

# Package ‘ASpediaFI’

March 29, 2021

**Type** Package

**Title** ASpedia-FI: Functional Interaction Analysis of Alternative Splicing Events

**Version** 1.4.0

**Date** 2020-04-01

**Author** Doyeong Yu, Kyubin Lee, Daejin Hyung, Soo Young Cho, Charny Park

**Maintainer** Doyeong Yu <parklab.bi@gmail.com>

**Description** This package provides functionalities for a systematic and integrative analysis of alternative splicing events and their functional interactions.

**License** GPL-3

**Encoding** UTF-8

**biocViews** AlternativeSplicing, Annotation, Coverage, GeneExpression, GeneSetEnrichment, GraphAndNetwork, KEGG, Network, NetworkInference, Pathways, Reactome, Transcription, Sequencing, Visualization

**LazyData** false

**RoxygenNote** 6.1.1

**Depends** R (>= 3.6.0), SummarizedExperiment, ROCR

**Imports** BiocParallel, GenomicAlignments, GenomicFeatures, GenomicRanges, IRanges, IVAS, Rsamtools, biomaRt, limma, S4Vectors, stats, DRaWR, GenomeInfoDb, Gviz, Matrix, dplyr, fgsea, reshape2, igraph, graphics, e1071, methods, rtracklayer, scales, grid, ggplot2, mGSZ, utils

**Suggests** knitr

**VignetteBuilder** knitr

**BugReports** <https://github.com/nachoryu/ASpediaFI>

**git\_url** <https://git.bioconductor.org/packages/ASpediaFI>

**git\_branch** RELEASE\_3\_12

**git\_last\_commit** d59c4a0

**git\_last\_commit\_date** 2020-10-27

**Date/Publication** 2021-03-29

## R topics documented:

|                  |    |
|------------------|----|
| analyzeFI        | 2  |
| annotateASevents | 3  |
| ASpediaFI-class  | 4  |
| exportNetwork    | 5  |
| GSE114922.fpkm   | 6  |
| GSE114922.psi    | 6  |
| quantifyPSI      | 7  |
| samples          | 8  |
| visualize        | 10 |

|              |           |
|--------------|-----------|
| <b>Index</b> | <b>11</b> |
|--------------|-----------|

---

|           |   |
|-----------|---|
| analyzeFI | <i>Functional interaction analysis of AS events</i> |
|-----------|---|

---

### Description

Analyze functional interactions of AS events using Discriminative Random Walk with Restart (DRaWR). It runs a DRaWR on a heterogeneous network containing genes, AS events, and pathways. It then performs GSEA on gene sets related to query genes.

### Usage

```
analyzeFI(object, query, expr, ppi = NULL, pathways = NULL,
          restart = 0.7, num.folds = 5, num.feats = 100, low.expr = 1,
          low.var = NULL, prop.na = 0.05, prop.extreme = 1,
          cor.threshold = 0.3)
```

### Arguments

|           |   |
|-----------|---|
| object    | Object of class ASpediaFI   |
| query     | a character vector or a data frame containing query genes   |
| expr      | a SummarizedExperiment object or matrix containing gene expression profiles (FPKM)  |
| ppi       | an igraph object containing known interactions between genes. If NULL, an igraph object containing human gene-gene interactions will be used. |
| pathways  | a GMT file or a named list of pathway gene sets. If NULL, a combined list of HALLMARK, KEGG, and REACTOME pathway gene sets will be used.     |
| restart   | a restart probability   |
| num.folds | the number of folds for cross-validation  |
| num.feats | the number of feature nodes to be retained in the final subnetwork  |
| low.expr  | Genes with mean expression below low.expr are excluded. AS events for corresponding genes are also excluded.                                  |
| low.var   | AS events with variance below low.var are excluded. If NULL, top 10,000 variable events are used for analysis.                                |
| prop.na   | AS events with the higher proportion of missing values than prop.na are excluded.   |

- prop.extreme AS events with the higher proportion of extreme values (0 or 1) than prop.extreme are excluded.
- cor.threshold a pair of AS event and gene with Spearman's correlation greater than cor.threshold are connected in a heterogeneous network.

**Value**

ASpediaFI object with results of functional interaction analysis

**References**

Blatti, C. et al. (2016). Characterizing gene sets using discriminative random walks with restart on heterogeneous biological networks. *Bioinformatics*, 32.

**Examples**

```
library(limma)
data(GSE114922.fpkm)
data(GSE114922.psi)
design <- cbind(WT = 1, MvsW = colData(GSE114922.psi)$condition == 'MUT')
fit <- lmFit(log2(GSE114922.fpkm + 1), design = design)
fit <- eBayes(fit, trend = TRUE)
tt <- topTable(fit, number = Inf, coef = 'MvsW')
query <- rownames(tt[tt$logFC > 1 & tt$P.Value < 0.1, ])
head(query)
## Not run:
GSE114922.ASpediaFI <- analyzeFI(
  GSE114922.ASpediaFI, query,
  GSE114922.fpkm
)

## End(Not run)
```

---

annotateASevents      *AS event annotation*

---

**Description**

Detect and annotate AS events from GTF. This function borrows code from the IVAS package.

**Usage**

```
annotateASevents(object, gtf.file, num.cores = 1)
```

**Arguments**

- object            Object of class ASpediaFI
- gtf.file          an input GTF file
- num.cores        the number of cores for parallel processing

**Value**

ASpediaFI object with a list of AS event annotations

## References

Han, S. et al. (2017). Genome wide discovery of genetic variants affecting alternative splicing patterns in human using bioinformatics method. *Genes & Genomics*, 39.

## Examples

```
fi <- new('ASpediaFI')
gtf <- system.file('extdata/GRCh38.subset.gtf', package = 'ASpediaFI')
fi <- annotateASevents(fi, gtf.file = gtf, num.cores = 1)
sapply(events(fi), length)
head(events(fi)$SE)
```

---

|                 |                        |
|-----------------|------------------------|
| ASpediaFI-class | <i>ASpediaFI class</i> |
|-----------------|------------------------|

---

## Description

ASpediaFI class is a wrapper of ASpediaFI functionalities and a container of inputs and outputs.

## Usage

```
ASpediaFI(sample.names, bam.files, conditions)
```

## Arguments

|              |  |
|--------------|--|
| sample.names | a character vector of sample names (or IDs)          |
| bam.files    | a character vector of paths to RNA-Seq BAM files     |
| conditions   | a vector of sample conditions (e.g. mutation status) |

## Value

ASpediaFI object

## Slots

**samples:** a data frame containing information about samples. The first three columns should be names, BAM file paths, and conditions.

**events:** a list of AS events extracted from a GTF file.

**gtf:** a GRanges object containing genomic features extracted from a GTF file.

**psi:** a SummarizedExperiment object containing AS event quantification

**network:** an igraph object containing a query-specific subnetwork as a result of DRaWR.

**gene.table, as.table, pathway.table:** data frames containing gene nodes, AS event nodes, and pathway nodes.

## Accessors

In the following, 'x' represents a ASpediaFI object:

`samples(x)`, `samples(x) <-value`: get or set sample information. value must be a data frame containing sample information.

`events(x)`, `events(x) <-value`: get or set AS event annotations. value must be a list of annotations.

`gtf(x)`, `gtf(x) <-value`: get or set a GRanges object containing GTF. value must be a GRanges object.

`psi(x)`, `psi(x) <-value`: get or set PSI values. value must be a SummarizedExperiment object.

`network(x)`, `network(x) <-value`: get or set final subnetwork. value must be an igraph object.

`gene.table(x)`, `gene.table(x) <-value`: get or set gene node tables. value must be a data frame containing information about gene nodes.

`as.table(x)`, `as.table(x) <-value`: get or set AS node tables. value must be a data frame containing information about AS nodes.

`pathway.table(x)`, `pathway.table(x) <-value`: get or set pathway node tables. value must be a data frame containing information about pathway nodes.

## Examples

```
bamWT <- system.file('extdata/GSM3167290.subset.bam', package = 'ASpediaFI')
GSE114922.ASpediaFI <- ASpediaFI(
  sample.names = 'GSM3167290',
  bam.files = bamWT, conditions = 'WT'
)
```

---

exportNetwork

*Export network to GML format*

---

## Description

Export a subnetwork pertaining to the given pathway to GML format which can be used in Cytoscape. If no pathway is given, the entire final subnetwork is exported.

## Usage

```
exportNetwork(object, node = NULL, file)
```

## Arguments

|                     |  |
|---------------------|--|
| <code>object</code> | Object of class ASpediaFI  |
| <code>node</code>   | the name of pathway. If NULL, the entire subnetwork is exported. |
| <code>file</code>   | the file name to export the network                              |

## Value

a GML file containing a subnetwork

**Examples**

```
library(igraph)
fi <- new('ASpediaFI', network = make_empty_graph(n = 0))
exportNetwork(fi, node = NULL, file = 'empty.gml')
```

---

`GSE114922.fpkm`*Example gene expression dataset*

---

**Description**

A matrix containing gene expression values. We downloaded RNA-Seq reads of 82 MDS patients from GEO database (GSE114922), aligned with STAR, and obtained FPKM values using RSEM.

**Usage**`GSE114922.fpkm`**Format**

An object of class `matrix` with 6275 rows and 40 columns.

**References**

Pellagatti, A. et al. (2018). Impact of spliceosome mutations on RNA splicing in myelodysplasia: dysregulated genes/pathways and clinical associations. *Blood*, 132.

**Examples**

```
data(GSE114922.fpkm)
```

---

`GSE114922.psi`*Example dataset containing PSI values*

---

**Description**

A `SummarizedExperiment` containing PSI values of 5,000 AS events. We downloaded RNA-Seq reads of 82 MDS patients from GEO database (GSE114922), aligned with STAR, and computed PSI values using rMATS. AS events with a lot of missing values or extreme values, or those on genes with low expression were filtered out and 5,000 most variable AS events were selected.

**Usage**`GSE114922.psi`**Format**

An object of class `SummarizedExperiment` with 10000 rows and 40 columns.

## References

Pellagatti, A. et al. (2018). Impact of spliceosome mutations on RNA splicing in myelodysplasia: dysregulated genes/pathways and clinical associations. *Blood*, 132.

## Examples

```
data(GSE114922.psi)
```

---

|             |                                |
|-------------|--------------------------------|
| quantifyPSI | <i>AS event quantification</i> |
|-------------|--------------------------------|

---

## Description

Compute PSI values of AS events. This function borrows code from the IMAS package.

## Usage

```
quantifyPSI(object, read.type = "paired", read.length, insert.size,  
            min.reads, num.cores = 1)
```

## Arguments

|             |  |
|-------------|--|
| object      | Object of class ASpediaFI                        |
| read.type   | a type of RNA-seq reads ('single' or 'paired')   |
| read.length | read length                                      |
| insert.size | insert size                                      |
| min.reads   | a minimum number of reads mapped to a given exon |
| num.cores   | the number of cores for parallel processing      |

## Value

ASpediaFI object with PSI values

## References

Han, S. et al. (2017). IMAS: Integrative analysis of Multi-omics data for Alternative Splicing. R package version 1.8.0.

## Examples

```
bamWT <- system.file('extdata/GSM3167290.subset.bam', package = 'ASpediaFI')  
GSE114922.ASpediaFI <- ASpediaFI(  
  sample.names = 'GSM3167290',  
  bam.files = bamWT, conditions = 'WT'  
)  
## Not run:  
GSE114922.ASpediaFI <- quantifyPSI(GSE114922.ASpediaFI,  
  read.type = 'paired',  
  read.length = 100, insert.size = 300,  
  min.reads = 3, num.cores = 1  
)  
## End(Not run)
```

---

samples

*ASpediaFI* accessors

---

## Description

ASpediaFI accessors

## Usage

```
samples(object, ...)
```

```
## S4 method for signature 'ASpediaFI'  
samples(object)
```

```
samples(object) <- value
```

```
## S4 replacement method for signature 'ASpediaFI'  
samples(object) <- value
```

```
events(object, ...)
```

```
## S4 method for signature 'ASpediaFI'  
events(object)
```

```
events(object) <- value
```

```
## S4 replacement method for signature 'ASpediaFI'  
events(object) <- value
```

```
psi(object, ...)
```

```
## S4 method for signature 'ASpediaFI'  
psi(object)
```

```
psi(object) <- value
```

```
## S4 replacement method for signature 'ASpediaFI'  
psi(object) <- value
```

```
gtf(object, ...)
```

```
## S4 method for signature 'ASpediaFI'  
gtf(object)
```

```
gtf(object) <- value
```

```
## S4 replacement method for signature 'ASpediaFI'  
gtf(object) <- value
```

```
network(object, ...)
```



```
## S4 method for signature 'ASpediaFI'
network(object)

network(object) <- value

## S4 replacement method for signature 'ASpediaFI'
network(object) <- value

gene.table(object, ...)

## S4 method for signature 'ASpediaFI'
gene.table(object)

gene.table(object) <- value

## S4 replacement method for signature 'ASpediaFI'
gene.table(object) <- value

as.table(object, ...)

## S4 method for signature 'ASpediaFI'
as.table(object)

as.table(object) <- value

## S4 replacement method for signature 'ASpediaFI'
as.table(object) <- value

pathway.table(object, ...)

## S4 method for signature 'ASpediaFI'
pathway.table(object)

pathway.table(object) <- value

## S4 replacement method for signature 'ASpediaFI'
pathway.table(object) <- value
```

### Arguments

|        |  |
|--------|--|
| object | an ASpediaFI object  |
| ...    | additional arguments to be passed  |
| value  | a value to replace. For details, please see <code>help(ASpediaFI)</code> . |

### Value

Slots of the ASpediaFI object

### Examples

```
fi <- new('ASpediaFI')

data('GSE114922.psi')
```

```
psi(fi) <- GSE114922.psi  
psi(fi)
```

---

visualize

*AS event and pathway visualization*

---

### Description

Visualize AS event or pathway. If an AS event node is given, the function modified from the `plotTranscripts` function in the `maser` package is used to visualize the event. If a pathway node is given, a subnetwork pertaining to the pathway is visualized.

### Usage

```
visualize(object, node, zoom = NULL, n = NULL)
```

### Arguments

|                     |   |
|---------------------|---|
| <code>object</code> | Object of class <code>ASpediaFI</code>  |
| <code>node</code>   | the name of AS event or pathway   |
| <code>zoom</code>   | a logical to determine if genomic coordinates are zoomed (for AS event visualization) |
| <code>n</code>      | the number of genes and AS events to be shown (for pathway visualization)             |

### Value

a plot demonstrating AS event or pathway

### References

Veiga, D. (2019). `maser`: Mapping Alternative Splicing Events to pRoteins. R package version 1.2.0. <https://github.com/DiogoVeiga/maser>

### Examples

```
## Not run:  
# Visualize AS event  
visualize(GSE114922.ASpediaFI,  
  node = as.table(GSE114922.ASpediaFI)$EventID[1],  
  zoom = FALSE  
)  
  
# Visualize pathway  
visualize(GSE114922.ASpediaFI, node = 'HALLMARK_HEME_METABOLISM', n = 10)  
  
## End(Not run)
```

# Index

## \* datasets

GSE114922.fpkms, 6

GSE114922.psi, 6

analyzeFI, 2

annotateASevents, 3

as.table(samples), 8

as.table,ASpediaFI-method(samples), 8

as.table<- (samples), 8

as.table<-,ASpediaFI-method(samples), 8

ASpediaFI(ASpediaFI-class), 4

ASpediaFI-accessor(samples), 8

ASpediaFI-class, 4

events(samples), 8

events,ASpediaFI-method(samples), 8

events<- (samples), 8

events<-,ASpediaFI-method(samples), 8

exportNetwork, 5

gene.table(samples), 8

gene.table,ASpediaFI-method(samples), 8

gene.table<- (samples), 8

gene.table<-,ASpediaFI-method  
(samples), 8

GSE114922.fpkms, 6

GSE114922.psi, 6

gtf(samples), 8

gtf,ASpediaFI-method(samples), 8

gtf<- (samples), 8

gtf<-,ASpediaFI-method(samples), 8

network(samples), 8

network,ASpediaFI-method(samples), 8

network<- (samples), 8

network<-,ASpediaFI-method(samples), 8

pathway.table(samples), 8

pathway.table,ASpediaFI-method  
(samples), 8

pathway.table<- (samples), 8

pathway.table<-,ASpediaFI-method  
(samples), 8

psi(samples), 8

psi,ASpediaFI-method(samples), 8

psi<- (samples), 8

psi<-,ASpediaFI-method(samples), 8

quantifyPSI, 7

samples, 8

samples,ASpediaFI-method(samples), 8

samples<- (samples), 8

samples<-,ASpediaFI-method(samples), 8

visualize, 10