

# 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 E $fdr$  value(s).

## 2.10 mlests

mlests is an optional vector of initial values for  $(\delta_0, \sigma_0)$  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  $\delta_0$ , 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  $5 \times 3$  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  $99 \times 2$  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. `p1fl`: the estimated subdensity of the `zz` elements that come from non-null tests. `p1fl` is scaled to sum to approximately  $(1-p_0)$  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 Efrd for the supplied multiples of the sample size to the Efrd 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

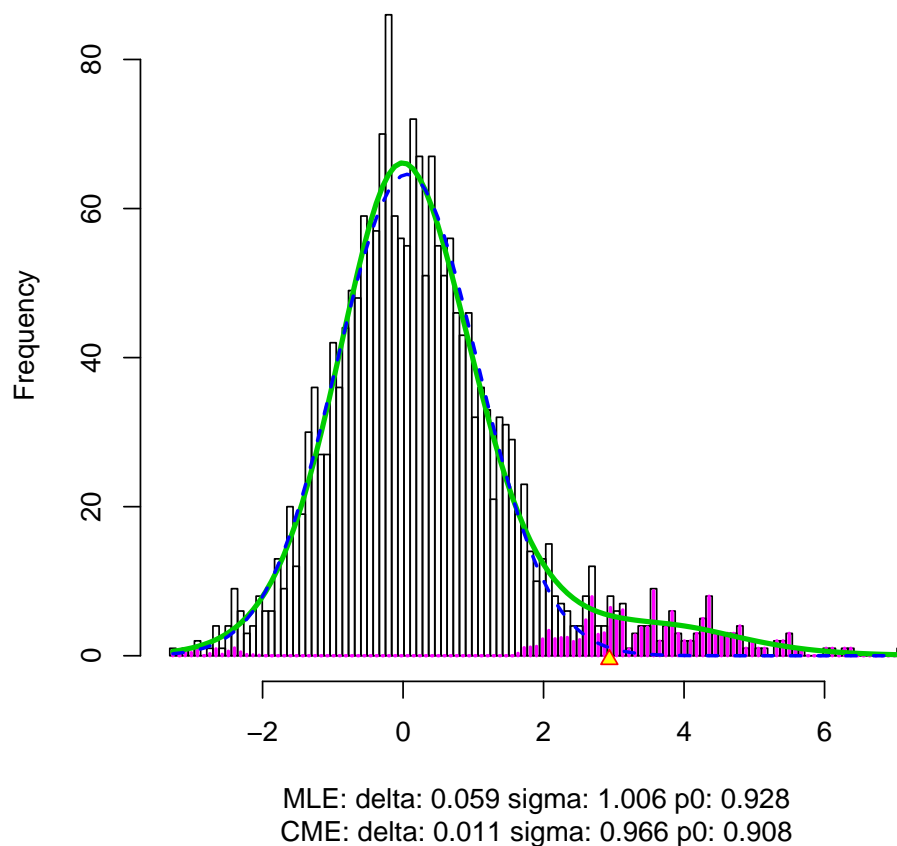
This simulation example involves 2000 “genes”, each of which has yielded a test statistic  $z_i$ , with  $z_i \sim N(\mu_i, 1)$ , independently for  $i = 1, 2, \dots, 2000$ .

Here  $\mu_i$  is the “true score” of gene  $i$ , which we observe only noisily. 1800 (90%) of the  $\mu_i$  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 < 0.2)

 [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  $\mu_i$ . So we can find the observed tail false discovery proportion.

```

> sum(which(w$fdr < 0.2) > 200)/sum(w$fdr < 0.2)

[1] 0.03636364

```

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

```

> w$mat[which(w$mat[, "fdr"] < 0.2)[1], "Fdrright"]

[1] 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.