locfdr Vignette
Complete Help Documentation
Including Usage Tips and Simulation Example

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This vignette includes locfdr's complete help documentation, including usage tips, which could not fit in the R help file. It also demonstrates usage of locfdr through an example using the simulated data included in the package.

1 Description and Usage

locfdr computes local false discovery rates, following the definitions and description in the references listed below.

```
locfdr(zz, bre=120, df=7, pct=0, pct0=1/4, nulltype=1, type=0, plot=1,
        mult, mlests, main=" ", sw=0)
```

2 Arguments

2.1 zz

zz is a vector of summary statistics, one for each case under consideration. In a microarray experiment, there would be one element of zz for each gene, perhaps a t-statistic comparing gene expression levels under two different conditions. The calculations assume a large number of cases, say `length(zz)` exceeding 200.

Results may be improved by transforming zz so that its elements are theoretically distributed as $N(0,1)$ under the null hypothesis. For example, when using t-statistics, transform them by `zz = qnorm(pt(t,df))`. Recentering and rescaling zz may be necessary if its central histogram looks very far removed from mean 0 and variance 1.

When using a permutation null distribution with sample zperm, transform the original statistics zorig by `zz = qnorm(ecdf(zperm)(zorig))`. Such transformation is especially important when the theoretical null option is invoked (see nulltype below).

2.2 bre

bre is the number of breaks in the discretization of the z-score axis, or a vector of breakpoints fully describing the discretization. If `length(zz)` is small, such as when the number of cases is less than about 1000, set bre to a number less than the default of 120.

2.3 df

df is the degrees of freedom for fitting the estimated density $f(z)$ (see type below). Larger values of df may be required if $f(z)$ has sharp bends or other irregularities. A warning is issued if the fitted curve does not adequately match the histogram counts. It is a good idea to use the plot option to view the histogram and fitted curve.

2.4 pct

pct is the excluded tail proportions of zz's when fitting f. The default `pct=0` includes the full range of zz's. pct can also be a 2-vector, describing the fitting range.

2.5 pct0

pct0 is the proportion of the zz distribution used in fitting the null density f_0 by central matching. If it is a 2-vector, e.g. `pct0=c(0.25,0.60)`, the range `[pct0[1], pct0[2]]` is used. If a scalar, `[pct0, 1-pct0]` is used.

2.6 nulltype

nulltype is the type of null hypothesis assumed in estimating f_0, for use in the fdr calculations.

- 0 is the theoretical null $N(0, 1)$, which assumes that zz has been scaled to have a $N(0, 1)$ distribution under the null hypothesis.
- 1 (the default) is the empirical null with parameters estimated by maximum likelihood.
- 2 is the empirical null with parameters estimated by central matching (see [3]).
- 3 is a "split normal" version of 2, in which $f_0(z)$ is allowed to have different scales on the two sides of the maximum.

Unless sw is set to 2 or 3, the theoretical, maximum likelihood, and central matching estimates all will be output in the matrix fp0, and both the theoretical and the specified nulltype will be used in the calculations output in mat, but only the specified nulltype is used in the calculation of the output fdr (local fdr estimates for every case).

2.7 type

type is the type of fitting used for f.

- 0 is a natural spline.
- 1 is a polynomial.

In either case, f is fit with degrees of freedom df (so total degrees of freedom including the intercept is df + 1).

2.8 plot

plot specifies the plots desired.

- 0 gives no plots.
- 1 (the default) gives a single plot showing the histogram of zz and fitted mixture density f (green solid curve) and null subdensity $p_0 f_0$ (blue dashed curve). Colored histogram bars indicate estimated non-null counts. Yellow triangles on the zz-axis indicate threshold values for $fdr(z) \leq 0.2$, if such cases exist.
- 2 also gives plot of fdr, and the right and left tail area Fdr curves.
- 3 gives instead the f_1 cdf of the estimated fdr curve, as in Figure 4 of [3].
- 4 gives all three plots.

We recommend setting plot to 1 or greater, to check the fit of $p_0 f_0$ to the histogram. (If the fit is poor, try a different nulltype or a different value of the mlests argument.)

2.9 mult

mult is an optional scalar multiple (or vector of multiples) of the sample size for calculation of the corresponding hypothetical Efdr value(s).

2.10 mlests

mlests is an optional vector of initial values for (δ_0, σ_0) in the maximum likelihood iteration. In addition, these are used to determine the interval over which the maximum likelihood estimation is performed. If, for example, zz was transformed quantile-wise from F statistics, most of zz's elements corresponding to interesting features will be positive. To shift the interval away from such elements, specify a negative initial value for δ_0, the first element of mlests. If the default results in a poor fit of $p_0 f_0$ to the histogram in the first plot, try setting mlests to move the estimates toward the values suggested by the histogram.

2.11 main

main is the main heading for the histogram plot.

2.12 sw

sw determines the type of output desired.

- 2 gives a list consisting of the last 5 values listed under Value below.
- 3 gives the square matrix of dimension bre-1 representing the influence function of $\log(fdr)$. The (i, j) entry of the matrix is the derivative of $\log(fdr)$ at the midpoint of bin i with respect to the count value of bin j.
- Any other value of sw returns a list consisting of the first 7 (8 if mult is supplied) values listed below.

3 Value

3.1 fdr

fdr is the estimated local false discovery rate for each case, using the selected type and nulltype.

3.2 fp0

fp0 is a matrix containing the estimated parameters delta (mean of f_0), sigma (standard deviation of f_0), and p0 (proportion of tests that are null), along with their estimated standard errors. If `nulltype<3`, fp0 is a 5×3 matrix, with columns representing delta, sigma, and p0 and rows representing nulltypes and estimate vs. standard error. If `nulltype==3`, the second column corresponds to the estimate of sigma for the left side of f_0, and a fourth column corresponds to the sigma estimate for the right.

3.3 Efdr

Efdr is the expected local false discovery rate for the non-null cases, a measure of the experiment's power as described in Section 3 of [3]. Large values of Efdr, say `Efdr>0.4`, indicate low power. Overall Efdr and right and left values are given, both for the specified nulltype and for nulltype 0. (If `nulltype==0`, values are given for nulltypes 1 and 0.)

3.4 cdf1

cdf1 is a 99×2 matrix giving the estimated cdf of fdr under the non-null distribution f_1. Large values of the cdf for small fdr values indicate good power. See Section 3 of [3]. Set plot to 3 or 4 to see the plot of cdf1.

3.5 mat

mat is a $(\text{bre} - 1) \times 11$ matrix, convenient for comparisons and plotting. Each row corresponds to a bin of the zz histogram, and the columns contain the following:

1. x: the midpoint of the bin.
2. fdr: the estimated local false discovery rate at x, calculated based on the specified type and nulltype (using `nulltype=1` if `nulltype=0` is specified).
3. Fdrleft: the left tail false discovery rate at x.
4. Fdrright: the right tail false discovery rate at x.
5. f: the mixture density estimate at x, calculated based on the specified type, df, and pct, scaled to sum to `length(zz)`.
6. f0: the null density estimate at x, calculated based on the specified nulltype (using `nulltype=1` if `nulltype=0` is specified) and pct0 and scaled to sum to `length(zz)`.
7. f0theo: the null density estimate at x, calculated using the theoretical null $N(0, 1)$ and scaled to sum to `length(zz)`.
8. fdrtheo: the local false discovery rate at x, calculated based on the specified type and `nulltype=0`.

9. counts: the number of elements of zz in the bin.

10. lfdrse: the delta-method estimate of the standard error of the log of the local false discovery rate for the specified nulltype. This estimate assumes independence of the zz values and should usually be considered as a lower bound on the true standard errors. See [3].

11. p1f1: the estimated subdensity of the zz elements that come from non-null tests. p1f1 is scaled to sum to approximately (1-p0) times `length(z)`, i.e. the estimated number of non-null tests.

3.6 z.2

z.2 is the interval along the zz-axis outside of which $fdr(z) < 0.2$, the locations of the yellow triangles in the histogram plot. If no elements of zz on the left or right satisfy the criterion, the corresponding element of z.2 is NA, and the corresponding triangle does not appear.

3.7 call

call is the function call.

3.8 mult

If the argument mult was supplied, the value mult is the vector of the ratios of the hypothetical Efdr for the supplied multiples of the sample size to the Efdr for the actual sample size.

3.9 pds

pds is the vector of estimates of p0, delta, and sigma.

3.10 x

x is the vector of bin midpoints.

3.11 f

f is the vector of estimated values of $f(x)$ at the bin midpoints.

3.12 pds.

pds. is the derivative of the estimates of p0, delta, and sigma with respect to the bin counts.

3.13 stdev

stdev is the vector of delta-method estimates of the standard deviations of the p0, delta, and sigma estimates.

4 Simulation Example

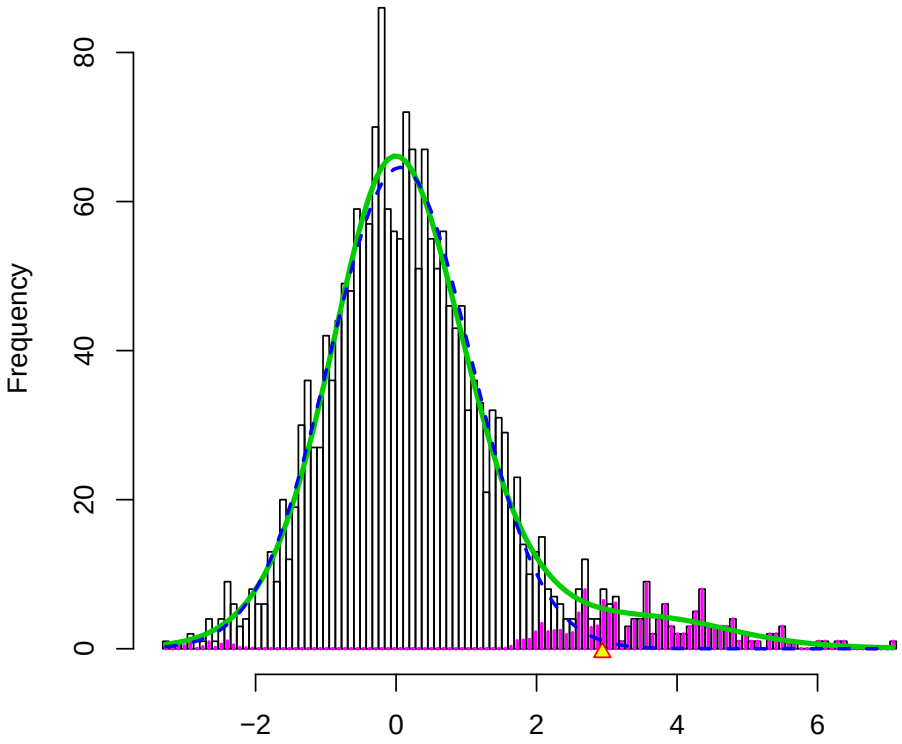
This simulation example involves 2000 "genes", each of which has yielded a test statistic z_i, with $z_i \sim N(\mu_i, 1)$, independently for $i = 1, 2, \ldots, 2000$.

Here μ_i is the "true score" of gene i, which we observe only noisily. 1800 (90%) of the μ_i values are zero; the remaining 200 (10%) are from a $N(3,1)$ distribution. The data are contained in the dataset `lfdrsim`, where the z_i are the column `zex`.

```
> library(locfdr)
> data(lfdrsim)
> zex <- lfdrsim[, 2]
```

If we are confident that the null z_i's are distributed as $N(0,1)$, we run `locfdr` with `nulltype=0`. Otherwise, we use the default `nulltype=1`, which uses empirical estimates of the null density parameters.

```
> w <- locfdr(zex)
```



In the figure, the green solid line is the spline-based estimate of the mixture density f. The blue dashed line is the null subdensity $p_0 f_0$, estimated by default by maximum likelihood (nulltype=1). Whichever nulltype is specified, `locfdr` returns a matrix `fp0` containing parameters of all three nulltypes and corresponding estimates of the proportion p_0 of cases that are null, along with standard errors. In this example, the null distribution is $N(0,1)$, and both the MLE and central matching estimates come close to this.

```
> w$fp0
```

```
           delta      sigma         p0
thest 0.00000000 1.00000000 0.93488483
theSD 0.00000000 0.00000000 0.01638130
mlest 0.05913609 1.00598987 0.92793692
mleSD 0.02853215 0.02970003 0.01121705
cmest 0.01137651 0.96576676 0.90831871
cmeSD 0.04211370 0.03380724 0.01381380
```

The output mat contains estimates of the local false discovery rates and other functions for each bin midpoint x.

```
> w$mat[1:5,]
```

```
             x       fdr   Fdrleft  Fdrright         f        f0    f0theo
[1,] -3.277130 0.4476285 0.4476285 0.9279369 0.5902186 0.2847162 0.3260307
[2,] -3.189391 0.4938541 0.4728980 0.9280787 0.7117024 0.3787727 0.4329734
[3,] -3.101651 0.5408582 0.4998939 0.9282333 0.8579789 0.5000824 0.5705853
[4,] -3.013912 0.5881378 0.5284586 0.9283997 1.0338087 0.6552407 0.7461681
[5,] -2.926172 0.6351747 0.5583867 0.9285759 1.2447492 0.8520333 0.9682989
       fdrtheo counts    lfdrse      p1f1
[1,] 0.5164208      1 0.5319658 0.3260199
[2,] 0.5687493      0 0.4945655 0.3602252
[3,] 0.6217304      1 0.4576673 0.3939340
[4,] 0.6747682      1 0.4214070 0.4257867
[5,] 0.7272533      2 0.3859218 0.4541160
```

The output fdr contains the local false discovery rate estimate for each z_i. One might use this vector to create a list of Interesting cases.

```
> which(w$fdr<.2)
```

```
  [1]    1    2    3    4    5    6    7    8    9   10   11   12   13   14   15
 [16]   16   17   18   19   20   21   23   24   25   26   27   28   29   30   31
 [31]   32   33   35   37   38   39   41   42   43   45   46   47   48   49   51
 [46]   52   54   55   56   57   58   59   60   61   62   63   66   67   69   70
 [61]   71   73   74   75   77   78   79   83   85   88   89   90   92   94   95
 [76]   96   98  100  103  104  106  107  109  112  113  118  121  122  125  127
 [91]  128  132  133  135  136  137  141  150  151  160  161  162  165  166  168
[106]  170  324 1508 1732 1898
```

Here 0.2 is a rule-of-thumb cut-off. In the simulated data, the first 200 cases have nonzero μ_i. So we can find the observed tail false discovery proportion.

```
> sum(which(w$fdr<.2)>200)/sum(w$fdr<.2)
```

```
[1] 0.03636364
```

The estimated tail FDR can be found from the `mat` output.

```
> w$mat[which(w$mat[,"fdr"]<.2)[1],"Fdrright"]
```

```
  Fdrright
0.03863531
```

The tail FDR is the mean local fdr over the entire tail and is therefore smaller than the local fdr cutoff.

References

[1] Efron, B. (2004) "Large-scale simultaneous hypothesis testing: the choice of a null hypothesis," *JASA*, **99**, pp. 96–104.

[2] Efron, B. (2005) "Local False Discovery Rates,"
`http://www-stat.stanford.edu/~brad/papers/False.pdf`

[3] Efron, B. (2006) "Size, Power, and False Discovery Rates,"
`http://www-stat.stanford.edu/~brad/papers/Size.pdf`

[4] Efron, B. (2006) "Correlation and Large-Scale Simultaneous Significance Testing," *JASA*, **102**, pp. 93–103.