

Workflow for analysis of raw data

Functions with their main arguments (see help pages for a complete description)

Step 1: import, check and pretreatment

```
microarraydata(file,
    norm.method = c("cyclicloess", "quantile", "scale", "none"))
RNAseqdata(file, transfo.method = c("rlog", "vst"))
continuousomicdata(file)
continuousanchoringdata(file)
```

Step 2: selection of significantly responsive items

```
itemselect(omicdata,
    select.method = c("quadratic", "linear", "ANOVA"), FDR)
```

Step 3: dose-response modelling for responsive items

drcfit(itemselect, information.criterion = c("AICc", "BIC", "AIC"))

Step 4: Computation of benchmark doses

bmdcalc(f, z = 1, x = 10, minBMD)

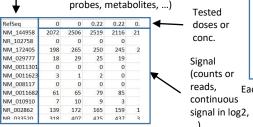
Step 5: Bootstrap to compute BMD confidence intervals

bmdboot(r, niter = 1000, conf.level = 0.95)

Format of data in input

Data can be imported from a .txt file (e.g. "mydata.txt") containing one row per item after a first row giving the doses or concentrations for each sample , with the first column corresponding to the identifier of each item. Alternatively an R object of class data.frame can be directly given in input, corresponding to the output of read.table(file, header = FALSE) on a file described as above.

Typical script for the workflow Identifiers of items (contigs, probes, metabolites, ...) O <- RNAseq(datafilename)



o <- RNAseq(datafilename) s <- itemselect(o) f <- drcfit(s) r <- bmdcalc(f) b <- bmdboot(r)</pre>

b\$res

Each function of this workflow returns a S3 class object that can printed and plotted.

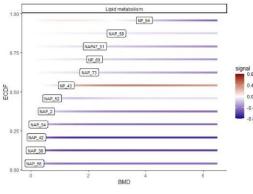
Other functions to help the interpretation of results within a multi-omics approach using a unique biological annotation

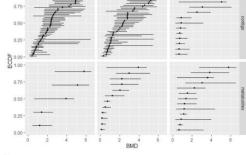
Functions taking as a first argument extendedres, a dataframe with the main workflow results (optionally gathering results obtained at different modelcular levels) extended with additional columns coding for example for the biological annotation of items (and for the molecular level if needed). Some lines of the workflow results can be replicated for items having more than one annotation (see help pages for a complete description of argument of those functions)

BMD plot

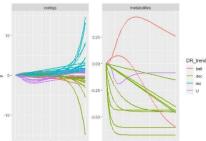
bmdplot(extendedres, add.CI, facetby, facetby2, shapeby, colorby, add.label, BMD log transfo)

BMD plot with gradient





bmdplotwithgradient(extendedres,
xmin, xmax, facetby, facetby2,
shapeby, add.label,
BMD_log_transfo)



Dose-response curves plot

curvesplot(extendedres, xmin, xmax, facetby, facetby2, colorby, dose_log_transfo = FALSE)

Trend plot

trendplot (extendedres, group, facetby)

Translation

Signal branslation

of other amme acids

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bell sensitivitypl

dec extendedres,

Sensitivity plot

Sensitivityplot(
extendedres, group,
colorby, BMDsummary =
c("first.quartile",
"median",
"median.and.IQR"),
BMD_log_transfo)

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