stopping bounds  $\alpha_1 \leq \alpha_0$  and the local level  $\alpha_2$  of the test after the second stage. These quantities are interrelated through the overall level condition. The function `tsT` calculates any of these quantities based on the others.

## Usage

```
tsT(typ, a = NA, a0 = NA, a1 = NA, a2 = NA)
```

## Arguments

<code>typ</code>	type of test: "b" for Bauer and Koehne (1994), "l" for Lehmacher and Wassmer (1999), "v" for Vandemeulebroecke (2006) and "h" for the horizontal conditional error function
<code>a</code>	$\alpha$ , the overall test level
<code>a0</code>	$\alpha_0$ , the futility stopping bound
<code>a1</code>	$\alpha_1$ , the efficacy stopping bound and local level of the test after the first stage
<code>a2</code>	$\alpha_2$ , the local level of the test after the second stage

## Details

An adaptive two-stage test can be viewed as a family of decreasing functions  $f[c](p_1)$  in the unit square. Each of these functions is a conditional error function, specifying the type I error conditional on the p-value  $p_1$  of the first stage. For example,  $f[c](p_1) = \min(1, c/p_1)$  corresponds to Fisher's combination test (Bauer and Koehne, 1994). Based on this function family, the test can be put into practice by specifying the desired overall level  $\alpha$ , stopping bounds  $\alpha_1 \leq \alpha_0$  and a parameter  $\alpha_2$ . After computing  $p_1$ , the test stops with or without rejection of the null hypothesis if  $p_1 \leq \alpha_1$  or  $p_1 > \alpha_0$ , respectively. Otherwise, the null hypothesis is rejected if and only if  $p_2 \leq f[c](p_1)$  holds for the p-value  $p_2$  of the second stage, where  $c$  is such that the local level of this latter test is  $\alpha_2$  (e.g.,  $c = c(\alpha_2) = \exp(-\chi_{4, \alpha_2}^2/2)$  for Fisher's combination test).

The four parameters  $\alpha$ ,  $\alpha_0$ ,  $\alpha_1$  and  $\alpha_2$  are interdependent: they must satisfy the level condition

$$\alpha_1 + \int_{\alpha_1}^{\alpha_0} cef_{\alpha_2}(p_1) dp_1 = \alpha,$$

where  $cef_{\alpha_2}$  is the conditional error function (of a specified family) with parameter  $\alpha_2$ . For example, this condition translates to

$$\alpha = \alpha_1 + c(\alpha_2) * (\log(\alpha_0) - \log(\alpha_1))$$

for Fisher's combination test (assuming that  $c(\alpha_2) < \alpha_1$ ; Bauer and Koehne, 1994). The function tsT calculates any of the four parameters based on the remaining ones. Currently, this is implemented for the following four tests: Bauer and Koehne (1994), Lehmacher and Wassmer (1999), Vandemeulebroecke (2006), and the horizontal conditional error function.

### Value

If three of the four quantities  $\alpha$ ,  $\alpha_0$ ,  $\alpha_1$  and  $\alpha_2$  are provided, tsT returns the fourth. If only  $\alpha$  and  $\alpha_0$  are provided, tsT returns  $\alpha_1$  under the condition  $\alpha_1 = \alpha_2$  (the so-called "Pocock-type").

If the choice of arguments is not allowed (e.g.,  $\alpha_0 < \alpha_1$ ) or when a test cannot be constructed with this choice of arguments (e.g.,  $\alpha_0 = 1$  and  $\alpha < \alpha_2$ ), tsT returns NA.

IMPORTANT: When the result is (theoretically) not unique, tsT returns the maximal  $\alpha_1$ , maximal  $\alpha_2$  or minimal  $\alpha_0$ .

In all cases, tsT returns the result for the test specified by typ.

### Note

The argument typ, and either exactly three of  $\alpha$ ,  $\alpha_0$ ,  $\alpha_1$  and  $\alpha_2$ , or only  $\alpha$  and  $\alpha_0$ , must be provided to tsT.

### Author(s)

Marc Vandemeulebroecke

### References

- Bauer, P., Koehne, K. (1994). Evaluation of experiments with adaptive interim analyses. *Biometrics* 50, 1029-1041.
- Lehmacher, W., Wassmer, G. (1999). Adaptive sample size calculations in group sequential trials. *Biometrics* 55, 1286-1290.
- Vandemeulebroecke, M. (2006). An investigation of two-stage tests. *Statistica Sinica* 16, 933-951.
- Vandemeulebroecke, M. (2008). Group sequential and adaptive designs - a review of basic concepts and points of discussion. *Biometrical Journal* 50, 541-557.

### See Also

[adaptTest](#) package description

**Examples**

```
## Example from Bauer and Koehne (1994): full level after final stage, alpha0 = 0.5
alpha <- 0.1
alpha2 <- 0.1
alpha0 <- 0.5
alpha1 <- tsT(typ="b", a=alpha, a0=alpha0, a2=alpha2)
plotCEF(typ="b", a2=alpha2, add=FALSE)
plotBounds(alpha1, alpha0)

## See how similar Lehmacher and Wassmer (1999) and Vandemeulebroecke (2006) are
alpha <- 0.1
alpha1 <- 0.05
alpha0 <- 0.5
alpha2l <- tsT(typ="l", a=alpha, a0=alpha0, a1=alpha1)
alpha2v <- tsT(typ="v", a=alpha, a0=alpha0, a1=alpha1)
plotCEF(typ="l", a2=alpha2l, add=FALSE)
plotCEF(typ="v", a2=alpha2v, col="red")
plotBounds(alpha1, alpha0)

## A remark about numerics
tsT(typ="b", a=0.1, a1=0.05, a0=0.5)
tsT(typ="b", a=0.1, a2=0.104877, a0=0.5)
tsT(typ="b", a=0.1, a2=tsT(typ="b", a=0.1, a1=0.05, a0=0.5), a0=0.5)

## An example of non-uniqueness: the maximal alpha1 is returned; any smaller value would also be valid
alpha <- 0.05
alpha0 <- 1
alpha2 <- 0.05
alpha1 <- tsT(typ="b", a=alpha, a0=alpha0, a2=alpha2)
tsT(typ="b", a0=alpha0, a1=alpha1, a2=alpha2)
tsT(typ="b", a0=alpha0, a1=alpha1/2, a2=alpha2)
```

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