# Package ‘nempi’

May 22, 2024

**Type**  Package  

**Title**  Inferring unobserved perturbations from gene expression data  

**Version**  1.12.0  

**Depends**  R (>= 4.1), mnem  

**Description**  Takes as input an incomplete perturbation profile and differential gene expression in log odds and infers unobserved perturbations and augments observed ones. The inference is done by iteratively inferring a network from the perturbations and inferring perturbations from the network. The network inference is done by Nested Effects Models.  

**License**  GPL-3  

**Encoding**  UTF-8  

**LazyData**  true  

**biocViews**  Software, GeneExpression, DifferentialExpression, DifferentialMethylation, GeneSignaling, Pathways, Network, Classification, NeuralNetwork, NetworkInference, ATACSeq, DNASEq, RNASeq, PooledScreens, CRISPR, SingleCell, SystemsBiology  

**Imports**  e1071, nnet, randomForest, naturalsort, graphics, stats, utils, matrixStats, epiNEM  

**VignetteBuilder**  knitr  

**Suggests**  knitr, BiocGenerics, rmarkdown, RUnit, BiocStyle  

**BugReports**  https://github.com/cbg-ethz/nempi/issues  

**URL**  https://github.com/cbg-ethz/nempi/  

**RoxygenNote**  7.1.1  

**git_url**  https://git.bioconductor.org/packages/nempi  

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Description

Builds and uses different classifiers to infer perturbation profiles

Usage

classpi(
  D,
  unknown = "",
  full = TRUE,
  method = "svm",
  size = NULL,
  MaxNWts = 10000,
  ...
)

Arguments

D 
  either a binary effects matrix or log odds matrix as for Nested Effects Models (see package 'nem')

unknown 
  colname of samples without mutation data, E.g. ""

full 
  if FALSE, does not change the known profiles

method 
  either one of svm, nn, rf

size 
  parameter for neural network (see package 'nnet')

MaxNWts 
  parameters for neural network (see package 'nnet')

... 
  additional parameters for mnem::nem
Value

plot

Author(s)

Martin Pirkl

Examples

D <- matrix(rnorm(1000*100), 1000, 100)
colnames(D) <- sample(seq_len(5), 100, replace = TRUE)
Gamma <- matrix(sample(c(0,1), 5*100, replace = TRUE, p = c(0.9, 0.1)), 5,
100)
Gamma <- apply(Gamma, 2, function(x) return(x/sum(x)))
Gamma[is.na(Gamma)] <- 0
rownames(Gamma) <- seq_len(5)
result <- classpi(D)

nempi

Main function for NEM based perturbation imputation.

Description

Infers perturbations profiles based on a sparse perturbation matrix and differential gene expression as log odds

Usage

nempi(
D,
unknown = "",
Gamma = NULL,
type = "null",
full = TRUE,
verbose = FALSE,
logtype = 2,
null = TRUE,
soft = TRUE,
combi = 1,
converged = 0.1,
complete = TRUE,
mw = NULL,
max_iter = 100,
keepphi = TRUE,
start = NULL,
phi = NULL,
...
Arguments

- **D**: either a binary effects matrix or log odds matrix as for Nested Effects Models (see package 'nem')
- **unknown**: colname of samples without mutation data, e.g. ""
- **Gamma**: matrix with expectations of perturbations, e.g. if you have a binary mutation matrix, just normalize the columns to have sum 1
- **type**: "null": does not use the unknown samples for inference at the start, "random" uses them in a random fashion (not recommended)
- **full**: if FALSE, does not change the known profiles
- **verbose**: if TRUE gives more output during inference
- **logtype**: log type for the log odds
- **null**: if FALSE does not use a NULL node for uninformative samples
- **soft**: if FALSE discretizes Gamma during the inference
- **combi**: if combi > 1, uses a more complex algorithm to infer combinatorial perturbations (experimental)
- **converged**: the absolute difference of log likelihood till convergence
- **complete**: if TRUE uses the complete-data log likelihood (recommended for many E-genes)
- **mw**: if NULL infers mixture weights, otherwise keeps them fixed
- **max_iter**: maximum iterations of the EM algorithm
- **keepphi**: if TRUE, uses the previous phi for the next inference, if FALSE always starts with start network (and empty and full)
- **start**: starting network as adjacency matrix
- **phi**: if not NULL uses only this phi and does not infer a new one
- **...**: additional parameters for the nem function (see package mnem, function nem or mnem::nem)

Value

nempi object

Author(s)

Martin Pirkl

Examples

```r
D <- matrix(rnorm(1000*100), 1000, 100)
oclumnames(D) <- sample(seq_len(5), 100, replace = TRUE)
Gamma <- matrix(sample(c(0,1), 5*100, replace = TRUE, p = c(0.9, 0.1)), 5, 100)
Gamma[is.na(Gamma)] <- 0
rownames(Gamma) <- seq_len(5)
result <- nempi(D, Gamma = Gamma)
```
nempibs

**Bootstrapping function**

**Description**

Bootstrap algorithm to get a more stable result.

**Usage**

nempibs(D, bsruns = 100, bssize = 0.5, replace = TRUE, ...)

**Arguments**

- **D**: either a binary effects matrix or log odds matrix as
- **bsruns**: number of bootstraps
- **bssize**: number of E-genes for each bootstrap
- **replace**: if TRUE, actual bootstrap, if False sub-sampling
- **...**: additional parameters for the function nempi

**Value**

list with aggregate Gamma and aggregate causal network phi

**Author(s)**

Martin Pirkl

**Examples**

D <- matrix(rnorm(1000*100), 1000, 100)
colnames(D) <- sample(seq_len(5), 100, replace = TRUE)
Gamma <- matrix(sample(c(0,1), 5*100, replace = TRUE, p = c(0.9, 0.1)), 5, 100)
Gamma[is.na(Gamma)] <- 0
rownames(Gamma) <- seq_len(5)
result <- nempibs(D, bsruns = 3, Gamma = Gamma)
Description

Compares the ground truth of a perturbation profile with the inferred profile

Usage

\[
pifit(x, y, D, unknown = \text{""}, \text{balanced} = \text{FALSE}, \text{propagate} = \text{TRUE}, \text{knowns} = \text{NULL})
\]

Arguments

- \(x\) object of class nempi
- \(y\) object of class mnemsim
- \(D\) data matrix
- \(unknown\) label for the unlabelled samples
- \(balanced\) if TRUE, computes balanced accuracy
- \(propagate\) if TRUE, propagates the perturbation through the network
- \(knowns\) subset of P-genes that are known to be perturbed (the other are neglected)

Value

list of different accuracy measures: true/false positives/negatives, correlation, area under the precision recall curve, (balanced) accuracy

Author(s)

Martin Pirkl

Examples

```r
library(mnem)
seed <- 42
Pgenes <- 10
Egenes <- 10
samples <- 100
uninform <- floor((Pgenes*Egenes)*0.1)
Nems <- mw <- 1
noise <- 1
multi <- c(0.2, 0.1)
set.seed(seed)
simmini <- simData(Sgenes = Pgenes, Egenes = Egenes,
                   Nems = Nems, mw = mw, nCells = samples,
                   uninform = uninform, multi = multi,
                   badCells = floor(samples*0.1))
data <- simmini$data
```
ones <- which(data == 1)
zeros <- which(data == 0)
data[ones] <- rnorm(length(ones), 1, noise)
data[zeros] <- rnorm(length(zeros), -1, noise)
lost <- sample(1:ncol(data), floor(ncol(data)*0.5))
colnames(data)[lost] <- ""
res <- nempi(data)
fit <- pifit(res, simmini, data)

plot.nempi

Plotting nempi

Description
Plot function for an object of class 'nempi'.

Usage
## S3 method for class 'nempi'
plot(x, barlist = list(), heatlist = list(), ...)

Arguments
x object of class 'nempi'
barlist additional arguments for function 'barplot' from package 'graphics'
heatlist additional arguments for function 'HeatmapOP' from package 'epiNEM'
... additional arguments for function 'plotDnf' from package 'mnem'

Value
Plots of the optimal network phi and perturbation matrix.

Author(s)
Martin Pirkl

Examples
D <- matrix(rnorm(1000*100), 1000, 100)
colnames(D) <- sample(seq_len(5), 100, replace = TRUE)
result <- nempi(D)
plot(result)
plotConvergence.nempi  

Plot convergence of EM

Description

Produces different convergence plots based on a nempi object

Usage

## S3 method for class 'nempi'
plotConvergence(x, type = "b", ...)

Arguments

x  
nempi object

type  
see ?plot.default

...  
additional parameters for plot

Value

plot

Author(s)

Martin Pirkl

Examples

D <- matrix(rnorm(1000*100), 1000, 100)
colnames(D) <- sample(seq_len(5), 100, replace = TRUE)
Gamma <- matrix(sample(c(0,1), 5*100, replace = TRUE, p = c(0.9, 0.1)), 5, 100)
Gamma[is.na(Gamma)] <- 0
rownames(Gamma) <- seq_len(5)
result <- nempi(D, Gamma = Gamma)
par(mfrow=c(2,3))
plotConvergence(result)
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