

# Package ‘nempi’

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**Type** Package

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

**Version** 1.16.0

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

**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, DNaseSeq, 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

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|         |                       |
|---------|-----------------------|
| classpi | <i>Classification</i> |
|---------|-----------------------|

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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 PirkI

**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 loglikelihood (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 Pirkel

**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 <- nempi(D, Gamma = Gamma)
```

---

|         |                               |
|---------|-------------------------------|
| nempibs | <i>Bootstrapping function</i> |
|---------|-------------------------------|

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**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 PirkI

**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 <- nempibs(D, bsruns = 3, Gamma = Gamma)
```

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pifit

*Accuracy computation*


---

### Description

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

### Usage

```
pifit(x, y, D, unknown = "", balanced = FALSE, propagate = TRUE, knowns = 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 PirkI

### Examples

```
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)

```

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plot.nempi

*Plotting nempi*


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## 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 Pirkel

## Examples

```

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

```

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plotConvergence.nempi *Plot convergence of EM*

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**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 Pirkel

**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 <- nempi(D, Gamma = Gamma)
par(mfrow=c(2,3))
plotConvergence(result)
```

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