

# Package ‘SynExtend’

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**Type** Package

**Title** Tools for Working With Synteny Objects

**Version** 1.16.0

**biocViews** Genetics, Clustering, ComparativeGenomics, DataImport

**Description** Shared order between genomic sequences provide a great deal of information. Synteny objects produced by the R package DECIPHER provides quantitative information about that shared order. SynExtend provides tools for extracting information from Synteny objects.

**Depends** R (>= 4.3.0), DECIPHER (>= 2.28.0)

**Imports** methods, Biostrings, S4Vectors, IRanges, utils, stats, parallel, graphics, grDevices, RSQLite, DBI

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---

BlastSeqs                      *Run BLAST queries from R*

---

### Description

Wrapper to run **BLAST** queries using the commandline BLAST tool directly from R. Can operate on an `XStringSet` or a FASTA file.

This function requires the BLAST+ commandline tools, which can be downloaded [here](#).

### Usage

```
BlastSeqs(seqs, BlastDB,
          blastType=c('blastn', 'blastp', 'tblastn', 'blastx', 'tblastx'),
          extraArgs='', verbose=TRUE)
```

### Arguments

|           |  |
|-----------|--|
| seqs      | Sequence(s) to run BLAST query on. This can be either an <code>XStringSet</code> or a path to a FASTA file.  |
| BlastDB   | Path to FASTA file in a pre-built BLAST Database. These can be built using either <code>MakeBlastDb</code> from R or the commandline <code>makeblastdb</code> function from BLAST+. For more information on building BLAST DBs, see <a href="#">here</a> . |
| blastType | Type of BLAST query to run. See 'Details' for more information on available types.   |
| extraArgs | Additional arguments to be passed to the BLAST query executed on the command line. This should be a single character string.   |
| verbose   | Should output be displayed?  |

### Details

BLAST implements multiple types of search. Available types are the following:

- `blastn`: Nucleotide sequences against database of nucleotide sequences
- `blastp`: Protein sequences against database of protein sequences
- `tblastn`: Protein sequences against translated database of nucleotide sequences

- `blastx`: Translated nucleotide sequences against database of protein sequences
- `tblastx`: Translated nucleotide sequences against translated database of nucleotide sequences

Different BLAST queries require different inputs. The function will throw an error if the input data does not match expected input for the requested query type.

Input sequences for `blastn`, `blastx`, and `tblastx` should be nucleotide data.

Input sequences for `blastp` and `tblastn` should be amino acid data.

Database for `blastn`, `tblastn`, `tblastx` should be nucleotide data.

Database for `blastp` and `blastx` should be amino acid data.

### Value

Returns a data frame ([data.frame](#)) of results of the BLAST query.

### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

### See Also

[MakeBlastDb](#)

### Examples

```
#
```

---

|                |   |
|----------------|---|
| BlockExpansion | <i>Attempt to expand blocks of paired features in a PairSummaries object.</i> |
|----------------|---|

---

### Description

Attempt to expand blocks of paired features in a `PairSummaries` object.

### Usage

```
BlockExpansion(Pairs,
               GapTolerance = 4L,
               DropSingletons = FALSE,
               Criteria = "PID",
               Floor = 0.5,
               NewPairsOnly = TRUE,
               DBPATH,
               Verbose = FALSE)
```

**Arguments**

|                |   |
|----------------|---|
| Pairs          | An object of class <code>PairSummaries</code> .   |
| GapTolerance   | Integer value indicating the diff between feature IDs that can be tolerated to view features as part of the same block. Set by default to 4L, implying that a single feature missing in a run of pairs will not cause the block to be split. Setting to 3L would imply that a diff of 3 between features, or a gap of 2 features, can be viewed as those features being part of the same block. |
| DropSingletons | Ignore solo pairs when planning expansion routes. Set to <code>FALSE</code> by default.   |
| Criteria       | Either "PID" or "Score", indicating which metric to use to keep or reject pairs.  |
| Floor          | Lower PID limit for keeping a pair that was evaluated during expansion.   |
| NewPairsOnly   | Logical indicating whether or not to return only the pairs that were kept from all expansion attempts, or to return a <code>PairSummaries</code> object with the new pairs folded in.   |
| DBPATH         | A file or connection pointing to the DECIPHER database supplied to <code>FindSynteny</code> for the original map construction.  |
| Verbose        | Logical indicating whether or not to display a progress bar and print the time difference upon completion.  |

**Details**

`BlockExpansion` uses a naive expansion algorithm to attempt to fill in gaps in blocks of paired features and to attempt to expand blocks of paired features.

**Value**

An object of class `PairSummaries`.

**Author(s)**

Nicholas Cooley <npc19@pitt.edu>

**See Also**

[PairSummaries](#), [NucleotideOverlap](#), [link{SubSetPairs}](#), [FindSynteny](#)

**Examples**

```
# this function will be deprecated soon,
# please see the new ExpandDiagonal() function.
library(RSQLite)
DBPATH <- system.file("extdata",
                      "Endosymbionts_v02.sqlite",
                      package = "SynExtend")

data("Endosymbionts_LinkedFeatures", package = "SynExtend")

Pairs <- PairSummaries(SyntenyLinks = Endosymbionts_LinkedFeatures,
                      PIDs = TRUE,
```

```

Score = TRUE,
DBPATH = DBPATH,
Verbose = TRUE)

data("Endosymbionts_Pairs01", package = "SynExtend")
Pairs02 <- BlockExpansion(Pairs = Pairs,
                          NewPairsOnly = FALSE,
                          DBPATH = DBPATH,
                          Verbose = TRUE)

```

---

BlockReconciliation    *Rejection scheme for asyntenic predicted pairs*

---

### Description

Take in a `PairSummaries` object and reject predicted pairs that conflict with syntenic blocks either locally or globally.

### Usage

```

BlockReconciliation(Pairs,
                    ConservativeRejection = TRUE,
                    Precedent = "Size",
                    PIDThreshold = NULL,
                    SCOREThreshold = NULL,
                    Verbose = FALSE)

```

### Arguments

|                                    |   |
|------------------------------------|---|
| <code>Pairs</code>                 | A <code>PairSummaries</code> object.  |
| <code>ConservativeRejection</code> | A logical defaulting to <code>TRUE</code> . By default only pairs that conflict within a syntenic block will be rejected. When <code>FALSE</code> any conflict will cause the rejection of the pair in the smaller block.   |
| <code>Precedent</code>             | A character vector of length 1, defaulting to "Size". Selector for whether function attempts to reconcile with block size as precedent, or mean block PID as precedent. Currently "Metric" will select mean block PID to set block precedent. Blocks of size 1 cannot reject other blocks. The default behavior causes the rejection of any set of predicted pairs that conflict with a larger block of predicted pairs. Switching to "Metric" changes this behavior to any block of size 2 or greater will reject any predicted pair that both conflicts with the current block, and is part of a block with a lower mean PID. |
| <code>PIDThreshold</code>          | Defaults to <code>NULL</code> , a numeric of length 1 can be used to retain pairs that would otherwise be rejected. Pairs that would otherwise be rejected that have a <code>PID &gt;= PIDThreshold</code> will be retained.  |

|                |   |
|----------------|---|
| SCOREThreshold | Defaults to NULL, a numeric of length 1 can be used retain pairs that would otherwise be rejected. Pairs that would otherwise be rejected that have a SCORE $\geq$ SCOREThreshold will be retained. |
| Verbose        | Logical indicating whether or not to display a progress bar and print the time difference upon completion.  |

### Details

If a given PairSummaries object contains predicted pairs that conflict, i.e. imply paralogy, or an “incorrect” and a “correct” ortholog prediction, these predictions will be reconciled. The function scrolls through pairs based on the size of the syntenic block that they are part of, from largest to smallest. When ConservativeRejection is TRUE only predicted pairs that exist within the syntenic block “space” will be removed, this option leaves room for conflicting predictions to remain if they are non-local to each other, or are on different indices. When ConservativeRejection is FALSE any pair that conflicts with a larger syntenic block will be rejected. This option forces only 1-1 feature pairings, for features are part of any syntenic block. Predicted pairs that represent a syntenic block size of 1 feature will not reject other pairs. PIDThreshold and SCOREThreshold can be used to retain pairs that would otherwise be rejected based on available assessments of their pairwise alignment.

### Value

A data.frame of class “data.frame” and “PairSummaries” of paired genes that are connected by syntenic hits. Contains columns describing the k-mers that link the pair. Columns “p1” and “p2” give the location ids of the the genes in the pair in the form “DatabaseIdentifier\_ContigIdentifier\_GeneIdentifier”. “ExactMatch” provides an integer representing the exact number of nucleotides contained in the linking k-mers. “TotalKmers” provides an integer describing the number of distinct k-mers linking the pair. “MaxKmer” provides an integer describing the largest k-mer that links the pair. A column titled “Consensus” provides a value between zero and 1 indicating whether the kmers that link a pair of features are in the same position in each feature, with 1 indicating they are in exactly the same position and 0 indicating they are in as different a position as is possible. The “Adjacent” column provides an integer value ranging between 0 and 2 denoting whether a feature pair’s direct neighbors are also paired. Gap filled pairs neither have neighbors, or are included as neighbors. The “TetDist” column provides the euclidean distance between oligonucleotide - of size 4 - frequencies between predicted pairs. “PIDType” provides a character vector with values of “NT” where either of the pair indicates it is not a translatable sequence or “AA” where both sequences are translatable. If users choose to perform pairwise alignments there will be a “PID” column providing a numeric describing the percent identity between the two sequences. If users choose to predict PIDs using their own, or a provided model, a “PredictedPID” column will be provided.

### Author(s)

Nicholas Cooley <npc19@pitt.edu>

### See Also

[FindSynteny](#), [Synteny-class](#), [PairSummaries](#)

**Examples**

```
# this function will be deprecated soon...
## Not run:
data("Endosymbionts_Pairs02", package = "SynExtend")
Pairs03 <- BlockReconciliation(Pairs = Endosymbionts_Pairs02,
                              ConservativeRejection = FALSE,
                              Verbose = TRUE)

## End(Not run)
```

---

 BuiltInEnsembles

*Pretrained EvoWeaver Ensemble Models*


---

**Description**

EvoWeaver has best performance with an ensemble method combining individual evidence streams. This data file provides pretrained models for ease of use. These models are trained on genes from *Streptomyces* species.

These models are used internally if the user does not provide their own model, and aren't explicitly designed to be accessed by the user.

See the examples for how to train your own ensemble model.

**Usage**

```
data("BuiltInEnsembles")
```

**Value**

The data contain a list of objects of class `glm`.

**Examples**

```
## Training own ensemble method to avoid
## using built-ins

exData <- get(data("ExampleStreptomycesData"))
ew <- EvoWeaver(exData$Genes[1:50])
datavals <- predict(ew, NoPrediction=TRUE)

# Make sure the actual values correspond to the right pairs!
# This example just picks random numbers
# Do not do this for your own models
actual_values <- sample(c(0,1), nrow(datavals), replace=TRUE)
datavals[, 'y'] <- actual_values
myModel <- glm(y~., datavals[, -c(1,2)], family='binomial')

predictionPW <- EvoWeaver(exData$Genes[51:60])
predict(predictionPW,
        PretrainedModel=myModel)
```



---

`CIDist_NullDist`*Simulated Null Distributions for CI Distance*

---

### Description

Simulated values of [Clustering Information Distance](#) for random trees with 4 to 200 shared leaves.

### Usage

```
data("CIDist_NullDist")
```

### Details

Each column of the matrix corresponds to the distribution of distances between random trees with the given number of leaves. This begins at `CI_DISTANCE_INTERNAL[, 1]` corresponding to 4 leaves, and ends at `CI_DISTANCE_INTERNAL[, 197]` corresponding to 200 leaves. Distances begin at 4 leaves since there is only one unrooted tree with 1, 2, or 3 leaves (so the distance between any given tree with less than 4 leaves is always 0).

Each row of the matrix corresponds to statistics for the given simulation set. The first row gives the minimum value, the next 9 give quantiles in `c(1%, 5%, 10%, 25%, 50%, 75%, 90%, 95%, 99%)`, and the last three rows give the max, mean, and sd (resp.).

### Value

A matrix `CI_DISTANCE_INTERNAL` with 197 columns and 13 rows.

### Source

Datafiles obtained from the [TreeDistData](#) package, published as part of Smith (2020).

### References

Smith, Martin R. *Information theoretic generalized Robinson–Foulds metrics for comparing phylogenetic trees*. *Bioinformatics*, 2020. **36**(20):5007-5013.

### Examples

```
data(CIDist_NullDist)
```

ClusterByK

*Predicted pair trimming using K-means.***Description**

A relatively simple k-means clustering approach to drop predicted pairs that belong to clusters with a PID centroid below a specified user threshold.

**Usage**

```
ClusterByK(SynExtendObject,
           UserConfidence = list("PID" = 0.3),
           ClusterScalar = 4,
           MaxClusters = 15L,
           ColSelect = c("p1featurelength",
                        "p2featurelength",
                        "TotalMatch",
                        "Consensus",
                        "PID",
                        "Score"),
           ColNorm = "Score",
           ShowPlot = FALSE,
           Verbose = FALSE)
```

**Arguments**

|                 |  |
|-----------------|--|
| SynExtendObject | An object of class PairSummaries.  |
| UserConfidence  | A named list of length 1 where the name identifies a column of the PairSummaries object, and the value identifies a user confidence. Every k-means cluster with a center value of the column value selected greater than the confidence is retained.   |
| ClusterScalar   | A numeric value used to scale selection of how many clusters are used in kmeans clustering. A transformed total within-cluster sum of squares value is fit to a right hyperbola, and a scaled half-max value is used to select cluster number. "ClusterScalar" is multiplied by the half-max to adjust cluster number selection. |
| MaxClusters     | Integer value indicating the largest number of clusters to test in a series of k-means clustering tests.   |
| ColSelect       | A character vector of column names indicating which columns to use for k-means clustering. When "p1featurelength", "p2featurelength", and "TotalMatch" are included together, they are morphed into a value representing the match size proportional to the longer of the two sequences.   |
| ColNorm         | A character vector of column names indicating columns the user would like to unit normalize. By default only set to "Score".   |
| ShowPlot        | Logical indicating whether or not to plot the CDFs for the PIDs of all k-means clusters for the determined cluster number.   |

Verbose Logical indicating whether or not to display a progress bar and print the time difference upon completion.

### Details

ClusterByK uses a naive k-means routine to select for predicted pairs that belong to clusters whose centroids are greater than or equal to the user specified column-value pair. This means that the confidence is not a minimum, and that pairs with values below the user confidence can be retained. The sum of within cluster sum of squares is used to approximate “knee” selection with the “ClusterScalar” value. With a “ClusterScalar” value of 1 the half-max of a right-hyperbola fitted to the sum of within-cluster sum of squares is used to pick the cluster number for evaluation, “ClusterScalar” is multiplied by the half-max to tune cluster number selection. ClusterByK returns the original object with an appended column and new attributes. The new column “ClusterID” is an integer value indicating which k-means cluster a candidate pair belongs to, while the attribute “Retain” is a named logical vector where the names correspond to ClusterIDs, and the logical value indicates whether the cluster center was above the user supplied column-value pair. This function is intended to be used at the genome-to-genome comparison level, and not say, at the level of an all-vs-all comparison of many genomes. It will work well in all-vs-all cases, but it is not optimized for that scale yet.

### Value

An object of class PairSummaries.

### Author(s)

Nicholas Cooley <npc19@pitt.edu>

### See Also

[SummarizePairs](#), [NucleotideOverlap](#), [FindSyteny](#), [ExpandDiagonal](#)

### Examples

```
data("Endosymbionts_Pairs01", package = "SynExtend")
Pairs02 <- ClusterByK(SynExtendObject = Endosymbionts_Pairs01)
```

---

dendrapply

*Apply a Function to All Nodes of a Dendrogram*

---

### Description

Apply function FUN to each node of a dendrogram recursively. When `y <- dendrapply(x, fn)`, then `y` is a dendrogram of the same graph structure as `x` and for each node, `y.node[j] <- FUN( x.node[j], ...)` (where `y.node[j]` is an (invalid!) notation for the `j`-th node of `y`). Also provides flexibility in the order in which nodes are evaluated.

NOTE: This man page is for the `dendrapply` function defined in the **SynExtend** package. See `?stats::dendrapply` for the default method (defined in the **stats** package).

**Usage**

```
dendrapply(X, FUN, ...,
           how = c("pre.order", "post.order"))
```

**Arguments**

|     |   |
|-----|---|
| X   | An object of class "dendrogram".  |
| FUN | An R function to be applied to each dendrogram node, typically working on its <a href="#">attributes</a> alone, returning an altered version of the same node.  |
| ... | potential further arguments passed to FUN.  |
| how | one of c("pre.order", "post.order"), or an unambiguous abbreviation. Determines if nodes should be evaluated according to an preorder (default) or postorder traversal. See details for more information. |

**Details**

"pre.order" preserves the functionality of the previous `dendrapply`. For each node `n`, `FUN` is applied first to `n`, then to `n[[1]]` (and any children it may have), then `n[[2]]` and its children, etc. Notably, each node is evaluated *prior to any* of its children.

"post.order" allows for calculations that depend on the children of a given node. For each node `n`, `FUN` is applied first to *all* children of `n`, then is applied to `n` itself. Notably, each node is evaluated *after all* of its children.

**Value**

Usually a dendrogram of the same (graph) structure as `X`. For that, the function must be conceptually of the form `FUN <- function(X) { attributes(X) <- .....; X }`, i.e., returning the node with some attributes added or changed.

If the function provided does not return the node, the result is a nested list of the same structure as `X`, or as close as can be achieved with the return values. If the function should only be applied to the leaves of `X`, consider using [rapply](#) instead.

**Warning**

`dendrapply` identifies leaf nodes as nodes such that `attr(node, 'leaf') == TRUE`, and internal nodes as nodes such that `attr(node, 'leaf') %in% c(NULL, FALSE)`. If you modify or remove this attribute, `dendrapply` may perform unexpectedly.

**Note**

The prior implementation of `dendrapply` was recursive and inefficient for dendrograms with many non-leaves. This version is no longer recursive, and thus should no longer cause issues stemming from insufficient C stack size (as mentioned in the 'Warning' in [dendrogram](#)).

**Author(s)**

Aidan Lakshman <ahl27@pitt.edu>

**See Also**

`as.dendrogram`, `lapply` for applying a function to each component of a list.

`rapply` is particularly useful for applying a function to the leaves of a dendrogram, and almost always be used when the function does not need to be applied to interior nodes due to significantly better performance.

**Examples**

```
require(graphics)

## a smallish simple dendrogram
dhc <- as.dendrogram(hc <- hclust(dist(USArrests), "ave"))
(dhc21 <- dhc[[2]][[1]])

## too simple:
dendrapply(dhc21, function(n) utils::str(attributes(n)))

## toy example to set colored leaf labels :
local({
  collab <- function(n) {
    if(is.leaf(n)) {
      a <- attributes(n)
      i <- i+1
      attr(n, "nodePar") <- c(a$nodePar, list(lab.col = mycols[i], lab.font = i%3))
    }
    n
  }
  mycols <- grDevices::rainbow(attr(dhc21,"members"))
  i <- 0
})
dL <- dendrapply(dhc21, collab)
op <- par(mfrow = 2:1)
plot(dhc21)
plot(dL) ## --> colored labels!
par(op)

## Illustrating difference between pre.order and post.order
dend <- as.dendrogram(hclust(dist(seq_len(4L))))

f <- function(x){
  if(!is.null(attr(x, 'leaf'))){
    v <- as.character(attr(x, 'label'))
  } else {
    v <- paste0(attr(x[[1]], 'newattr'), attr(x[[2]], 'newattr'))
  }
  attr(x, 'newattr') <- v
  x
}

# trying with default, note character(0) entries
preorder_try <- dendrapply(dend, f)
```

```
dendrapply(preorder_try, \x){ print(attr(x, 'newattr')); x })

## trying with postorder, note that children nodes will already
## have been populated, so no character(0) entries
postorder_try <- dendrapply(dend, f, how='post.order')
dendrapply(postorder_try, \x){ print(attr(x, 'newattr')); x })
```

---

DisjointSet

*Return single linkage clusters from PairSummaries objects.*


---

### Description

Takes in a PairSummaries object and return a list of identifiers organized into single linkage clusters.

### Usage

```
DisjointSet(Pairs,
            Verbose = FALSE)
```

### Arguments

|         |  |
|---------|--|
| Pairs   | A PairSummaries object.  |
| Verbose | Logical indicating whether to print progress bars and messages. Defaults to FALSE. |

### Details

Takes in a PairSummaries object and return a list of identifiers organized into single linkage clusters.

### Value

Returns a list of character vectors representing IDs of sequence features, typically genes.

### Author(s)

Nicholas Cooley <npc19@pitt.edu>

### See Also

[FindSynteny](#), [Synteny-class](#), [PairSummaries](#), [FindSets](#)

### Examples

```
data("Endosymbionts_Pairs03", package = "SynExtend")

Sets <- DisjointSet(Pairs = Endosymbionts_Pairs03,
                  Verbose = TRUE)
```

---

DPhyloStatistic      *D-Statistic for Binary States on a Phylogeny*

---

### Description

Calculates if a presence/absence pattern is random, Brownian, or neither with respect to a given phylogeny.

### Usage

```
DPhyloStatistic(dend, PAPProfile, NumIter = 1000L)
```

### Arguments

|            |  |
|------------|--|
| dend       | An object of class <code>dendrogram</code>   |
| PAPProfile | A vector representing presence/absence of binary traits. See Details for more information. |
| NumIter    | Number of iterations to simulate for random permutation analysis.                          |

### Details

This function implements the D-Statistic for binary traits on a phylogeny, as introduced in Fritz and Purvis (2009). The statistic is the following ratio:

$$\frac{D_{obs} - D_b}{D_r - D_b}$$

Here  $D_{obs}$  is the D value for the input data,  $D_b$  is the value under simulated Brownian evolution, and  $D_r$  is the value under random permutation of the input data. The D value measures the sum of sister clade differences in a phylogeny weighted by branch lengths. A score close to 1 indicates phylogenetically random distribution, and a score close to 0 indicates the trait likely evolved under Brownian motion. Scores can fall outside this range; these scores are only intended as benchmark points on the scale. See the original paper cited in References for more information.

The input `PAPProfile` supports a number of formatting options:

- Character vector, where each element is a label of the dendrogram. Presence in the character vector indicates presence of the trait in the corresponding label.
- Integer vector of length equivalent to the number of leaves, comprised of 0s and 1s. 0 indicates absence in the corresponding leaf, and 1 indicates presence.
- Logical vector of length equivalent to number of leaves. FALSE indicates absence in the corresponding leaf, and TRUE indicates presence.

See Examples for a demonstration of each case.

### Value

Returns a numerical value. Values close to 0 indicate random distribution, and values close to 1 indicate a Brownian distribution.

**Author(s)**

Aidan Lakshman <ahl27@pitt.edu>

**References**

Fritz S.A. and Purvis A. *Selectivity in Mammalian Extinction Risk and Threat Types: a New Measure of Phylogenetic Signal Strength in Binary Traits*. Conservation Biology, 2010. **24**(4):1042-1051.

**Examples**

```
#####
### Replicating results from Table 1 in original paper ###
#####

# creates a dendrogram with 16 leaves and branch lengths all 1
distMat <- suppressWarnings(matrix(1:17, nrow=16, ncol=16))
testDend <- as.dendrogram(hclust(as.dist(distMat)))
testDend <- dendrapply(testDend, \x){
  attr(x, 'height') <- attr(x, 'height') / 2
  return(x)
})
attr(testDend[[1]], 'height') <- attr(testDend[[2]], 'height') <- 3
attr(testDend, 'height') <- 4
plot(testDend)

set.seed(123)

# extremely clumped (should be close to -2.4)
DPhyloStatistic(testDend, as.character(1:8))

# clumped Brownian (should be close to 0)
DPhyloStatistic(testDend, as.character(c(1,2,5,6,10,12,13,14)))

# random (should be close to 1.0)
DPhyloStatistic(testDend, as.character(c(1,4:6,10,13,14,16)))

# overdispersed (should be close to 1.9)
DPhyloStatistic(testDend, as.character(seq(2,16,by=2)))

#####
### Different ways to create PAPfiles ###
#####

allLabs <- as.character(labels(testDend))

# All these ways create a PAPfile with
# presence in members 1:4
# and absence in members 5:16

# numeric vector:
c(rep(1,4), rep(0, length(allLabs)-4))
```



```
# logical vector:
c(rep(TRUE,4), rep(FALSE, length(allLabs)-4))

# character vector:
allLabs[1:4]
```

---

Endosymbionts\_GeneCalls

*Example genecalls*

---

### **Description**

A named list of DataFrames.

### **Usage**

```
data("Endosymbionts_GeneCalls")
```

### **Details**

Example genecalls.

### **Value**

A named list.

### **Examples**

```
data(Endosymbionts_GeneCalls)
```

---

Endosymbionts\_LinkedFeatures

*Example synteny links*

---

### **Description**

An object of class LinkedPairs.

### **Usage**

```
data("Endosymbionts_LinkedFeatures")
```

### **Details**

An object of class LinkedPairs.

**Value**

An object of class `LinkedPairs`.

**Examples**

```
data(Endosymbionts_LinkedFeatures)
```

---

Endosymbionts\_Pairs01 *Example predicted pairs*

---

**Description**

An object of class `PairSummaries`.

**Usage**

```
data("Endosymbionts_Pairs01")
```

**Details**

An object of class `PairSummaries`.

**Value**

An object of class `PairSummaries`.

**Examples**

```
data(Endosymbionts_Pairs01)
```

---

Endosymbionts\_Pairs02 *Example predicted pairs*

---

**Description**

An object of class `PairSummaries` where blocks have been expanded.

**Usage**

```
data("Endosymbionts_Pairs02")
```

**Details**

An object of class `PairSummaries`.

**Value**

An object of class PairSummaries.

**Examples**

```
data(Endosymbionts_Pairs02)
```

---

Endosymbionts\_Pairs03 *Example predicted pairs*

---

**Description**

An object of class PairSummaries where blocks have been expanded and competitors have been rejected.

**Usage**

```
data("Endosymbionts_Pairs03")
```

**Details**

An object of class PairSummaries.

**Value**

An object of class PairSummaries.

**Examples**

```
data(Endosymbionts_Pairs03)
```

---

Endosymbionts\_Sets *A list of disjoint sets.*

---

**Description**

A named list of disjoint sets representing hypothetical COGs.

**Usage**

```
data("Endosymbionts_Sets")
```

**Details**

A named list of disjoint sets representing hypothetical COGs.

**Value**

A named list of disjoint sets representing hypothetical COGs.

**Examples**

```
data(Endosymbionts_Sets)
```

---

Endosymbionts\_Synteny *A synteny object*

---

**Description**

An object of class Synteny.

**Usage**

```
data("Endosymbionts_Synteny")
```

**Details**

An object of class Synteny.

**Value**

An object of class Synteny.

**Examples**

```
data(Endosymbionts_Synteny)
```

---

EstimateExoLabel *Estimate ExoLabel Disk Consumption*

---

**Description**

Estimate the total disk consumption for [ExoLabel](#).

**Usage**

```
EstimateExoLabel(num_v, avg_degree=1,
                 num_edges=num_v*avg_degree,
                 node_name_length=8L)
```

### Arguments

|                  |  |
|------------------|--|
| num_v            | Approximate number of total unique nodes in the network.     |
| avg_degree       | Average degree of each node in the network.                  |
| num_edges        | Approximate total number of edges in the network.            |
| node_name_length | Approximate average length of each node name, in characters. |

### Details

This function provides a rough estimate of the total disk space required to run [ExoLabel](#) for a given input network. `avg_degree` and `num_edges` need not both be specified. The function prints out the estimated size of the original edgelist files, the estimated disk space to be consumed by [ExoLabel](#), and the approximate ratio of disk space relative to the original file.

`node_name_length` specifies the average length of the node names—since the names themselves must be stored on disk, this contributes to the overall size. For relatively short node names (1-16 characters) this has a negligible impact on overall disk consumption.

### Value

Returns a vector of length three, showing the estimated total edgelist file size, estimated disk consumption, and ratio of the two. All sizes are shown in bytes.

### Note

Estimating the average node label size is challenging, and unfortunately it does have a relatively large effect on the estimated edgelist file size. This function should be used for **rough** estimations of sizing, not absolute values. Errors in estimation of rough node name size will have a larger impact on edgelist file estimation than on the [ExoLabel](#) disk usage, so users can have higher confidence in estimated [ExoLabel](#) consumption.

### Author(s)

Aidan Lakshman <AHL27@pitt.edu>

### See Also

[ExoLabel](#)

### Examples

```
# 100,000 nodes, average degree 2
EstimateExoLabel(num_v=100000, avg_degree=2)

# 10,000 nodes, 50,000 edges
EstimateExoLabel(num_v=10000, num_edges=50000)
```

---

|                |   |
|----------------|---|
| EstimRearrScen | <i>Estimate Genome Rearrangement Events with Double Cut and Join Operations</i> |
|----------------|---|

---

### Description

Take in a [Synteny](#) object and return predicted rearrangement events.

### Usage

```
EstimRearrScen(SyntenyObject, NumRuns = -1,
               Mean = FALSE, MinBlockLength = -1,
               Verbose = TRUE)
```

### Arguments

|                |   |
|----------------|---|
| SyntenyObject  | <a href="#">Synteny</a> object, as obtained from running <a href="#">FindSynteny</a> . Expected input is unichromosomal sequences, though multichromosomal sequences are supported.   |
| NumRuns        | Numeric; Number of times to simulate scenarios. The default value of -1 (and all non-positive values) runs each analysis for $\sqrt{b}$ iterations, where b is the number of unique breakpoints.  |
| Mean           | Logical; If TRUE, returns the mean number of inversions and transpositions found. If FALSE, returns the scenario corresponding to the minimum total number of operations across all runs. This parameter only affects the number of inversions and transpositions reported; the specific scenario returned is one of the runs that resulted in a minimum value. |
| MinBlockLength | Numeric; Minimum size of syntenic blocks to use for analysis. The default value accepts all blocks. Set to a larger value to ignore sections of short mutations that could be the result of SNPs or other small-scale mutations.  |
| Verbose        | Logical; indicates whether or not to display a progress bar and print the time difference upon completion.  |

### Details

EstimRearrScen is an implementation of the Double Cut and Join (DCJ) method for analyzing large scale mutation events.

The DCJ model is commonly used to model genome rearrangement operations. Given a genome, we can create a connected graph encoding the order of conserved genomic regions. Each syntenic region is split into two nodes, with one encoding the beginning and one encoding the end (beginning and end defined relative to the direction of transcription). Each node is then connected to the two nodes it is adjacent to in the genome.

For example, given a genome with 3 syntenic regions  $a - b - c$  such that  $b$  is transcribed in the opposite direction relative to  $a, c$ , our graph would consist of nodes and edges  $a1 - a2 - b2 - b1 - c1 - c2$ .

Given two genomes, we derive syntenic regions between the two samples and then construct two of these graph structures. A DCJ operation is one that cuts two connections of a common color and creates two new edges. The goal of the DCJ model is to rearrange the graph of the first genome into the second genome using DCJ operations. The DCJ distance is defined as the minimum number of DCJ operations to transform one graph into another.

It can be easily shown that inversions can be performed with a single DCJ operation, and block interchanges/order rearrangements can be performed with a sequence of two DCJ operations. DCJ distance defines a metric space, and prior work has demonstrated algorithms for fast computation of the DCJ distance.

However, DCJ distance inherently incentivizes inversions over block interchanges due to the former requiring half as many DCJ operations. This is a strong assumption, and there is no evidence to support gene order rearrangements occurring half as often as gene inversions.

This implementation incentivizes minimum number of total events rather than total number of DCJs. As the search space is large and multiple sequences of events can be equally parsimonious, this algorithm computes multiple scenarios with random sequences of operations to try to find the minimum amount of events. Users can choose to receive the best found solution or the mean number of events from all solutions.

## Value

An  $N \times N$  matrix of lists with the same shape as the input Synteny object. This is wrapped into a `GenRearr` object for pretty printing.

The diagonal corresponds to total sequence length of the corresponding genome.

In the upper triangle, entry  $[i, j]$  corresponds to the percent hits between genome  $i$  and genome  $j$ . In the lower triangle, entry  $[i, j]$  contains a List object with 5 properties:

- `$Inversions` and `$Transpositions` contain the (Mean/min) number of estimated inversions and transpositions (resp.) between genome  $i$  and genome  $j$ .
- `$pct_hits` contains percent hits between the genomes.
- `$Scenario` shows the sequence of events corresponding to the minimum rearrangement scenario found. See below for details.
- `$Key` provides a mapping between syntenic blocks and genome positions. See below for details.

The `print.GenRearr` method prints this data out as a matrix, with the diagonal showing the number of chromosomes and the lower triangle displaying  $xI, yT$ , where  $x, y$  the number of inversions and transpositions (resp.) between the corresponding entries.

The `$Scenario` entry describes a sequences of steps to rearrange one genome into another, as found by this algorithm. The goal of the DCJ model is to rearrange the second genome into the first. Thus, with  $N$  syntenic regions total, we can arbitrarily choose the syntenic blocks in genome 1 to be ordered  $1, 2, \dots, N$ , and then have genome 2 numbers relative to that.

As an example, suppose genome 1 has elements  $A B E(r) G$  and genome 2 has elements  $E B(r) A(r) G$ , with  $X(r)$  denoting block  $X$  has reversed direction of transcription. We can then arbitrarily assign blocks to numbers such that genome 1 is  $(1\ 2\ 3\ 4)$  and genome 2 is  $(3\ -2\ -1\ 4)$ , where a negative indicates reversed direction of transcription relative to the corresponding syntenic block in genome 1.

Each entry in `$Scenario` details an operation, the result after that operation, and the number of blocks involved in the operation. If we reversed the middle two entries of genome 2, the entry in `$Scenario` would be:

```
inversion: 3 1 2 4 { 2 }
```

Here we inverted the whole block (-2 -1) into (1 2). We could then finish the rearrangement by performing a transposition to move block 3 between 2 and 4. The entries of `$Scenario` in this case would be the following:

```
Original: 3 -2 -1 4
```

```
inversion: 3 1 2 4 { 2 }
```

```
block interchange: 1 2 3 4 { 3 }
```

Step 1 is the original state of genome 2, step 2 inverts 2 elements to arrive at (3 1 2 4), and then step 3 moves one element to arrive at (1 2 3 4).

It is important to note that the numbered genomic regions in `$Scenario` are not genes, they are blocks of conserved syntenic regions between the genomes. These blocks may not match up with the original blocks from the Synteny object, since some are combined during pre-processing to expedite calculations.

`$Key` is a mapping between these numbered regions and the original genomic regions. This is a 5 column matrix with the following columns (in order):

1. `start1`: Nucleotide position for the first nucleotide in of the syntenic region on genome 1.
2. `start2`: Same as `start1`, but for genome 2
3. `length`: Length of block, in nucleotides
4. `rel_direction_on_2`: 1 if the blocks have the same transcriptional direction on both genomes, and 0 if the direction is reversed in genome 2
5. `index1`: Label of the genetic region used in `$Scenario` output

### Author(s)

Aidan Lakshman (<ahl27@pitt.edu>)

### References

Friedberg, R., Darling, A. E., & Yancopoulos, S. (2008). Genome rearrangement by the double cut and join operation. *Bioinformatics*, 385-416.

### See Also

[FindSynteny](#)

[Synteny](#)

### Examples

```
db <- system.file("extdata", "Influenza.sqlite", package="DECIPHER")
synteny <- FindSynteny(db)
synteny
```



```

rearrs <- EstimRearrScen(synteny)

rearrs          # view whole object
rearrs[[2,1]]  # view details on Genomes 1 and 2

```

---

EvoWeaver

*EvoWeaver: Predicting Protein Functional Association Networks*


---

## Description

EvoWeaver is an S3 class with methods for predicting functional association using protein or gene data. EvoWeaver implements multiple algorithms for analyzing coevolutionary signal between genes, which are combined into overall predictions on functional association. For details on predictions, see [predict.EvoWeaver](#).

## Usage

```

EvoWeaver(ListOfData, MySpeciesTree=NULL, NoWarn=FALSE)

## S3 method for class 'EvoWeaver'
SpeciesTree(ew, Verbose=TRUE, Processors=1L)

```

## Arguments

|               |   |
|---------------|---|
| ListOfData    | A list of gene data, where each entry corresponds to information on a particular gene. List must contain either dendrograms or vectors, and cannot contain a mixture. If list is composed of dendrograms, each dendrogram is a gene tree for the corresponding entry. If list is composed of vectors, vectors should be numeric or character vectors denoting the genomes containing that gene. |
| MySpeciesTree | An object of class 'dendrogram' representing the overall species tree for the list provided in ListOfData.  |
| NoWarn        | Several algorithms depend on having certain data. When a EvoWeaver object is initialized, it automatically selects which algorithms can be used given the input data. By default, EvoWeaver will notify the user of algorithms that cannot be used with warnings. Setting NoWarn=TRUE will suppress these messages.   |
| ew            | An object of class EvoWeaver  |
| Verbose       | Should output be displayed when calculating species tree?   |
| Processors    | Number of processors to use. Set to NULL to automatically use the maximum amount of processors.   |

## Details

EvoWeaver expects input data to be a list. All entries must be one of the following:

1. ListOfData[[i]] = c('ID#1', 'ID#2', ..., 'ID#k')

2. (a) `ListOfData[[i]] = c('i1_d1_p1', 'i2_d2_p2', ..., 'ik_dk_pk')`  
 (b) `ListOfData[[i]] = c('i1_d1_s1_p1', 'i2_d2_s2_p2', ..., 'ik_dk_sk_pk')`
3. `ListOfData[[i]] = dendrogram(...)`

In (1), each `ID#i` corresponds to the unique identifier for genome #i. For entry #j in the list, the presence of `'ID#i'` means genome #i has an ortholog for gene/protein #j.

Case (2a) is the same as (1), just with the formatting of names slightly different. Each entry is of the form `i_d_p`, where `i` is the unique identifier for the genome, `d` is which chromosome the ortholog is located, and `p` is what position the ortholog appears in on that chromosome. `p` must be a numeric, while the other entries can be any value.

Case (2b) is a variation on (2a), adding in an identifier `s`. This value must be 0 or 1, corresponding to whether the gene is on the forward or reverse strand. Whether 0 denotes forward or reverse is inconsequential as long as the scheme is consistent.

Case (3) expects gene trees for each gene, with labeled leaves corresponding to each source genome. If `ListOfData` is in this format, taking `labels(ListOfData[[i]])` should produce a character vector that matches the format of one of the previous cases.

*See the Examples section for illustrative examples.*

*Whenever possible, provide a full set of dendrogram objects with leaf labels in form (2b). This will allow the most algorithms to run. What follows is a more detailed description of which inputs allow which algorithms.*

EvoWeaver requires input of scenario (3) to use distance matrix methods, and requires input of scenario (2) (or (3) with leaves labeled according to (2)) for gene organization analyses. Transcriptional direction analysis requires input of scenario (2b). Sequence-level methods require dendrograms with sequence information included as the state attribute in each leaf node.

Note that ALL entries must belong to the same category—a combination of character vectors and dendrograms is not allowed.

Prediction of a functional association network is done using `predict(EvoWeaverObject)`. See [predict.EvoWeaver](#) for more information.

The `SpeciesTree` function takes in an object of class `EvoWeaver` and returns a species tree. If the object was not initialized with a species tree, it calculates one using [SuperTree](#). The species tree for a `EvoWeaver` object can be set with `attr(ew, 'speciesTree') <- ...`

## Value

Returns a `EvoWeaver` object.

## Author(s)

Aidan Lakshman <ahl27@pitt.edu>

## See Also

[predict.EvoWeaver](#), [ExampleStreptomycesData](#), [BuiltInEnsembles](#), [SuperTree](#)

**Examples**

```

# I'm using gene to mean either a gene or protein

## Imagine we have the following 4 genomes:
## (each letter denotes a distinct gene)
##   Genome 1: a b c d
##   Genome 2: d c e
##   Genome 3: b a e
##   Genome 4: a e

## We have 5 total genes: (a,b,c,d,e)
##   a is present in genomes 1, 3, 4
##   b is present in genomes 1, 3
##   c is present in genomes 1, 2
##   d is present in genomes 1, 2
##   e is present in genomes 2, 3, 4

## Constructing a EvoWeaver object according to (1):
l <- list()
l[['a']] <- c('1', '3', '4')
l[['b']] <- c('1', '3')
l[['c']] <- c('1', '2')
l[['d']] <- c('1', '2')
l[['e']] <- c('2', '3', '4')

## Each value of the list corresponds to a gene
## The associated vector shows which genomes have that gene
pwCase1 <- EvoWeaver(l)

## Constructing a EvoWeaver object according to (2):
## Here we need to add in the chromosome and the position
## As we only have one chromosome,
## we can just set that to 1 for all.
## Position can be identified with knowledge, or with
## FindGenes(...) from DECIPHER.

## In this toy case, genomes are small so it's simple.
l <- list()
l[['a']] <- c('1_1_1', '3_1_2', '4_1_1')
l[['b']] <- c('1_1_2', '3_1_1')
l[['c']] <- c('1_1_3', '2_1_2')
l[['d']] <- c('1_1_4', '2_1_1')
l[['e']] <- c('2_1_3', '3_1_3', '4_1_2')

pwCase2a <- EvoWeaver(l)

## If we want transcriptional information, we need an
## value corresponding to the strand of each gene
## Notice that the genome identifier need not be numeric,
## but the strand identifier must be 0 or 1
l <- list()
l[['a']] <- c('a_1_0_1', 'c_1_1_2', 'd_1_0_1')

```

```

l[['b']] <- c('a_1_1_2', 'c_1_1_1')
l[['c']] <- c('a_1_1_3', 'b_1_0_2')
l[['d']] <- c('a_1_0_4', 'b_1_0_1')
l[['e']] <- c('b_1_0_3', 'c_1_0_3', 'd_1_0_2')

## For Case 3, we just need dendrogram objects for each
# l[['a']] <- dendrogram(...)
# l[['b']] <- dendrogram(...)
# l[['c']] <- dendrogram(...)
# l[['d']] <- dendrogram(...)
# l[['e']] <- dendrogram(...)

## Leaf labels for these will be the same as the
## entries in Case 1.

```

## Description

EvoWeaver incorporates four classes of prediction, each with multiple methods and algorithms. Colocalization (Coloc) methods examine conservation of relative location and transcriptional direction of genetic regions within the genome.

predict.EvoWeaver currently supports three Coloc methods:

- 'Coloc'
- 'ColocMoran'
- 'TranscripMI'

## Details

All distance matrix methods require a EvoWeaver object initialized with gene locations using the three or four number code. See [EvoWeaver](#) for more information on input data types.

The built-in Coloc examines relative location of genes within genomes as evidence of interaction. For a given pair of genes, the score is given by  $\sum_G e^{1-|dI_G|}$ , where  $G$  the set of genomes and  $dI_G$  the difference in index between the two genes in genome  $G$ . Using gene index instead of number of base pairs avoids bias introduced by gene and genome length.

ColocMoran measures the extent to which gene distances are preserved across a phylogeny. This function uses the same initial scoring scheme as Coloc, but can handle paralogs. The raw scores are passed into [MoransI](#) to calculate spatial autocorrelation. "Space" is taken as  $e^{-C}$ , where  $C$  is the Cophenetic distance matrix calculated from the species tree of the inputs. As such, this method requires a species tree as input, which can be calculated from a set of gene trees using [SuperTree](#).

TranscripMI uses mutual information of the transcriptional direction of each pair of genes. Conservation of relative transcriptional direction between gene pairs has been shown to imply functional association in prior work. This algorithm requires that the EvoWeaver object is initialized with a four number code, with the third number either 0 or 1, denoting whether the gene is on the forward or reverse strand. The mutual information is calculated as:

$$\sum_{x \in X} \sum_{y \in Y} (-1)^{(x \neq y)} P_{(X,Y)}(x, y) \log \left( \frac{P_{(X,Y)}(x, y)}{P_X(x)P_Y(y)} \right)$$

Here  $X = Y = \{0, 1\}$ ,  $x$  is the direction of the gene with lower index,  $y$  is the direction of the gene with higher index, and  $P_{(T)}(t)$  is the probability of  $T = t$ . Note that this is a weighted MI as introduced by Beckley and Wright (2021). The mutual information is augmented by the addition of a single pseudocount to each value, and normalized by the joint entropy of  $X, Y$ . P-values are calculated using Fisher's Exact Test on the contingency table.

### Value

None.

### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

### References

Beckley, Andrew and E. S. Wright. *Identification of antibiotic pairs that evade concurrent resistance via a retrospective analysis of antimicrobial susceptibility test results*. *The Lancet Microbe*, 2021. **2**(10): 545-554.

Korbel, J. O., et al., *Analysis of genomic context: prediction of functional associations from conserved bidirectionally transcribed gene pairs*. *Nature Biotechnology*, 2004. **22**(7): 911-917.

Moran, P. A. P., *Notes on Continuous Stochastic Phenomena*. *Biometrika*, 1950. **37**(1): 17-23.

### See Also

[EvoWeaver](#)

[predict.EvoWeaver](#)

[EvoWeaver Phylogenetic Profiling Predictors](#)

[EvoWeaver Phylogenetic Structure Predictors](#)

[EvoWeaver Sequence-Level Predictors](#)

---

EvoWeaver-PPPreds

*Phylogenetic Profiling Predictions for EvoWeaver*

---

### Description

EvoWeaver incorporates four classes of prediction, each with multiple methods and algorithms. Phylogenetic Profiling (PP) methods examine conservation of gain/loss events within orthology groups using phylogenetic profiles constructed from presence/absence patterns.

predict.EvoWeaver currently supports seven PP methods:

- 'Jaccard'

- 'Hamming'
- 'MutualInformation'
- 'PAPV'
- 'CorrGL'
- 'ProfDCA'
- 'Behdenna'
- 'GainLoss'

## Details

Most PP methods are compatible with a `EvoWeaver` object initialized with any input type. See [EvoWeaver](#) for more information on input data types.

All of these methods use presence/absence (PA) profiles, which are binary vectors such that 1 implies the corresponding genome has that particular gene, and 0 implies the genome does not have that particular gene.

Methods `Hamming` and `Jaccard` use Hamming and Jaccard distance (respectively) of PA profiles to determine overall score.

`MutualInformation` uses mutual information of PA profiles to determine score, employing a weighting scheme such that 11 and 00 give positive information, and 10 and 01 give negative information.

`PAPV` calculates a p-value for PA profiles using Fisher's Exact Test. The returned score is provided as `1-p_value` so that larger scores indicate more significance, and smaller scores indicate less significance. This rescaling is consistent with the other similarity metrics in `EvoWeaver`. This can be used with `Jaccard`, `Hamming`, or `MutualInformation` to weight raw scores by statistical significance.

`ProfDCA` uses the direct coupling analysis algorithm introduced by Weigt et al. (2005) to determine direct information between PA profiles. This approach has been validated on PA profiles in Fukunaga and Iwasaki (2022), though the implementation in `EvoWeaver` forsakes the persistent contrastive divergence method in favor of the algorithm from Lokhov et al. (2018) for increased speed and exact solutions. Note that this algorithm is still extremely slow relative to the other methods despite the aforementioned runtime improvements.

`Behdenna` implements the method detailed in Behdenna et al. (2016) to find statistically significant interactions using co-occurrence of gain/loss events mapped to ancestral states on a species tree. This method requires a species tree as input. If the `EvoWeaver` object is initialized with dendrogram objects, `SuperTree` will be used to infer a species tree.

`GainLoss` uses a similar method to `Behdenna`. This method uses Fitch Parsimony to infer where events were gained or lost on a species tree, and then looks for distance between these gain/loss events. Unlike `Behdenna`, this method takes into account the types of events (ex. gain/gain and loss/loss are treated differently than gain/loss). This method requires a species tree as input. If the `EvoWeaver` object is initialized with dendrogram objects, `SuperTree` will be used to infer a species tree.

`CorrGL` infers where events were gained or lost on a species tree as in method `GainLoss`, then uses a Pearson's correlation coefficient weighted by p-value to infer similarity.

## Value

None.

**Author(s)**

Aidan Lakshman <ahl27@pitt.edu>

**References**

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- Date, S.V. and E.M. Marcotte, *Discovery of uncharacterized cellular systems by genome-wide analysis of functional linkages*. Nature Biotechnology, 2003. **21**(9): p. 1055-1062.
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- Pellegrini, M., et al., *Assigning protein function by comparative genome analysis: Protein phylogenetic profiles*. Proceedings of the National Academy of Sciences, 1999. **96**(8) p. 4285-4288
- Weigt, M., et al., *Identification of direct residue contacts in protein-protein interaction by message passing*. Proceedings of the National Academy of Sciences, 2009. **106**(1): p. 67-72.

**See Also**

- [EvoWeaver](#)
- [predict.EvoWeaver](#)
- [EvoWeaver Phylogenetic Structure Predictors](#)
- [EvoWeaver Gene Organization Predictors](#)
- [EvoWeaver Sequence-Level Predictors](#)

---

EvoWeaver-PSPreds

*Phylogenetic Structure Predictions for EvoWeaver*

---

**Description**

EvoWeaver incorporates four classes of prediction, each with multiple methods and algorithms. Phylogenetic Structure (PS) methods examine conservation of overall evolutionary rates within orthology groups using distance matrices constructed from each gene tree.

predict.EvoWeaver currently supports three PS methods:

- 'MirrorTree'
- 'ContextTree'
- 'TreeDistance'

## Details

All distance matrix methods require a `EvoWeaver` object initialized with dendrogram objects. See [EvoWeaver](#) for more information on input data types.

The `MirrorTree` method was introduced by Pazos et al. (2001). This method builds distance matrices using a nucleotide substitution model, and then calculates coevolution between gene families using the Pearson correlation coefficient of the upper triangle of the two corresponding matrices.

Experimental analysis has shown data in the upper triangle is heavily redundant and rapidly overwhelms available system memory. Previous work has incorporated dimensionality reduction such as SVD to reduce the dimensionality of the data, but this prevents parallelization of the data and doesn't solve memory issues (since SVD takes as input the entire matrix with columns corresponding to upper triangle values). `EvoWeaver` instead uses a seeded random projection following Achlioptas (2001) to reduce the dimensionality of the data in a reproducible and parallel-compatible way. We also utilize Spearman's  $\rho$ , which outperforms Pearson's  $r$  following dimensionality reduction.

Subsequent work by Pazos et al. (2005) and Sato et al. (2005, 2006) found multiple ways to improve predictions from the initial `MirrorTree` method. These methods incorporate additional phylogenetic context, and are thus called `ContextTree` methods. These improvements include correcting for overall evolutionary rate using a species tree and/or using projection vectors. The built-in `ContextTree` method implements a species tree correction, and weights the resulting score by the normalized Hamming distance of the presence/absence profiles. This can correct for gene trees with low overlap that achieve spuriously high scores via random projection. Additional correction measures are implemented in the `MTCorrection` argument.

The `TreeDistance` method uses phylogenetic tree distance to quantify differences between gene trees. This method implements a number of metrics and groups them together to improve overall runtime. The default tree distance method is normalized Robinson-Foulds distance due to its lower computational complexity. Other methods can be specified using the `TreeMethods` argument, which expects a character vector containing one or more of the following:

- "CI": [Clustering Information Distance](#)
- "RF": [Robinson-Foulds Distance](#)
- "JRF": [Jaccard-Robinson-Foulds Distance](#)
- "Nye": [Nye Similarity](#)
- "KF": [Kuhner-Felsenstein Distance](#)
- "all": All of the above methods

See the links above for more information and references. All of these metrics are accessible using the [PhyloDistance](#) method. Method "JRF" defaults to a  $k$  value of 4, but this can be specified further if necessary using the `JRFk` input parameter. Higher values of  $k$  approach the value of Robinson-Foulds distance, but these have a negligible impact on performance so use of the default parameter is encouraged for simplicity. Multiple metrics can be specified.

## Value

None.

## Author(s)

Aidan Lakshman <ahl27@pitt.edu>



## References

- Achlioptas, Dimitris. *Database-friendly random projections*. Proceedings of the Twentieth ACM SIGMOD-SIGACT-SIGART Symposium on Principles of Database Systems, 2001. p. 274-281.
- Pazos, F. and A. Valencia, *Similarity of phylogenetic trees as indicator of protein-protein interaction*. Protein Engineering, Design and Selection, 2001. **14**(9): p. 609-614.
- Pazos, F., et al., *Assessing protein co-evolution in the context of the tree of life assists in the prediction of the interactome*. J Mol Biol, 2005. **352**(4): p. 1002-15.
- Sato, T., et al., *The inference of protein-protein interactions by co-evolutionary analysis is improved by excluding the information about the phylogenetic relationships*. Bioinformatics, 2005. **21**(17): p. 3482-9.
- Sato, T., et al., *Partial correlation coefficient between distance matrices as a new indicator of protein-protein interactions*. Bioinformatics, 2006. **22**(20): p. 2488-92.

## See Also

[EvoWeaver](#)  
[predict.EvoWeaver](#)  
[EvoWeaver Phylogenetic Profiling Predictors](#)  
[EvoWeaver Gene Organization Predictors](#)  
[EvoWeaver Sequence-Level Predictors](#)  
[PhyloDistance](#)

---

EvoWeaver-SLPreds

*Sequence-Level Predictions for EvoWeaver*

---

## Description

EvoWeaver incorporates four classes of prediction, each with multiple methods and algorithms. Sequence-Level (SL) methods examine conservation of patterns in sequence data, commonly exhibited due to physical interactions between proteins.

predict.EvoWeaver currently supports three SL methods:

- 'ResidueMI'
- 'NVDI'
- 'Ancestral'

## Details

All residue methods require a EvoWeaver object initialized with dendrogram objects and ancestral states. See [EvoWeaver](#) for more information on input data types.

The ResidueMI method looks at mutual information between sites in a multiple sequence alignment (MSA). This approach extends prior work in Martin et al. (2005). Each site from the first gene group is paired with the site from the second gene group that maximizes their mutual information.

The NVDT method uses the natural vector encoding method introduced in Zhao et al. (2022). This encodes each gene sequences as a 92-dimensional vector, with the following entries:

$$N(S) = (n_A, n_C, n_G, n_T, \quad \mu_A, \mu_C, \mu_G, \mu_T, \quad D_2^A, D_2^C, D_2^G, D_2^T, \quad n_{AA}, n_{AC}, \dots, n_{TT},$$

Here  $n_X$  is the raw total count of nucleotide  $X$  (or di/trinucleotide). For single nucleotides, we also calculate  $\mu_X$ , the mean location of nucleotide  $X$ , and  $D_2^X$ , the second moment of the location of nucleotide  $X$ . The overall natural vector for a COG is calculated as the normalized mean vector from the natural vectors of all component gene sequences. Interaction scores are computed using Pearson's R between each COG's natural vector. These di/trinucleotide counts are by default excluded, but can be included using the `extended=TRUE` argument. Using the extended counts has shown minimal increased accuracy at the cost of slower runtime in benchmarking.

The `Ancestral` method calculates coevolution by looking at correlation of residue mutations near the leaves of each respective gene tree.

### Value

None.

### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

### References

Martin, L. C., Gloor, G. B., Dunn, S. D. & Wahl, L. M. *Using information theory to search for co-evolving residues in proteins*. *Bioinformatics*, 2005. **21**(4116-4124).

Zhao, N., et al., *Protein-protein interaction and non-interaction predictions using gene sequence natural vector*. *Nature Communications Biology*, 2022. **5**(652).

### See Also

[EvoWeaver](#)

[predict.EvoWeaver](#)

[EvoWeaver Phylogenetic Profiling Predictors](#)

[EvoWeaver Phylogenetic Structure Predictors](#)

[EvoWeaver Gene Organization Predictors](#)

**Description**

EvoWeb objects are outputted from `predict.EvoWeaver`.

This class wraps the `simMat` object with some other diagnostic information intended to help interpret the output of `EvoWeaver` predictions..

**Details**

`predict.EvoWeaver` returns a `EvoWeb` object, which bundles some methods to make formatting and printing of results slightly nicer. This currently only implements a plot function, but future functionality is in the works.

**Value**

An object of class "EvoWeb", which inherits from "simMat".

**Author(s)**

Aidan Lakshman <ahl27@pitt.edu>

**See Also**

`predict.EvoWeaver`

`simMat`

`plot.EvoWeb`

**Examples**

```
#####  
## Prediction with built-in model and data  
#####  
  
exData <- get(data("ExampleStreptomycesData"))  
  
# Subset isn't necessary but is faster for a working example  
ew <- EvoWeaver(exData$Genes[1:10])  
  
evoweb <- predict(ew, Method='Jaccard')  
  
# print out results as an adjacency matrix  
print(evoweb)  
  
# print out results as a pairwise data.frame  
as.data.frame(evoweb)
```

---

ExampleStreptomycesData

*Example EvoWeaver Input Data from Streptomyces Species*

---

### Description

Data from Streptomyces species to test [EvoWeaver](#) functionality.

### Usage

```
data("ExampleStreptomycesData")
```

### Details

This dataset contains a number of Clusters of Orthologous Genes (COGs) and a species tree for use with EvoWeaver. This dataset showcases an example of using EvoWeaver with a list of vectors. Entries in each vector are formatted correctly for use with co-localization prediction. Each COG *i* contains entries of the form *a\_b\_c*, indicating that the gene was found in genome *a* on chromosome *b*, and was at the *c*'th location. The original dataset is comprised of 301 unique genomes.

### Value

The data contain two elements, Genes and Tree. Genes is a list of presence/absence vectors in the input required for [EvoWeaver](#). Tree is a species tree used for additional input.

### See Also

[EvoWeaver](#)

### Examples

```
exData <- get(data("ExampleStreptomycesData"))
ew <- EvoWeaver(exData$Genes)
# Subset isn't necessary but is faster for a working example
predict(ew, Subset=1:10, MySpeciesTree=exData$Tree)
```

---

ExoLabel

*ExoLabel: Out of Memory Fast Label Propagation*

---

### Description

Runs Fast Label Propagation using disk space for constant memory complexity.

**Usage**

```
ExoLabel(edgelistfiles, outfile=tempfile(),
         mode=c("undirected", "directed"),
         add_self_loops=FALSE,
         ignore_weights=FALSE,
         normalize_weights=FALSE,
         iterations=0L,
         return_table=FALSE,
         consensus_cluster=FALSE,
         verbose=interactive(),
         sep='\t',
         tempfiledir=tempdir(),
         cleanup_files=TRUE)
```

**Arguments**

|                                |  |
|--------------------------------|--|
| <code>edgelistfiles</code>     | Character vector of files to be processed. Each entry should be a machine-interpretable path to an edgelist file. See Details for expected format.   |
| <code>outfile</code>           | File to write final clusters to. Optional, defaults to a temporary file.   |
| <code>mode</code>              | String specifying whether edges should be interpreted as undirected (default) or directed. Can be "undirected", "directed", or an unambiguous abbreviation.  |
| <code>add_self_loops</code>    | Should self loops be added to the network? If TRUE, adds self loops of weight 1.0 to all vertices. If set to numeric value <i>w</i> , adds self loops of weight <i>w</i> to all nodes. Note that this takes place prior to edge weight normalization (if requested).   |
| <code>ignore_weights</code>    | Should weights be ignored? If TRUE, all edges will be treated as an edge of weight 1. Must be set to TRUE if any of <code>edgelistfiles</code> are two-column tables (start->end only, lacking a weights column).  |
| <code>normalize_weights</code> | Should weights be normalized? If TRUE, each vertex's edge weights are normalized such that the outgoing edges have weight 1. This normalization is done after adding self loops.   |
| <code>iterations</code>        | Number of iterations to run fast label propagation algorithm for. Set to a value of 0 or less for infinite iterations.   |
| <code>return_table</code>      | Should result of clustering be returned as a file, or a <code>data.frame</code> object? If FALSE, returns a character vector corresponding to the path of <code>outfile</code> . If TRUE, parses <code>outfile</code> using <code>read.table</code> and returns the result. Not recommended for very large graphs. |
| <code>consensus_cluster</code> | Should consensus clustering be used? If TRUE, runs the clustering algorithm nine times and forms a consensus clustering based on the agreement of each run. Can be set to a double to control the number of iterations, see Details for more information.  |
| <code>verbose</code>           | Should status messages (output, progress, etc.) be displayed while running?  |
| <code>sep</code>               | Character that separates entries on a line in each file in <code>edgelistfiles</code> . Defaults to tab, as would be expected in a <code>.tsv</code> formatted file. Set to <code>,</code> for a <code>.csv</code> file.   |

|                            |   |
|----------------------------|---|
| <code>tempfiledir</code>   | Character vector corresponding to the location where temporary files used during execution should be stored. Defaults to R's <code>tempdir</code> .                             |
| <code>cleanup_files</code> | Should intermediary files be deleted when the process completes? Note that <code>outfile</code> will only be deleted if <code>return_table=TRUE AND cleanup_files=TRUE</code> . |

### Details

Very large graphs require too much RAM for processing on some machines. In a graph containing billions of nodes and edges, loading the entire structure into RAM is rarely feasible. This implementation uses disk space for storing representations of each graph. While this is slower than computing on RAM, it allows this algorithm to scale to graphs of enormous size while only taking a small amount of RAM. Local benchmarking resulting in a plateau of approximately 100MB of RAM consumption for arbitrarily sized networks. If your graph is small enough to fit into RAM, consider using the `LP_igraph()` function instead.

This function expects a set of `edgelist` files, provided as a vector of filepaths. Each entry in the file is expected to be in the following:

```
VERTEX1<sep>VERTEX2<sep>WEIGHT<linesep>
```

This line defines a single edge between vertices `VERTEX1` and `VERTEX2` with weight `WEIGHT`. `VERTEX1` and `VERTEX2` are strings corresponding to vertex names, `WEIGHT` is a numeric value that can be interpreted as a double. The separators `<sep>` and `<linesep>` correspond to the arguments `sep` and `linesep`, respectively. The default arguments work for standard `.tsv` formatting, i.e., a file of three columns of tab-separated values.

If `ignore_weight=TRUE`, the file can be formatted as:

```
VERTEX1<sep>VERTEX2<linesep>
```

Note that the `v1 v2 w` format is still accepted for `ignore_weight=FALSE`, but the specified weights will be ignored.

Consensus clustering can be enabled by setting `consensus_cluster=TRUE`. Consensus clustering runs this algorithm on the graph multiple times, transforming weight values according to a sigmoid function. By default, this runs nine times for sigmoids with scale 0.5 and shape `c(0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.33, 1.67, 2.0)` collapsing weights below 0.1 to zero. The resulting clusters form a network such that the edge weight between any two nodes connected in the initial graph is the proportion of clusters they shared over clustering runs. This network is used for a final label propagation run, which identifies the consensus clusters. Users can specify a numeric vector as input to `consensus_cluster`, which will override the default shape parameters and number of iterations.

### Value

If `return_table=TRUE`, returns a `data.frame` object with two columns. The first column contains the name of each vertex, and the second column contains the cluster it was assigned to.

If `return_table=FALSE`, returns a character vector of length 1. This vector contains the path to the file where clusters were written to. The file is formatted as a `.tsv`, with each line containing two tab separated columns (vertex name, assigned cluster)

### Warning

While this algorithm can scale to very large graphs, it does have some internal limitations. First, nodes must be comprised of no more than 254 characters. If this limitation is restrictive, please feel

free to contact me. Alternatively, you can increase the size yourself by changing the definition of `MAX_NODE_NAME_SIZE` in `src/outmem_graph.c`. This limitation is provided to decrease memory overhead and improve runtime, but arbitrary values are possible.

Second, nodes are indexed using 64-bit unsigned integers, with 0 reserved for other values. This means that the maximum possible number of nodes available is  $2^{64}-2$ , which is about 18.5 quintillion.

Third, this algorithm uses disk space to store large objects. As such, please ensure you have sufficient disk space for the graph you intend to process. I've tried to put safeguards in the code itself, but funky stuff can happen when the OS runs out of space.

The disk space required by this algorithm is equivalent to  $56V + LV + 16E$ , where  $V$  the number of unique vertices,  $L$  the average length of each vertex label, and  $E$  the number of edges. We can instead represent this purely in terms of vertices by setting  $D$  to the average degree of each node. The total disk space required is thus  $(56 + L + 16D)V$ . If you'd like to estimate the disk consumption of this algorithm, use the `EstimateExoLabel` function.

### Author(s)

Aidan Lakshman <AHL27@pitt.edu>

### References

Traag, V.A., Subelj, L. Large network community detection by fast label propagation. *Sci Rep* **13**, 2701 (2023). <https://doi.org/10.1038/s41598-023-29610-z>

### See Also

[EstimateExoLabel](#)

### Examples

```
num_verts <- 20L
num_edges <- 20L
all_verts <- sample(letters, num_verts)
all_edges <- vapply(seq_len(num_edges),
  \ (i) paste(c(sample(all_verts, 2L),
    as.character(round(runif(1),3))),
    collapse='\t'),
  character(1L))
edgefile <- tempfile()
if(file.exists(edgefile)) file.remove(edgefile)
writeLines(all_edges, edgefile)
res <- ExoLabel(edgefile, return_table=TRUE)
print(res)
```

---

|                |   |
|----------------|---|
| ExpandDiagonal | <i>Attempt to expand blocks of paired features in a PairSummaries object.</i> |
|----------------|---|

---

### Description

Attempt to expand blocks of paired features in a PairSummaries object.

### Usage

```
ExpandDiagonal(SynExtendObject,
               FeatureSeqs,
               DataBase,
               InheritConfidence = TRUE,
               GapTolerance = 100L,
               DropSingletons = FALSE,
               UserConfidence = list("PID" = 0.3),
               Verbose = FALSE)
```

### Arguments

|                   |  |
|-------------------|--|
| SynExtendObject   | An object of class PairSummaries.  |
| FeatureSeqs       | An object of class FeatureSeqs.  |
| DataBase          | A character string pointing to a SQLite database, or a connection to a DECIPHER database.  |
| InheritConfidence | A logical indicating whether or not to inherit the user specified column-value pairs assigned to the input object.   |
| GapTolerance      | Integer value indicating the diff between feature IDs that can be tolerated to view features as part of the same block. Set by default to 100L.  |
| DropSingletons    | Ignore solo pairs when planning expansion routes. Set to FALSE by default.   |
| UserConfidence    | A named list of length 1 where the name identifies a column of the PairSummaries object, and the value identifies a user confidence. Every k-means cluster with a center value of the column value selected greater than the confidence is retained. |
| Verbose           | Logical indicating whether or not to display a progress bar and print the time difference upon completion.   |

### Details

ExpandDiagonal uses a naive expansion algorithm to attempt to fill in gaps in blocks of paired features and to attempt to expand blocks of paired features.

### Value

An object of class PairSummaries.



**Author(s)**

Nicholas Cooley <npc19@pitt.edu>

**See Also**

[PairSummaries](#), [NucleotideOverlap](#), [link{SubSetPairs}](#), [FindSynteny](#)

**Examples**

```
DBPATH <- system.file("extdata",
                      "Endosymbionts_v02.sqlite",
                      package = "SynExtend")

data("Endosymbionts_LinkedFeatures", package = "SynExtend")
Endosymbiont_Seqs <- PrepareSeqs(SynExtendObject = Endosymbionts_LinkedFeatures,
                                DataBase = DBPATH,
                                Verbose = TRUE)

data("Endosymbionts_Pairs02", package = "SynExtend")
Pairs03 <- ExpandDiagonal(SynExtendObject = Endosymbionts_Pairs02,
                          DataBase = DBPATH,
                          FeatureSeqs = Endosymbiont_Seqs,
                          Verbose = TRUE)
```

---

ExtractBy

*Extract and organize DNASTringSetss.*

---

**Description**

Return organized DNASTringSets based on three currently supported object combinations. First return a single DNASTringSet of feature sequences from a DFrame of genecalls and a DNASTringSet of the source assembly. Second return a list of DNASTringSets of predicted pairs from a PairSummaries object and a character string of the location of a DECIPHER SQLite database. Third return a list of DNASTringSets of predicted single linkage communities from a PairSummaries object, a character string of the location of a DECIPHER SQLite database, and a list of identifiers generated by DisjointSet.

**Usage**

```
ExtractBy(x,
          y,
          z,
          Verbose = FALSE)
```

**Arguments**

|         |  |
|---------|--|
| x       | A PairSummaries object, or if y is a DNASTringSet, a DFrame of gene calls such as one generated by gffToDataFrame.   |
| y       | A character vector of length 1 indicating the location of a DECIPHER SQLite database. Or, if x is a DFrame, a DNASTringSet of the assembly the gene calls are called from. |
| z       | Optional; a list of identifiers generated by DisjointSet. Or any list built along a similar format with identifiers paired to the PairSummaries object.                    |
| Verbose | Logical indicating whether to print progress bars and messages. Defaults to FALSE.   |

**Details**

All sequences are forced into the same direction based on the Strand column supplied by either the gene calls DFrame specified by x, or the GeneCalls attribute of the PairSummaries object specified by y.

**Value**

Return a DNASTringSet, or list of DNASTringSets arranged depending upon the objects supplied. See description.

**Author(s)**

Nicholas Cooley <npc19@pitt.edu>

**See Also**

[FindSynteny](#), [Synteny-class](#), [PairSummaries](#), [DisjointSet](#)

**Examples**

```
DBPATH <- system.file("extdata",
                     "Endosymbionts_v02.sqlite",
                     package = "SynExtend")
data("Endosymbionts_Pairs03", package = "SynExtend")
data("Endosymbionts_Sets", package = "SynExtend")

# extract the first 10 disjoint sets
Sets <- ExtractBy(x = Endosymbionts_Pairs03,
                 y = DBPATH,
                 z = Endosymbionts_Sets[1:10],
                 Verbose = TRUE)

# extract just the pairs
Sets <- ExtractBy(x = Endosymbionts_Pairs03,
                 y = DBPATH,
                 Verbose = TRUE)
```

FastQFromSRR

*Get Sequencing Data from the SRA***Description**

Get sequencing data from the SRA.

**Usage**

```
FastQFromSRR(SRR,
             ARGS = list("--gzip" = NULL,
                        "--skip-technical" = NULL,
                        "--readids" = NULL,
                        "--read-filter" = "pass",
                        "--dumpbase" = NULL,
                        "--split-3" = NULL,
                        "--clip" = NULL),
             KEEPFILES = FALSE)
```

**Arguments**

|           |   |
|-----------|---|
| SRR       | A character vector of length 1 representing an SRA Run Accession, such as one that would be passed to the <code>prefetch</code> , <code>fastq-dump</code> , or <code>fasterq-dump</code> functions in the SRAToolkit.   |
| ARGS      | A list representing key and value sets used to construct the call to <code>fastq-dump</code> , multi-argument values are passed to <code>paste</code> directly and should be structured accordingly.  |
| KEEPFILES | Logical indicating whether or not keep the downloaded fastq files outside of the R session. If TRUE, downloaded files will be moved to R's working directory with the default names assigned by <code>fastq-dump</code> . If FALSE - the default, they are removed and only the list of <code>QualityScaledDNASringSets</code> returned by the function are retained. |

**Details**

`FastQFromSRR` is a barebones wrapper for `fastq-dump`, it is set up for convenience purposes only and does not add any additional functionality. Requires a functioning installation of the SRAToolkit.

**Value**

A list of `QualityScaledDNASringSets`. The composition of this list will be determined by `fastq-dump`'s splitting arguments.

**Author(s)**

Nicholas Cooley <npc19@pitt.edu>

**Examples**

```
x <- "ERR10466327"  
y <- FastQFromSRR(SRR = x)
```

---

**FindSets***Find all single linkage clusters in an undirected pairs list.*

---

**Description**

Take in a pair of vectors representing the columns of an undirected pairs list and return the single linkage clusters.

**Usage**

```
FindSets(p1,  
         p2,  
         Verbose = FALSE)
```

**Arguments**

|         |  |
|---------|--|
| p1      | Column 1 of a pairs matrix or list.  |
| p2      | Column 2 of a pairs matrix or list.  |
| Verbose | Logical indicating whether or not to display a progress bar and print the time difference upon completion. |

**Details**

FindSets uses a version of the union-find algorithm to collect single linkage clusters from a pairs list. Currently meant to be used inside a wrapper function, but left exposed for user convenience.

**Value**

A two column matrix with the first column being input nodes, and the second the node representing a single linkage cluster.

**Author(s)**

Nicholas Cooley <npc19@pitt.edu>

**See Also**

[PairSummaries](#)

**Examples**

```

set.seed(1986)
m <- cbind(as.integer(sample(30, size = 25,
                           replace = TRUE)),
           as.integer(sample(35, size = 25,
                           replace = TRUE)))

Levs <- unique(c(m[, 1],
                m[, 2]))
m <- cbind("1" = as.integer(factor(x = m[, 1L],
                                  levels = Levs)),
          "2" = as.integer(factor(x = m[, 2L],
                                  levels = Levs)))

z <- FindSets(p1 = m[, 1],
              p2 = m[, 2])

```

---

FitchParsimony

*Calculate ancestral states using Fitch Parsimony*


---

**Description**

Ancestral states for binary traits can be inferred from presence/absence patterns at the tips of a dendrogram using Fitch Parsimony. This function works for an arbitrary number of states on bifurcating dendrogram objects.

**Usage**

```

FitchParsimony(dend, num_traits, traits_list,
               initial_state=rep(0L,num_traits),
               fill_ambiguous=TRUE)

```

**Arguments**

|                             |   |
|-----------------------------|---|
| <code>dend</code>           | An object of class 'dendrogram'   |
| <code>num_traits</code>     | The number of traits to inferred, as an integer.  |
| <code>traits_list</code>    | A list of character vectors, where the <i>i</i> 'th entry corresponds to the leaf labels that have the trait <i>i</i> . |
| <code>initial_state</code>  | The state assumed for the root node. Set to NULL to disable autofilling the root state.                                 |
| <code>fill_ambiguous</code> | If TRUE, states that remain ambiguous after completion of the algorithm are filled in randomly.                         |

**Details**

Fitch Parsimony allows for fast inference of ancestral states of binary traits. The algorithm proceeds in three steps.

First, traits are inferred upwards based on child nodes. If the child nodes have the same state (1/1 or 0/0), then the parent node is also set to that state. If the states are different, the parent node is set to 2, denoting an ambiguous entry. If one child is ambiguous and the other is not, the parent is set to the non-ambiguous entry.

Second, traits are inferred downward to attempt to fill in ambiguous entries. If a node is not ambiguous but its child is, the child's state is set to the parent state. If specified, the root node's state is set to `initial_state` prior to this step.

Third, traits that remain ambiguous are optionally filled in (only if `fill_ambiguous` is set to TRUE). This proceeds by randomly setting ambiguous traits to either 1 or 0.

The result is stored in the `FitchState` attribute within each node.

**Value**

A dendrogram with attribute `FitchState` set for each node, where this attribute is a binary vector of length `num_traits`.

**Note**

It's `FitchParsimony` because this implementation is entirely in R, as opposed to internal `SynExtend` methods that utilize a slightly faster C-based implementation that is not user-exposed.

**Author(s)**

Aidan Lakshman <ahl27@pitt.edu>

**References**

Fitch, Walter M. *Toward defining the course of evolution: minimum change for a specific tree topology*. *Systematic Biology*, 1971. **20**(4): p. 406-416.

**Examples**

```
d <- as.dendrogram(hclust(dist(USArrests), "ave"))
labs <- labels(d)

# Defining some presence absence patterns
set.seed(123L)
pa_1 <- sample(labs, 15L)
pa_2 <- sample(labs, 20L)

# inferring ancestral states
fpd <- FitchParsimony(d, 2L, list(pa_1, pa_2))

# Checking a state
attr(fpd[[1L]], 'FitchState')
```

```

# Visualizing the results for the first pattern
# Tips show P/A patterns, edges show gain/loss (green/red)
fpd <- dendrapply(fpd, \(x){
  ai <- 1L
  s <- attr(x, 'FitchState')
  l <- list()

  if(is.leaf(x)){
    # coloring tips based presence/absence
    l$col <- ifelse(s[ai]==1L, 'green', 'red')
    l$pch <- 19
    attr(x, 'nodePar') <- 1
  } else {
    # coloring edges based on gain/loss
    for(i in seq_along(x)){
      sc <- attr(x[[i]], 'FitchState')
      if(s[ai] != sc[ai]){
        l$col <- ifelse(s[ai] == 1L, 'red', 'green')
      } else {
        l$col <- 'black'
      }
      attr(x[[i]], 'edgePar') <- 1
    }
  }

  x
}, how='post.order')
plot(fpd, leaflab='none')

```

---

Generic

*Model for predicting PID based on k-mer statistics*

---

### Description

Though the function `PairSummaries` provides an argument allowing users to ask for alignments, given the time consuming nature of that process on large data, models are provided for predicting PIDs of pairs based on k-mer statistics without performing alignments.

### Usage

```
data("Generic")
```

### Details

A model for predicting the PID of a pair of sequences based on the k-mers that were used to link the pair.

### Value

The format is an object of class “glm”.

**Examples**

```
data(Generic)
```

---

|                |  |
|----------------|--|
| gffToDataFrame | <i>Generate a DataFrame of gene calls from a gff3 file</i> |
|----------------|--|

---

**Description**

Generate a DataFrame of gene calls from a gff3 file

**Usage**

```
gffToDataFrame(GFF,
               AdditionalAttrs = NULL,
               AdditionalTypes = NULL,
               RawTableOnly = FALSE,
               Verbose = FALSE)
```

**Arguments**

|                 |  |
|-----------------|--|
| GFF             | A url or filepath specifying a gff3 file to import   |
| AdditionalAttrs | A vector of character strings to designate the attributes to pull. Default Attributes include: "ID", "Parent", "Name", "gbkey", "gene", "product", "protein_id", "gene_biotype", "transl_table", and "Note".                   |
| AdditionalTypes | A vector of character strings to query from the the "Types" column. Default types are limited to "Gene" and "Pseudogene", but any possible entry for "Type" in a gff3 format can be added, such as "rRNA", or "CRISPR_REPEAT". |
| RawTableOnly    | Logical specifying whether to return the raw imported GFF without complex parsing. Remains as a holdover from function construction and debugging. For simple gff3 import see <code>rtracklayer::import</code> .               |
| Verbose         | Logical specifying whether to print a progress bar and time difference.  |

**Details**

Import a gff file into a rectangular parsable object.

**Value**

A DataFrame with relevant information extracted from a GFF.

**Author(s)**

Nicholas Cooley <npc19@pitt.edu>



**Examples**

```
ImportedGFF <- gffToDataFrame(GFF = system.file("extdata",
                                             "GCF_021065005.1_ASM2106500v1_genomic.gff.gz",
                                             package = "SynExtend"),
                             Verbose = TRUE)
```

---

 LinkedPairs

*Tables of where syntenic hits link pairs of genes*


---

**Description**

Syntenic blocks describe where order is shared between two sequences. These blocks are made up of exact match hits. These hits can be overlaid on the locations of sequence features to clearly illustrate where exact sequence similarity is shared between pairs of sequence features.

**Usage**

```
## S3 method for class 'LinkedPairs'
print(x,
      quote = FALSE,
      right = TRUE,
      ...)
```

**Arguments**

|       |  |
|-------|--|
| x     | An object of class <code>LinkedPairs</code> .                        |
| quote | Logical indicating whether to print the output surrounded by quotes. |
| right | Logical specifying whether to right align strings.                   |
| ...   | Other arguments for <code>print</code> .                             |

**Details**

Objects of class `LinkedPairs` are stored as square matrices of list elements with `dimnames` derived from the `dimnames` of the object of class `"Synteny"` from which it was created. The diagonal of the matrix is only filled if `OutputFormat "Comprehensive"` is selected in `NucleotideOverlap`, in which case it will be filled with the gene locations supplied to `GeneCalls`. The upper triangle is always filled, and contains location information in nucleotide space for all syntenic hits that link features between sequences in the form of an integer matrix with named columns. `"QueryGene"` and `"SubjectGene"` correspond to the integer rownames of the supplied gene calls. `"QueryIndex"` and `"SubjectIndex"` correspond to `"Index1"` and `"Index2"` columns of the source `synteny` object position. Remaining columns describe the exact positioning and size of extracted hits. The lower triangle is not filled if `OutputFormat "Sparse"` is selected and contains relative displacement positions for the 'left-most' and 'right-most' hit involved in linking the particular features indicated in the related line up the corresponding position in the upper triangle.

The object serves only as a simple package for input data to the `PairSummaries` function, and as such may not be entirely user friendly. However it has been left exposed to the user should they find this data interesting.

**Value**

An object of class "LinkedPairs".

**Author(s)**

Nicholas Cooley <npc19@pitt.edu>

---

MakeBlastDb

*Create a BLAST Database from R*

---

**Description**

Wrapper to create **BLAST** databases for subsequent queries using the commandline BLAST tool directly from R. Can operate on an [XStringSet](#) or a FASTA file.

This function requires the BLAST+ commandline tools, which can be downloaded [here](#).

**Usage**

```
MakeBlastDb(seqs, dbtype=c('prot', 'nucl'),
            dbname=NULL, dbpath=NULL,
            extraArgs='', createDirectory=FALSE,
            verbose=TRUE)
```

**Arguments**

|                 |   |
|-----------------|---|
| seqs            | Sequence(s) to create a BLAST database from. This can be either an <a href="#">XStringSet</a> or a path to a FASTA file.                        |
| dbtype          | Either 'prot' for amino acid input, or 'nucl' for nucleotide input.   |
| dbname          | Name of the resulting database. If not provided, defaults to a random string prefixed by blastdb.   |
| dbpath          | Path where database should be created. If not provided, defaults to <a href="#">TMPDIR</a> .  |
| extraArgs       | Additional arguments to be passed to the query executed on the command line. This should be a single character string.                          |
| createDirectory | Should a directory be created for the database if it doesn't exist? If FALSE, the function will throw an error instead of creating a directory. |
| verbose         | Should output be displayed?   |

**Details**

This offers a quick way to create BLAST databases from R. This function essentially wraps the makeblastdb commandline function. All arguments supported by makeblastdb are supported in the extraArgs argument.

**Value**

Returns a length 2 named character vector specifying the name of the BLAST database and the path to it.

**Author(s)**

Aidan Lakshman <ahl27@pitt.edu>

**See Also**

[BlastSeqs](#)

**Examples**

#

---

MoransI

*Moran's I Spatial Autocorrelation Index*

---

**Description**

Calculates Moran's *I* to measure spatial autocorrelation for a set of signals dispersed in space.

**Usage**

MoransI(values, weights, alternative='two.sided')

**Arguments**

|             |  |
|-------------|--|
| values      | Numeric vector containing signals for each point in space.   |
| weights     | Distances between each point in space. This should be a numeric object of class <a href="#">dist</a> with Size attribute equivalent to the length of values.                               |
| alternative | For hypothesis testing against the null of no spatial correlation, how should a p-value be calculated? Should be one of c("two.sided", "less", "greater"), or an unambiguous abbreviation. |

**Details**

Moran's *I* is a measure of how much the spatial arrangement of a set of datapoints correlates with the value of each datapoint. The index takes a value in the range  $[-1, 1]$ , with values close to 1 indicating high correlation between location and value (points have increasingly similar values as they increase in proximity), values close to -1 indicating anticorrelation (points have increasingly different values as they increase in proximity), and values close to 0 indicating no correlation.

The value itself is calculated as:

$$I = \frac{N \sum_i \sum_j w_{ij} (x_i - \bar{x})(x_j - \bar{x})}{W \sum_i (x_i - \bar{x})^2}$$

Here,  $N$  is the number of points,  $w_{ij}$  is the distance between points  $i$  and  $j$ ,  $W = \sum_{i,j} w_{ij}$  (the sum of all the weights),  $x_i$  is the value of point  $i$ , and  $\bar{x}$  is the sample mean of the values.

Moran's  $I$  has a closed form calculation for variance and expected value, which are calculated within this function. The full form of the variance is fairly complex, but all the equations are available for reference [here](#).

A p-value is estimated using the expected value and variance using a null hypothesis of no spatial autocorrelation, and the alternative hypothesis specified in the `alternative` argument. Note that if fewer than four datapoints are supplied, the variance of Moran's  $I$  is infinite. The function will return a standard deviation of `Inf` and a p-value of 1 in this case.

### Value

A `list` object containing the following named values:

- `observed`: The value of Moran's  $I$  (numeric in the range  $[-1, 1]$ ).
- `expected`: The expected value of Moran's  $I$  for the input data.
- `sd`: The standard deviation of Moran's  $I$  for the input data.
- `p.value`: The p-value for the input data, calculated with the alternative hypothesis as specified in `alternative`.

### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

### References

Moran, P. A. P., *Notes on Continuous Stochastic Phenomena*. Biometrika, 1950. **37**(1): 17-23.

Gittleman, J. L. and M. Kot., *Adaptation: Statistics and a Null Model for Estimating Phylogenetic Effects*. Systematic Zoology, 1990. **39**:227-241.

### Examples

```
# Make a distance matrix for a set of 50 points
# These are just random numbers in the range [0.1,2]
NUM_POINTS <- 50
distmat <- as.dist(matrix(runif(NUM_POINTS**2, 0.1, 2),
                             ncol=NUM_POINTS))

# Generate some random values for each of the points
vals <- runif(NUM_POINTS, 0, 3)

# Calculate Moran's I
MoransI(vals, distmat, alternative='two.sided')

# effect size should be pretty small
# and p-value close to 0.5
# since this is basically random data
```

---

NucleotideOverlap      *Tabulating Pairs of Genomic Sequences*

---

### Description

A function for concisely tabulating where genomic features are connected by syntenic hits.

### Usage

```
NucleotideOverlap(SytenyObject,
                  GeneCalls,
                  LimitIndex = FALSE,
                  AcceptContigNames = TRUE,
                  Verbose = FALSE)
```

### Arguments

- |                   |  |
|-------------------|--|
| SytenyObject      | An object of class “Syteny” built from the <code>FindSyteny</code> in the package DECIPHER.  |
| GeneCalls         | A named list of objects of class “DFrame” built from <code>gffToDataFrame</code> , objects of class “GRanges” imported from <code>rtracklayer::import</code> , or objects of class “Genes” created from the DECIPHER function <code>FindGenes</code> . “DFrame”s built by “ <code>gffToDataFrame</code> ” can be used directly, while “GRanges” objects may also be used with limited functionality. Using a “GRanges” object will force all alignments to nucleotide alignments. Objects of class “Genes” generated by <code>FindGenes</code> function equivalently to those produced by <code>gffToDataFrame</code> . Using a “GRanges” object will force <code>LimitIndex</code> to TRUE. |
| LimitIndex        | Logical indicating whether to limit which indices in a syteny object to query. FALSE by default, when TRUE only the first sequence in all selected identifiers will be used. <code>LimitIndex</code> can be used to skip analysis of plasmids, or solely query a single chromosome.  |
| AcceptContigNames | Match names of contigs between gene calls object and syteny object. Where relevant, the first white space and everything following are removed from contig names. If “TRUE”, <code>NucleotideOverlap</code> assumes that the contigs at each position in the syteny object and “GeneCalls” object are in the same order. Is automatically set to TRUE when “GeneCalls” are of class “GRanges”.   |
| Verbose           | Logical indicating whether or not to display a progress bar and print the time difference upon completion.   |

### Details

Builds a matrix of lists that contain information about linked pairs of genomic features.

**Value**

An object of class “LinkedPairs”. “LinkedPairs” is fundamentally just a list in the form of a matrix. The lower triangle of the matrix is populated with matrices that contain all kmer hits from the “Synteny” object that link features from the “GeneCalls” object. The upper triangle is populated by matrices of the summaries of those hits by feature. The diagonal is populated by named vectors of the lengths of the contigs, much like in the “Synteny” object. The “LinkedPairs” object also contains a “GeneCalls” attribute that contains the user supplied features in a slightly more trimmed down form. This allows users to only need to supply gene calls once and not again in the “PairSummaries” function.

**Author(s)**

Nicholas Cooley <npc19@pitt.edu>

**See Also**

[FindSynteny](#), [Synteny-class](#)

**Examples**

```
data("Endosymbionts_GeneCalls", package = "SynExtend")
data("Endosymbionts_Synteny", package = "SynExtend")

Links <- NucleotideOverlap(SyntenyObject = Endosymbionts_Synteny,
                          GeneCalls = Endosymbionts_GeneCalls,
                          LimitIndex = FALSE,
                          Verbose = TRUE)
```

---

PairSummaries

*Summarize connected pairs in a LinkedPairs object*

---

**Description**

Takes in a “LinkedPairs” object and gene calls, and returns a data.frame of paired features.

**Usage**

```
PairSummaries(SyntenyLinks,
              DBPATH,
              PIDs = FALSE,
              Score = FALSE,
              IgnoreDefaultStringSet = FALSE,
              Verbose = FALSE,
              Model = "Generic",
              DefaultTranslationTable = "11",
              AcceptContigNames = TRUE,
              OffSetsAllowed = NULL,
              Storage = 1,
              ...)
```

**Arguments**

|                         |   |
|-------------------------|---|
| Syntenylinks            | A LinkedPairs object. In previous versions of this function, a GeneCalls object was also required, but this object is now carried forward from NucleotideOverlap inside the LinkedPairs object.   |
| DBPATH                  | A SQLite connection object or a character string specifying the path to the database file constructed from DECIPHER's Seqs2DB function. This path is always required as "PairsSummaries" always computes the tetramer distance between paired sequences.  |
| PIDs                    | Logical indicating whether to provide a PID for each pair. If TRUE all pairs will be aligned using DECIPHER's AlignProfiles. This step can be time consuming, especially for large numbers of pairs. Default is FALSE.  |
| Score                   | Logical indicating whether to provide a length normalized score with DECIPHER's ScoreAlignment function. If TRUE all pairs will be aligned using DECIPHER's AlignProfiles. This step can be time consuming, especially for large numbers of pairs. Default is FALSE.  |
| IgnoreDefaultStringSet  | Logical indicating alignment type preferences. If FALSE (the default) pairs that can be aligned in amino acid space will be aligned as an AAStringSet. If TRUE all pairs will be aligned in nucleotide space. For PairSummaries to align the translation of a pair of sequences, both sequences must be tagged as coding in the "GeneCalls" object, and be the correct width for translation.   |
| Verbose                 | Logical indicating whether or not to display a progress bar and print the time difference upon completion.  |
| Model                   | A character string specifying a model to use to predict PIDs without performing an alignment. By default this argument is "Generic" specifying a generic PID prediction model based on PIDs computed from a randomly selected set of genomes. Currently no other models are included. Users may also supply their own model of type "glm" if they so desire in the form of an RData file. This model will need to take in some, or of the columns of statistics per pair that PairSummaries supplies. |
| DefaultTranslationTable | A character used to set the default translation table for translate. Is passed to getGeneticCode. Used when no translation table is specified in the "GeneCalls" object.  |
| AcceptContigNames       | Match names of contigs between gene calls object and syntenylinks object. Where relevant, the first white space and everything following are removed from contig names. If TRUE, PairSummaries assumes that the contigs at each position in the syntenylinks object and "GeneCalls" object are in the same order. Is automatically set to TRUE when "GeneCalls" are of class "GRanges". Is currently TRUE by default.   |
| OffsetsAllowed          | Defaults to NULL. Supplying an integer vector will indicate gap sizes to attempt to fill. A value of 2 will attempt to span gaps of size 1. If a vector larger than 1 is provided, i.e. c(2, 3), will attempt to query all gap sizes implied by the vector, in this case gaps of size 1 and 2.  |

|         |   |
|---------|---|
| Storage | Numeric indicating the approximate size a user wishes to allow for holding StringSets in memory to extract gene sequences, in “Gigabytes”. The lower Storage is set, the more likely that PairSummaries will need to reaccess StringSets when extracting gene sequences. The higher Storage is set, the more sequences PairSummaries will attempt to hold in memory, avoiding the need to re-access the source database many times. Set to 1 by default, indicating that PairSummaries can store a “Gigabyte” of sequences in memory at a time. |
| ...     | Arguments to be passed to AlignProfiles, and DistanceMatrix.  |

### Details

The LinkedPairs object generated by NucleotideOverlap is a container for raw data that describes possible orthologous relationships, however ultimate assignment of orthology is up to user discretion. PairSummaries generates a clear table with relevant statistics for a user to work with as they choose. The option to align all pairs, though onerous can allow users to apply a hard threshold to predictions by PID, while built in models can allow more expedient thresholding from predicted PIDs.

### Value

A data.frame of class “data.frame” and “PairSummaries” of paired genes that are connected by syntenic hits. Contains columns describing the k-mers that link the pair. Columns “p1” and “p2” give the location ids of the the genes in the pair in the form “DatabaseIdentifier\_ContigIdentifier\_GeneIdentifier”. “ExactMatch” provides an integer representing the exact number of nucleotides contained in the linking k-mers. “TotalKmers” provides an integer describing the number of distinct k-mers linking the pair. “MaxKmer” provides an integer describing the largest k-mer that links the pair. A column titled “Consensus” provides a value between zero and 1 indicating whether the kmers that link a pair of features are in the same position in each feature, with 1 indicating they are in exactly the same position and 0 indicating they are in as different a position as is possible. The “Adjacent” column provides an integer value ranging between 0 and 2 denoting whether a feature pair’s direct neighbors are also paired. Gap filled pairs neither have neighbors, or are included as neighbors. The “TetDist” column provides the euclidean distance between oligonucleotide - of size 4 - frequencies between predicted pairs. “PIDType” provides a character vector with values of “NT” where either of the pair indicates it is not a translatable sequence or “AA” where both sequences are translatable. If users choose to perform pairwise alignments there will be a “PID” column providing a numeric describing the percent identity between the two sequences. If users choose to predict PIDs using their own, or a provided model, a “PredictedPID” column will be provided.

### Author(s)

Nicholas Cooley <npc19@pitt.edu>

### See Also

[FindSyteny](#), [Syteny-class](#), [NucleotideOverlap](#)

### Examples

```
# this function will be deprecated soon,
```



```
# please see the new SummarizePairs() function.
DBPATH <- system.file("extdata",
                      "Endosymbionts_v02.sqlite",
                      package = "SynExtend")

data("Endosymbionts_LinkedFeatures", package = "SynExtend")

Pairs <- PairSummaries(SytenyLinks = Endosymbionts_LinkedFeatures,
                      PIDs = FALSE,
                      DBPATH = DBPATH,
                      Verbose = TRUE)
```

---

PhyloDistance

*Calculate Distance between Unrooted Phylogenies*


---

### Description

Calculates distance between two unrooted phylogenies using a variety of metrics.

### Usage

```
PhyloDistance(dend1, dend2,
              Method=c("CI", "RF", "KF", "JRF"),
              RawScore=FALSE, JRFExp=2)
```

### Arguments

|          |  |
|----------|--|
| dend1    | An object of class dendrogram, representing an unrooted bifurcating phylogenetic tree.   |
| dend2    | An object of class dendrogram, representing an unrooted bifurcating phylogenetic tree.   |
| Method   | Method to use for calculating tree distances. The following values are supported: "CI", "RF", "KF", "JRF". See Details for more information.   |
| RawScore | If FALSE, returns distance between the two trees. If TRUE, returns the component values used to calculate the distance. This may be preferred for methods like GRF. See the pages specific to each algorithm for more information on what values are reported. |
| JRFExp   | k-value used in calculation of JRF Distance. Unused if Method is not "JRF".  |

### Details

This function implements a variety of tree distances, specified by the value of Method. The following values are supported, along with links to documentation pages for each function:

- "RF": [Robinson-Foulds Distance](#)
- "CI": [Clustering Information Distance](#)
- "JRF": [Jaccard-Robinson-Foulds Distance](#), equivalent to the Nye Distance Metric when  $JRFVa1=1$

- "KF": [Kuhner-Felsenstein Distance](#)

Information on each of these algorithms, how scores are calculated, and references to literature can be found at the above links. Method "CI" is selected by default due to recent work showing this method as the most robust tree distance metric under general conditions.

### Value

Returns a normalized distance, with 0 indicating identical trees and 1 indicating maximal difference. If the trees have no leaves in common, the function will return 1.

If RawScore=TRUE, returns a vector of the components used to calculate the distance. This is typically a length 3 vector, but specific details can be found on the description for each algorithm.

### Note

Note that this function requires the input dendrograms to be labeled alike (ex. leaf labeled abc in dend1 represents the same species as leaf labeled abc in dend2). Labels can easily be modified using [dendrapply](#).

### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

### See Also

[Robinson-Foulds Distance](#)  
[Clustering Information Distance](#)  
[Jaccard-Robinson-Foulds Distance](#)  
[Kuhner-Felsenstein Distance](#)

### Examples

```
# making some toy dendrograms
set.seed(123)
dm1 <- as.dist(matrix(runif(64, 0.5, 5), ncol=8))
dm2 <- as.dist(matrix(runif(64, 0.5, 5), ncol=8))

tree1 <- as.dendrogram(hclust(dm1))
tree2 <- as.dendrogram(hclust(dm2))

# Robinson-Foulds Distance
PhyloDistance(tree1, tree2, Method="RF")

# Clustering Information Distance
PhyloDistance(tree1, tree2, Method="CI")

# Kuhner-Felsenstein Distance
PhyloDistance(tree1, tree2, Method="KF")

# Nye Distance Metric
```

```
PhyloDistance(tree1, tree2, Method="JRF", JRFExp=1)

# Jaccard-Robinson-Foulds Distance
PhyloDistance(tree1, tree2, Method="JRF", JRFExp=2)
```

---

PhyloDistance-CIDist    *Clustering Information Distance*

---

### Description

Calculate distance between two unrooted phylogenies using mutual clustering information of branch partitions.

### Details

This function is called as part of [PhyloDistance](#) and calculates tree distance using the clustering information approach first described in Smith (2020). This function iteratively pairs internal tree branches of a phylogeny based on their similarity, then scores overall similarity as the sum of these measures. The similarity score is then converted to a distance by normalizing by the average entropy of the two trees. This metric has been demonstrated to outperform numerous other metrics in capabilities; see the original publication cited in References for more information.

Users may wish to use the actual similarity values rather than a distance metric; the option to specify `RawScore=TRUE` is provided for this case. Distance is calculated as  $\frac{M-S}{M}$ , where  $M = \frac{1}{2}(H_1 + H_2)$ ,  $H_i$  is the entropy of the  $i$ 'th tree, and  $S$  is the similarity score between them. As shown in the original publication, this satisfies the necessary requirements to be considered a distance metric. Setting `RawScore=TRUE` will instead return a vector with  $(S, H_1, H_2, p)$ , where  $p$  is an approximation for the two sided p-value of the result based on random simulations from Smith (2020).

### Value

Returns a normalized distance, with 0 indicating identical trees and 1 indicating maximal difference. Note that branch lengths are not considered, so two trees with different branch lengths may return a distance of 0.

If `RawScore=TRUE`, returns a named length 4 vector with the first entry the similarity score, subsequent entries the entropy values for each tree, and the last entry the approximate p-value for the result based on simulations.

If the trees have no leaves in common, the function will return 1 if `RawScore=FALSE`, and `c(0, NA, NA, NA)` if `TRUE`.

### Note

Note that this function requires the input dendrograms to be labeled alike (ex. leaf labeled abc in dend1 represents the same species as leaf labeled abc in dend2). Labels can easily be modified using [dendrapply](#).

**Author(s)**

Aidan Lakshman <ahl27@pitt.edu>

**References**

Smith, Martin R. *Information theoretic generalized Robinson–Foulds metrics for comparing phylogenetic trees*. *Bioinformatics*, 2020. **36**(20):5007-5013.

**Examples**

```
# making some toy dendrograms
set.seed(123)
dm1 <- as.dist(matrix(runif(64, 0.5, 5), ncol=8))
dm2 <- as.dist(matrix(runif(64, 0.5, 5), ncol=8))

tree1 <- as.dendrogram(hclust(dm1))
tree2 <- as.dendrogram(hclust(dm2))

# get RF distance
PhyloDistance(tree1, tree2, Method="CI")

# get similarity score with individual entropies
PhyloDistance(tree1, tree2, Method="CI", RawScore=TRUE)
```

---

PhyloDistance-JRFDist *Jaccard-Robinson-Foulds Distance*

---

**Description**

Calculate JRF distance between two unrooted phylogenies.

**Details**

This function is called as part of [PhyloDistance](#) and calculates the Jaccard-Robinson-Foulds distance between two unrooted phylogenies. Each dendrogram is first pruned to only internal branches implying a partition in the shared leaf set; trivial partitions (where one leaf set contains 1 or 0 leaves) are ignored.

The total score is calculated by pairing branches and scoring their similarity. For a set of two branches  $A, B$  that partition the leaves into  $(A_1, A_2)$  and  $(B_1, B_2)$  (resp.), the distance between the branches is calculated as:

$$2 - 2 \left( \frac{|X \cap Y|}{|X \cup Y|} \right)^k$$

where  $X \in (A_1, A_2)$ ,  $Y \in (B_1, B_2)$  are chosen to maximize the score of the pairing, and  $k$  the value of `ExpVal`. The sum of these scores for all branches produces the overall distance between the two trees, which is then normalized by the number of branches in each tree.

There are a few special cases to this distance. If `ExpVal=1`, the distance is equivalent to the metric introduced in Nye et al. (2006). As `ExpVal` approaches infinity, the value becomes close to the (non-Generalized) Robinson Foulds Distance.

### Value

Returns a normalized distance, with 0 indicating identical trees and 1 indicating maximal difference.

If `RawScore=TRUE`, returns a named length 3 vector with the first entry the summed distance score over the branch pairings, and the subsequent entries the number of partitions for each tree.

If the trees have no leaves in common, the function will return 1 if `RawScore=FALSE`, and `c(0, NA, NA)` if `TRUE`.

### Note

Note that this function requires the input dendrograms to be labeled alike (ex. leaf labeled abc in `dend1` represents the same species as leaf labeled abc in `dend2`). Labels can easily be modified using [dendrapply](#).

### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

### References

Nye, T. M. W., Liò, P., & Gilks, W. R. *A novel algorithm and web-based tool for comparing two alternative phylogenetic trees*. *Bioinformatics*, 2006. **22**(1): 117–119.

Böcker, S., Canzar, S., & Klau, G. W.. *The generalized Robinson-Foulds metric*. *Algorithms in Bioinformatics*, 2013. **8126**: 156–169.

### Examples

```
# making some toy dendrograms
set.seed(123)
dm1 <- as.dist(matrix(runif(64, 0.5, 5), ncol=8))
dm2 <- as.dist(matrix(runif(64, 0.5, 5), ncol=8))

tree1 <- as.dendrogram(hclust(dm1))
tree2 <- as.dendrogram(hclust(dm2))

# Nye Metric
PhyloDistance(tree1, tree2, Method="JRF", JRFExp=1)

# Jaccard-RobinsonFoulds
PhyloDistance(tree1, tree2, Method="JRF", JRFExp=2)

# Good approximation to RF Dist (note RFDist is much faster for this)
PhyloDistance(tree1, tree2, Method="JRF", JRFExp=1000)
PhyloDistance(tree1, tree2, Method="RF")
```

---

**PhyloDistance-KFDist** *Kuhner-Felsenstein Distance*

---

**Description**

Calculate KF distance between two unrooted phylogenies.

**Details**

This function is called as part of [PhyloDistance](#) and calculates Kuhner-Felsenstein distance between two unrooted phylogenies. Each dendrogram is first pruned to only internal branches implying a partition in the shared leaf set; trivial partitions (where one leaf set contains 1 or 0 leaves) are ignored. The total score is calculated as the sum of squared differences between lengths of branches implying equivalent partitions. If a particular branch is unique to a given tree, it is treated as having length 0 in the other tree. The final score is normalized by the sum of squared lengths of all internal branches of both trees, resulting in a final distance that ranges from 0 to 1.

**Value**

Returns a normalized distance, with 0 indicating identical trees and 1 indicating maximal difference. If the trees have no leaves in common, the function will return 1.

**Note**

Note that this function requires the input dendrograms to be labeled alike (ex. leaf labeled abc in dend1 represents the same species as leaf labeled abc in dend2). Labels can easily be modified using [dendrapply](#).

**Author(s)**

Aidan Lakshman <ahl27@pitt.edu>

**References**

Robinson, D.F. and Foulds, L.R. *Comparison of phylogenetic trees*. *Mathematical Biosciences*, 1987. **53**(1–2): 131–147.

Kuhner, M. K. and Felsenstein, J. *Simulation comparison of phylogeny algorithms under equal and unequal evolutionary rates*. *Molecular Biology and Evolution*, 1994. **11**: 459–468.

**Examples**

```
# making some toy dendrograms
set.seed(123)
dm1 <- as.dist(matrix(runif(64, 0.5, 5), ncol=8))
dm2 <- as.dist(matrix(runif(64, 0.5, 5), ncol=8))

tree1 <- as.dendrogram(hclust(dm1))
tree2 <- as.dendrogram(hclust(dm2))
```

```
# get KF distance
PhyloDistance(tree1, tree2, Method="KF")
```

---

PhyloDistance-RFDist *Robinson-Foulds Distance*

---

## Description

Calculate RF distance between two unrooted phylogenies.

## Details

This function is called as part of [PhyloDistance](#) and calculates Robinson-Foulds distance between two unrooted phylogenies. Each dendrogram is first pruned to only internal branches implying a partition in the shared leaf set; trivial partitions (where one leaf set contains 1 or 0 leaves) are ignored. The total score is calculated as the number of unique partitions divided by the total number of partitions in both trees. Setting `RawScore=TRUE` will instead return a vector with  $(P_{shared}, P_1, P_2)$ , corresponding to the shared partitions and partitions in the first and second trees (respectively).

This algorithm incorporates some optimizations from Pattengale et al. (2007) to improve computation time of the original fast RF algorithm detailed in Day (1985).

## Value

Returns a normalized distance, with 0 indicating identical trees and 1 indicating maximal difference. Note that branch lengths are not considered, so two trees with different branch lengths may return a distance of 0.

If `RawScore=TRUE`, returns a named length 3 vector with the first entry the number of unique partitions, and the subsequent entries the number of partitions for each tree.

If the trees have no leaves in common, the function will return 1 if `RawScore=FALSE`, and `c(0, NA, NA)` if `TRUE`.

## Note

Note that this function requires the input dendrograms to be labeled alike (ex. leaf labeled abc in dend1 represents the same species as leaf labeled abc in dend2). Labels can easily be modified using [dendrapply](#).

## Author(s)

Aidan Lakshman <ahl27@pitt.edu>

## References

- Robinson, D.F. and Foulds, L.R. *Comparison of phylogenetic trees*. *Mathematical Biosciences*, 1987. **53**(1–2): 131–147.
- Day, William H.E. *Optimal algorithms for comparing trees with labeled leaves*. *Journal of classification*, 1985. **2**(1): 7-28.
- Pattengale, N.D., Gottlieb, E.J., and Moret, B.M. *Efficiently computing the Robinson-Foulds metric*. *Journal of computational biology*, 2007. **14**(6): 724-735.

## Examples

```
# making some toy dendrograms
set.seed(123)
dm1 <- as.dist(matrix(runif(64, 0.5, 5), ncol=8))
dm2 <- as.dist(matrix(runif(64, 0.5, 5), ncol=8))

tree1 <- as.dendrogram(hclust(dm1))
tree2 <- as.dendrogram(hclust(dm2))

# get RF distance
PhyloDistance(tree1, tree2, Method="RF")

# get number of unique splits per tree
PhyloDistance(tree1, tree2, Method="RF", RawScore=TRUE)
```

---

plot.EvoWeb

*Plot predictions in a EvoWeb object*

---

## Description

EvoWeb objects are outputted from [predict.EvoWeaver](#).

This function plots the predictions in the object using a force-directed embedding of connections in the adjacency matrix.

*This function is still a work in progress.*

## Usage

```
## S3 method for class 'EvoWeb'
plot(x, NumSims=10,
      Gravity=0.05, Coulomb=0.1, Connection=5,
      MoveRate=0.25, Cutoff=0.2, ColorPalette=topo.colors,
      Verbose=TRUE, ...)
```



### Arguments

|              |  |
|--------------|--|
| x            | A EvoWeb object. See <a href="#">EvoWeb</a>  |
| NumSims      | Number of iterations to run the model for.   |
| Gravity      | Strength of Gravity force. See 'Details'.  |
| Coulomb      | Strength of Coulomb force. See 'Details'.  |
| Connection   | Strength of Connective force. See 'Details'.   |
| MoveRate     | Controls how far each point moves in each iteration.   |
| Cutoff       | Cutoff value; if $\text{abs}(\text{val}) < \text{Cutoff}$ , that Connection is shrunk to zero.   |
| ColorPalette | Color palette for graphing. Valid inputs are any palette available in <code>palette.pals()</code> . See <a href="#">palette</a> for more info. |
| Verbose      | Logical indicating whether to print progress bars and messages. Defaults to TRUE.  |
| ...          | Additional parameters for consistency with generic.  |

### Details

This function plots the EvoWeb object using a force-directed embedding. This embedding has three force components:

- Gravity Force: Attractive force pulling nodes towards  $(0, 0)$
- Coulomb Force: Repulsive force pushing close nodes away from each other
- Connective Force: Tries to push node connections to equal corresponding values in the adjacency matrix

The parameters in the function are sufficient to get an embedding, though users are welcome to try to tune them for a better visualization. This function is meant to aid with visualization of the adjacency matrix, not for concrete analyses of clusters.

The function included in this release is early stage. Next release cycle will update this function with an updated version of this algorithm to improve plotting, visualization, and runtime.

### Value

No return value; creates a plot in the graphics window.

### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

### See Also

[predict.EvoWeaver](#)

[EvoWeb](#)

**Examples**

```
exData <- get(data("ExampleStreptomycesData"))
ew <- EvoWeaver(exData$Genes)

# Subset isn't necessary but is faster for a working example
# Same w/ method='Jaccard'
evoweb <- predict(ew, Method='Jaccard', Subset=1:50)

plot(evoweb)
```

---

predict.EvoWeaver      *Make predictions with EvoWeaver objects*

---

**Description**

This S3 method predicts pairwise functional associations between gene groups encoded in a [EvoWeaver](#) object. This returns an object of type [EvoWeb](#), which is essentially an adjacency matrix with some extra S3 methods to make printing cleaner.

**Usage**

```
## S3 method for class 'EvoWeaver'
predict(object, Method='Ensemble',
        Subset=NULL, Processors=1L,
        MySpeciesTree=SpeciesTree(object),
        PretrainedModel=NULL,
        NoPrediction=FALSE,
        ReturnRawData=FALSE, Verbose=TRUE, ...)
```

**Arguments**

|            |   |
|------------|---|
| object     | A <a href="#">EvoWeaver</a> object  |
| Method     | Method(s) to use for prediction. This can be a character vector with multiple entries for predicting using multiple methods. See 'Details' for more information.  |
| Subset     | Subset of data to predict on. This can either be a vector or a 2xN matrix.<br>If a vector, prediction proceeds for all possible pairs of elements specified in the vector (either by name, for character vector, or by index, for numeric vector). For example, subset=1:3 will predict for pairs (1,2), (1,3), (2,3).<br>If a matrix, subset is interpreted as a matrix of pairs, where each row of the matrix specifies a pair to evaluate. These can also be specified by name (character) or by index (numeric).<br>subset=rbind(c(1,2),c(1,3),c(2,3)) produces equivalent functionality to subset=1:3. |
| Processors | Number of cores to use for methods that support multithreaded execution. Setting to NULL or a negative value will use the value of detectCores(), or one core if the number of available cores cannot be determined. See Note for more information.   |

|                 |   |
|-----------------|---|
| MySpeciesTree   | Phylogenetic tree of all genomes in the dataset. Required for Method=c('ContextTree', 'GainLoss', 'CorrGL', 'ColocMoran', 'Behdenna'). 'Behdenna' requires a rooted, bifurcating tree (other values of Method can handle arbitrary trees). Note that EvoWeaver can automatically infer a species tree if initialized with dendrogram objects.   |
| PretrainedModel | A pretrained model for use with ensemble predictions. If unspecified when Method='Ensemble', the program will use built-in models (see <a href="#">BuiltInEnsembles</a> ). See the examples for how to train an ensemble method to pass to PretrainedModel. Has no effect if Method != 'Ensemble'.  |
| NoPrediction    | For Method='Ensemble', should data be returned prior to making predictions? If TRUE, this will instead return a <a href="#">data.frame</a> object with predictions from each algorithm for each pair. This dataframe is typically used to train an ensemble model.<br>If FALSE, EvoWeaver will return predictions for each pair (using user model if provided or a built-in otherwise). |
| ReturnRawData   | Internal parameter used for ensemble predictions. Should not be set by the user.  |
| Verbose         | Logical indicating whether to print progress bars and messages. Defaults to TRUE.   |
| ...             | Additional parameters for other predictors and consistency with generic.  |

## Details

predict.EvoWeaver wraps several methods to create an easy interface for multiple prediction types. Method='Ensemble' is the default value, but each of the component analyses can also be accessed. The following is a list of all algorithms implemented in EvoWeaver (\* denotes algorithms used in the EvoWeaver publication):

- 'Ensemble': Ensemble prediction combining individual coevolutionary predictors. See Note below.
- \* 'Jaccard': Jaccard distance of Presence/Absence (P/A) profiles
- 'Hamming': Hamming distance of P/A profiles
- \* 'MutualInformation': MI of P/A profiles
- \* 'PAPV': 1-p\_value of P/A profiles
- 'ProfDCA': Direct Coupling Analysis of P/A profiles
- 'Behdenna': Analysis of Gain/Loss events following Behdenna et al. (2016)
- \* 'CorrGL': Correlation of ancestral Gain/Loss events
- \* 'GainLoss': Score-based method based on distance between inferred ancestral Gain/Loss events
- \* 'MirrorTree': MirrorTree using Random Projection for dimensionality reduction
- \* 'ContextTree': MirrorTree with Random Projection correcting for species tree and P/A conservation
- \* 'Coloc': Co-localization analysis

- \* 'ColocMoran': Co-localization analysis using [Moran's I](#) for phylogenetic correction and significance
- \* 'TranscripMI': Mutual Information of Transcriptional Direction
- \* 'NVDI': Correlation of distribution of sequence level residues following Zhao et al. (2022)
- \* 'ResidueMI': Mutual information of sites in multiple sequence alignment

The best performing individual predictors are `c('CorrGL', 'GainLoss', 'MirrorTree', 'Jaccard')`. Users interesting in running quick analyses should use `c('CorrGL', 'GainLoss', 'Jaccard')`.

Additional information and references for each prediction algorithm can be found at the following pages:

- [EvoWeaver Phylogenetic Profiling Methods](#)
- [EvoWeaver Phylogenetic Structure Methods](#)
- [EvoWeaver Gene Organization Methods](#)
- [EvoWeaver Sequence-Level Methods](#)

This returns a `EvoWeb` object, an S3 class that makes formatting and printing of results slightly nicer. See [EvoWeb](#) for more information.

Different methods require different types of input. The constructor `EvoWeaver` will notify the user which methods are runnable with the given data. Method Ensemble automatically selects the methods that can be run with the given input data.

See [EvoWeaver](#) for more information on input data types.

## Value

Returns a `EvoWeb` object. See [EvoWeb](#) for more info.

## Note

The current ensemble method included with `EvoWeaver` is out of date. `EvoWeaver`'s publication used a random forest model from the `randomForest` package for prediction. The next release of `EvoWeaver` will include multiple new built-in ensemble methods, but in the interim users are recommended to rely on `randomForest` or `neuralnet`. Planned algorithms are random forests and feed-forward neural networks. Feel free to contact me regarding other models you would like to see added.

If `NumCores` is set to `NULL`, `EvoWeaver` will use one less core than is detected, or one core if `detectCores()` cannot detect the number of available cores. This is because of a recurring issue on my machine where the R session takes all available cores and is then locked out of forking processes, with the only solution to restart the entire R session. This may be an issue specific to ARM Macs, but out of an abundance of caution I've made the default setting to be slightly slower but guarantee completion rather than risk bricking a machine.

## Author(s)

Aidan Lakshman <ahl27@pitt.edu>

**See Also**[EvoWeaver](#)[EvoWeb](#)[EvoWeaver Phylogenetic Profiling Predictors](#)[EvoWeaver Phylogenetic Structure Predictors](#)[EvoWeaver Gene Organization Predictors](#)[EvoWeaver Sequence-Level Predictors](#)**Examples**

```
#####
## Prediction with built-in model and data
#####

exData <- get(data("ExampleStreptomycesData"))
ew <- EvoWeaver(exData$Genes[1:50])

# Subset isn't necessary but is faster for a working example
evoweb1 <- predict(ew, Subset=1:10, MySpeciesTree=exData$Tree)

# print out results as an adjacency matrix
evoweb1

#####
## Training own ensemble model
#####

datavals <- predict(ew, NoPrediction=TRUE)

actual_values <- sample(c(0,1), nrow(datavals), replace=TRUE)
# This example just picks random numbers
# ***Do not do this for your own models***

# Make sure the actual values correspond to the right pairs!
datavals[, 'y'] <- actual_values
myModel <- glm(y~., datavals[, -c(1,2)], family='binomial')

testEvoWeaverObject <- EvoWeaver(exData$Genes[51:60])
evoweb2 <- predict(testEvoWeaverObject,
                  PretrainedModel=myModel)

# Print result as a matrix of pairwise scores
evoweb2
```

**Description**

Given a SynExtend object with a GeneCalls attribute, and a DECIPHER database, return all gene sequences and their translations.

**Usage**

```
PrepareSeqs(SynExtendObject,  
            DataBase,  
            DefaultTranslationTable = "11",  
            Identifiers = NULL,  
            Storage = 1,  
            Verbose = FALSE)
```

**Arguments**

|                         |  |
|-------------------------|--|
| SynExtendObject         | An object of class PairSummaries or of LinkedPairs. Object must have a GeneCalls attribute.                                |
| DataBase                | A character string pointing to a SQLite database, or a connection to a DECIPHER database.                                  |
| DefaultTranslationTable | A character vector of length 1 identifying the translation table to use if one is not supplied in the GeneCalls attribute. |
| Identifiers             | By default NULL, but can be used to supply a vector of character identifiers for returning a subset of prepared sequences. |
| Storage                 | A soft memory limit for how much space to allow when building the resulting object. Translated to Gb.                      |
| Verbose                 | Logical indicating whether or not to display a progress bar and print the time difference upon completion.                 |

**Details**

PrepareSeqs returns the sequences of genes and their translations where appropriate.

**Value**

An object of class FeatureSeqs.

**Author(s)**

Nicholas Cooley <npc19@pitt.edu>

**See Also**

[SummarizePairs](#), [NucleotideOverlap](#), [FindSynteny](#)

**Examples**

```
DBPATH <- system.file("extdata",
                      "Endosymbionts_v02.sqlite",
                      package = "SynExtend")

data("Endosymbionts_LinkedFeatures", package = "SynExtend")
CurrentSeqs <- PrepareSeqs(SynExtendObject = Endosymbionts_LinkedFeatures,
                          DataBase = DBPATH,
                          Verbose = TRUE)
```

---

SelectByK

*Predicted pair trimming using K-means.*


---

**Description**

A relatively simple k-means clustering approach to drop predicted pairs that belong to clusters with a PID centroid below a specified user threshold.

**Usage**

```
SelectByK(Pairs,
          UserConfidence = 0.5,
          ClusterScalar = 1,
          MaxClusters = 15L,
          ReturnAllCommunities = FALSE,
          Verbose = FALSE,
          ShowPlot = FALSE,
          RetainHighest = TRUE)
```

**Arguments**

|                      |  |
|----------------------|--|
| Pairs                | An object of class PairSummaries.  |
| UserConfidence       | A numeric value greater than 0 and less than 1 that represents a minimum PID centroid that users believe represents a TRUE predicted pair.   |
| ClusterScalar        | A numeric value used to scale selection of how many clusters are used in kmeans clustering. Total within-cluster sum of squares are fit to a right hyperbola, and the half-max is used to select cluster number. "ClusterScalar" is multiplied by the half-max to adjust cluster number selection. |
| MaxClusters          | Integer value indicating the largest number of clusters to test in a series of k-means clustering tests.   |
| ReturnAllCommunities | A logical value, if "TRUE", function returns of a list where the second position is a list of "PairSummaries" tables for each k-means cluster. By default is "FALSE", returning only a "PairSummaries" object of the retained predicted pairs.   |

|               |  |
|---------------|--|
| ShowPlot      | Logical indicating whether or not to plot the CDFs for the PIDs of all k-means clusters for the determined cluster number.                       |
| Verbose       | Logical indicating whether or not to display a progress bar and print the time difference upon completion.                                       |
| RetainHighest | Logical indicating whether to retain the cluster with the highest PID centroid in the case where the PID is below the specified user confidence. |

### Details

SelectByK uses a naive k-means routine to select for predicted pairs that belong to clusters whose centroids are greater than or equal to the user specified PID confidence. This means that the confidence is not a minimum, and that pairs with PIDs below the user confidence can be retained. The sum of within cluster sum of squares is used to approximate “knee” selection with the user supplied “ClusterScalar” value. By default, with a “ClusterScalar” value of 1 the half-max of a right-hyperbola fitted to the sum of within-cluster sum of squares is used to pick the cluster number for evaluation, “ClusterScalar” is multiplied by the half-max to tune cluster number selection. This function is intended to be used at the genome-to-genome comparison level, and not say, at the level of an all-vs-all comparison of many genomes.

### Value

An object of class `PairSummaries`.

### Author(s)

Nicholas Cooley <npc19@pitt.edu>

### See Also

[PairSummaries](#), [NucleotideOverlap](#), [link{SubSetPairs}](#), [FindSynteny](#)

### Examples

```
# this function will be deprecated soon,
# please see the new ClusterByK() function.

DBPATH <- system.file("extdata",
                      "Endosymbionts_v02.sqlite",
                      package = "SynExtend")

data("Endosymbionts_LinkedFeatures", package = "SynExtend")

Pairs <- PairSummaries(SyntenyLinks = Endosymbionts_LinkedFeatures,
                      PIDs = TRUE,
                      Score = TRUE,
                      DBPATH = DBPATH,
                      Verbose = TRUE)

Pairs02 <- SelectByK(Pairs = Pairs)
```



---

|                    |   |
|--------------------|---|
| SequenceSimilarity | <i>Return a numeric value that represents the similarity between two aligned sequences as determined by a provided substitution matrix.</i> |
|--------------------|---|

---

### Description

Takes in a DNASTringSet or AAStringSet representing a pairwise alignment and a substitution matrix such as those present in PFASUM, and return a numeric value representing sequence similarity as defined by the substitution matrix.

### Usage

```
SequenceSimilarity(Seqs,  
                  SubMat,  
                  penalizeGapLetter = TRUE,  
                  includeTerminalGaps = TRUE,  
                  allowNegative = TRUE)
```

### Arguments

|                     |  |
|---------------------|--|
| Seqs                | A DNASTringSet or AAStringSet of length 2.   |
| SubMat              | A named matrix representing a substitution matrix. If left "NULL" and "Seqs" is a AAStringSet, the 40th "PFASUM" matrix is used. If left "NULL" and "Seqs" is a DNASTringSet, a matrix with only the diagonal filled with "1"'s is used. |
| penalizeGapLetter   | A logical indicating whether or not to penalize Gap-Letter matches. Defaults to "TRUE".  |
| includeTerminalGaps | A logical indicating whether or not to penalize terminal matches. Defaults to "TRUE".  |
| allowNegative       | A logical indicating whether or not allow negative scores. Defaults to "TRUE". If "FALSE" scores that are returned as less than zero are converted to zero.  |

### Details

Takes in a DNASTringSet or AAStringSet representing a pairwise alignment and a substitution matrix such as those present in PFASUM, and return a numeric value representing sequence similarity as defined by the substitution matrix.

### Value

Returns a single numeric.

### Author(s)

Erik Wright <ESWRIGHT@pitt.edu> Nicholas Cooley <npc19@pitt.edu>

**See Also**

[AlignSeqs](#), [AlignProfiles](#), [AlignTranslation](#), [DistanceMatrix](#)

**Examples**

```
db <- system.file("extdata", "Bacteria_175seqs.sqlite", package = "DECIPHER")
dna <- SearchDB(db, remove = "all")
alignedDNA <- AlignSeqs(dna[1:2])

DNAPlaceholder <- diag(15)
dimnames(DNAPlaceholder) <- list(DNA_ALPHABET[1:15],
                                 DNA_ALPHABET[1:15])

SequenceSimilarity(Seqs = alignedDNA,
                   SubMat = DNAPlaceholder,
                   includeTerminalGaps = TRUE,
                   penalizeGapLetter = TRUE,
                   allowNegative = TRUE)
```

---

simMat

*Similarity Matrices*

---

**Description**

The `simMat` object is an internally utilized class that provides similar functionality to the `dist` object, but with matrix-like accessors.

Like `dist`, this object stores values as a vector, reducing memory by making use of assumed symmetry. `simMat` currently only supports numeric data types.

**Usage**

```
## Create a blank sym object
simMat(VALUE, neleM, NAMES=NULL, DIAG=FALSE)

## S3 method for class 'vector'
as.simMat(x, NAMES=NULL, DIAG=TRUE, ...)

## S3 method for class 'matrix'
as.simMat(x, ...)

## S3 method for class 'simMat'
print(x, ...)

## S3 method for class 'simMat'
as.matrix(x, ...)

## S3 method for class 'simMat'
```

```

as.data.frame(x, ...)

## S3 method for class 'simMat'
Diag(x, ...)

## S3 replacement method for class 'simMat'
Diag(x) <- value

```

### Arguments

|       |  |
|-------|--|
| VALUE | Numeric (or NA_real_) indicating placeholder values. A vector of values can be provided for this function if desired.  |
| nelem | Integer; number of elements represented in the matrix. This corresponds to the number of rows and columns of the object, so setting nelem=10 would produce a 10x10 matrix.   |
| NAMES | Character (Optional); names for each row/column. If provided, this should be a character vector of length equal to nelem.  |
| DIAG  | Logical; Is the diagonal included in the data? If FALSE, the constructor generates 1s for the diagonal.  |
| x     | Various; for print and Diag, the "simMat" object to print. For as.vector or as.matrix, the vector or matrix (respectively). Note that as.matrix expects a symmetric matrix—providing a non-symmetric matrix will take only the upper triangle and produce a warning. |
| value | Numeric; value(s) to replace diagonal with.  |
| ...   | Additional parameters provided for consistency with generic.   |

### Details

The simMat object has a very similar format to dist objects, but with a few notable changes:

- simMat objects have streamlined print and show methods to make displaying large matrices better. print accepts an additional argument n corresponding to the maximum number of rows/columns to print before truncating.
- simMat objects support matrix-style get/set operations like s[1,] or s[1,3:5]
- simMat objects allow any values on the diagonal, rather than just zeros as in dist objects.
- simMat objects support conversion to matrices and data.frame objects
- simMat objects implement get/set Diag() methods. Note usage of capitalized Diag; this is to avoid conflicts and weirdness with using base diag.

See the examples for details on using these features.

The number of elements printed when calling print or show on a simMat object is determined by the "SynExtend.simMat" option.

**Value**

simMat and as.simMat return an object of class "simMat". Internally, the object stores the upper triangle of the matrix similar to how dist stores objects.

The object has the following attributes (besides "class" equal to "simMat"):

nrow                    the number of rows in the matrix implied by the vector  
 NAMES                  the names of the rows/columns

as.matrix(s) returns the equivalent matrix to a "simMat" object.

as.data.frame(s) returns a data.frame object corresponding to pairwise similarities.

**Author(s)**

Aidan Lakshman <ahl27@pitt.edu>

**Examples**

```
## Creating a blank simMat object initialized to zeros
s <- simMat(0, nelem=20)
s

## Print out 5 rows instead of 10
print(s, n=5)

## Create a simMat object with 5 entries from a vector
dimn <- 5
vec <- 1:(dimn*(dimn-1) / 2)
s1 <- as.simMat(vec, DIAG=FALSE)
s1

## Here we include the diagonal
vec <- 1:(dimn*(dimn+1) / 2)
s2 <- as.simMat(vec, DIAG=TRUE)
s2

## Subsetting
s2[1,]
s2[1,3:4]
# all entries except first row
s2[-1,]
# all combos not including 1
s2[-1,-1]

## Replace values (automatically recycled)
s2[1,] <- 10
s2

## Get/set diagonal
Diag(s1)
Diag(s1) <- 5
s1
```

---

subset.dendrogram      *Subsetting dendrogram objects*

---

### Description

Subsets dendrogram objects based on leaf labels. Subsetting can either be by leaves to keep, or leaves to remove.

NOTE: This man page is specifically for subset.dendrogram, see ?base::subset for the generic subset function defined for vectors, matrices, and data frames.

### Usage

```
## S3 method for class 'dendrogram'  
subset(x, subset, invert=FALSE, ...)
```

### Arguments

|        |   |
|--------|---|
| x      | An object of class 'dendrogram'                                 |
| subset | A vector of labels to keep (see invert).                        |
| invert | If set to TRUE, subset to only the leaves <i>not</i> in subset. |
| ...    | Additional arguments for consistency with generic.              |

### Value

An object of class 'dendrogram' corresponding to the subsetted tree.

### Note

If none of the labels specified in the subset argument appear in the tree (or if all do when invert=TRUE), a warning is thrown and an empty object of class 'dendrogram' is returned.

### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

### See Also

[subset](#)

**Examples**

```
d <- as.dendrogram(hclust(dist(USArrests), "ave"))

# Show original dendrogram
plot(d)

# Subset to first 10 labels
d1 <- subset(d, labels(d)[1:10])
plot(d1)

# Subset d1 to all except the first 2 labels
d2 <- subset(d1, labels(d1)[1:2], invert=TRUE)
plot(d2)
```

---

SubSetPairs

*Subset a "PairSummaries" object.*


---

**Description**

For a given object of class "PairSummaries", pairs based on either competing predictions, user thresholds on prediction statistics, or both.

**Usage**

```
SubSetPairs(CurrentPairs,
            UserThresholds,
            RejectCompetitors = TRUE,
            RejectionCriteria = "PID",
            WinnersOnly = TRUE,
            Verbose = FALSE)
```

**Arguments**

- CurrentPairs** An object of class "PairSummaries". Can also take in a generic "data.frame", as long as the feature naming scheme is the same as that followed by all SynExtend functions.
- UserThresholds** A named vector where values indicate a threshold for statistics to be above, and names designate which statistic to threshold on.
- RejectCompetitors** A logical that defaults to "TRUE". Allowing users to choose to remove competing predictions. When set to "FALSE", no competitor rejection is performed. When "TRUE" all competing pairs with the exception of the best pair as determined by "RejectionCriteria" are rejected. Can additionally be set to a numeric or integer, in which case only competing predictions below that value are dropped.
- RejectionCriteria** A character indicating which column value competitor rejection should reference. Defaults to "PID".

|             |   |
|-------------|---|
| WinnersOnly | A logical indicating whether or not to return just the pairs that are selected. Defaults to “TRUE” to return a subset object of class “PairSummaries”. When “FALSE”, function returns a list of two “PairSummaries” objects, one of the selected pairs, and the second of the rejected pairs. |
| Verbose     | Logical indicating whether or not to display a progress bar and print the time difference upon completion.  |

### Details

SubSetPairs uses a naive competitor rejection algorithm to remove predicted pairs when nodes are predicted to be paired to multiple nodes within the same index.

### Value

An object of class “PairSummaries”, or a list of two “PairSummaries” objects.

### Author(s)

Nicholas Cooley <npc19@pitt.edu>

### See Also

[PairSummaries NucleotideOverlap](#)

### Examples

```
# expected to be deprecated soon...
data("Endosymbionts_Pairs03", package = "SynExtend")
# remove competitors under default conditions
Pairs2 <- SubSetPairs(CurrentPairs = Endosymbionts_Pairs03,
                      Verbose = TRUE)

THRESH <- c(0.5, 21)
names(THRESH) <- c("Consensus", "TotalMatch")
# remove pairs only based on user defined thresholds
Pairs3 <- SubSetPairs(CurrentPairs = Endosymbionts_Pairs03,
                      UserThresholds = THRESH,
                      RejectCompetitors = FALSE,
                      Verbose = TRUE)
```

---

SummarizePairs

*Provide summaries of hypothetical orthologs.*

---

### Description

Given the correct set of SynExtend objects and a DECIPHER database, return a data.frame of summarized genomic feature pairs. SummarizePairs will collect all the linked genomic features in the supplied [LinkedPairs-class](#) object and return descriptions of the alignments of those features.

**Usage**

```
SummarizePairs(SynExtendObject,
               FeatureSeqs,
               DataBase,
               AlignmentFun = "AlignProfiles",
               RetainAnchors = FALSE,
               DefaultTranslationTable = "11",
               KmerSize = 5,
               IgnoreDefaultStringSet = FALSE,
               Verbose = FALSE,
               ShowPlot = FALSE,
               Processors = 1,
               ...)
```

**Arguments**

|                         |   |
|-------------------------|---|
| SynExtendObject         | An object of class <code>LinkedPairs</code> -class.   |
| FeatureSeqs             | An object of class <code>FeatureSeqs</code> .   |
| DataBase                | A character string pointing to a SQLite database, or a connection to a DECIPHER database.   |
| AlignmentFun            | A character string specifying a link{DECIPHER} alignment function. Currently only supports <a href="#">AlignProfiles</a> and <a href="#">AlignPairs</a> . |
| RetainAnchors           | An argument that only affects <a href="#">AlignPairs</a> ; provide the kmer hits supplied by <a href="#">FindSynteny</a> as alignment anchors.            |
| DefaultTranslationTable | A character vector of length 1 identifying the translation table to use if one is not supplied in the <code>GeneCalls</code> attribute.                   |
| KmerSize                | An integer specifying what Kmer size to collect Kmer distance between sequences at.   |
| IgnoreDefaultStringSet  | A soft memory limit for how much space to allow when building the resulting object. Translated to Gb.   |
| Verbose                 | Logical indicating whether or not to display a progress bar and print the time difference upon completion.  |
| ShowPlot                | Logical indicating whether or not to provide a plot of features collected by the function.  |
| Processors              | An integer value indicating how many processors to supply to <a href="#">AlignPairs</a> .   |
| ...                     | Additional arguments to pass to interior functions. Currently not implemented.  |

**Details**

`SummarizePairs` collects features describing each linked feature pair. These include an alignment PID, an alignment Score, a Kmer distance, a consensus score for the linking hits –or whether or not linking hits are in similar places in each feature– and a few other features.



**Value**

An object of class PairSummaries.

**Author(s)**

Nicholas Cooley <npc19@pitt.edu>

**See Also**

[PrepareSeqs](#), [NucleotideOverlap](#), [FindSynteny](#), [LinkedPairs-class](#)

**Examples**

```
DBPATH <- system.file("extdata",
                     "Endosymbionts_v02.sqlite",
                     package = "SynExtend")

data("Endosymbionts_LinkedFeatures", package = "SynExtend")
Endosymbiont_Seqs <- PrepareSeqs(SynExtendObject = Endosymbionts_LinkedFeatures,
                               DataBase = DBPATH,
                               Verbose = TRUE)
SummarizedPairs <- SummarizePairs(SynExtendObject = Endosymbionts_LinkedFeatures,
                                 FeatureSeqs = Endosymbiont_Seqs,
                                 DataBase = DBPATH)
```

---

SuperTree

*Create a Species Tree from Gene Trees*

---

**Description**

Given a set of unrooted gene trees, creates a species tree. This function works for rooted gene trees, but may not accurately root the resulting tree.

**Usage**

```
SuperTree(myDendList, NAMEFUN=NULL, Verbose=TRUE, Processors=1)
```

**Arguments**

|            |  |
|------------|--|
| myDendList | List of dendrogram objects, where each entry is an unrooted gene tree.   |
| NAMEFUN    | Optional input specifying a function to apply to each leaf to convert gene tree leaf labels into species names. This function should take as input a character vector and return a character vector of the same size. By default equals NULL, indicating that gene tree leaves are already labeled with species identifiers. See details for more information. |
| Verbose    | Should output be displayed?  |
| Processors | Number of processors to use for calculating the final species tree.  |

## Details

This implementation follows the ASTRID algorithm for estimating a species tree from a set of unrooted gene trees. Input gene trees are not required to have identical species sets, as the algorithm can handle missing entries in gene trees. The algorithm essentially works by averaging the Cophenetic distance matrices of all gene trees, then constructing a neighbor-joining tree from the resulting distance matrix. See the original paper linked in the references section for more information.

If two species never appear together in a gene tree, their distance cannot be estimated in the algorithm and will thus be missing. SuperTree handles this by imputing the value using the distances available with data-interpolating empirical orthogonal functions (DINEOF). This approach has relatively high accuracy even up to high levels of missingness. Eigenvector calculation speed is improved using a Lanczos algorithm for matrix compression.

SuperTree allows an optional argument called NAMEFUN to apply a renaming step to leaf labels. Gene trees as constructed by other functions in SynExtend (ex. [DisjointSet](#)) often include other information aside from species name when labeling genes, but SuperTree requires that leaf nodes of the gene tree are labeled with just an identifier corresponding to which species/genome each leaf is from. Duplicate values are allowed. See the examples section for more details on what this looks like and how to handle it.

## Value

A [dendrogram](#) object corresponding to the species tree constructed from input gene trees.

## Author(s)

Aidan Lakshman <ah127@pitt.edu>

## References

Vachaspati, P., Warnow, T. *ASTRID: Accurate Species TRees from Internode Distances*. BMC Genomics, 2015. **16** (Suppl 10): S3.

Taylor, M.H., Losch, M., Wenzel, M. and Schröter, J. *On the sensitivity of field reconstruction and prediction using empirical orthogonal functions derived from gappy data*. Journal of Climate, 2013. **26**(22): 9194-9205.

## See Also

[TreeLine](#), [SuperTreeEx](#)

## Examples

```
# Loads a list of dendrograms
# each is a gene tree from Streptomyces genomes
data("SuperTreeEx", package="SynExtend")

# Notice that the labels of the tree are in #_#_# format
# See the man page for SuperTreeEx for more info
labs <- labels(exData[[1]])
labs
```

```
# The first number corresponds to the species,  
# so we need to trim the rest in each leaf label  
namefun <- function(x) gsub("([0-9A-Za-z]*)_.*", "\\1", x)  
namefun(labs) # trims to just first number  
  
# This function replaces gene identifiers with species identifiers  
# we pass it to NAMEFUN  
# Note NAMEFUN should take in a character vector and return a character vector  
tree <- SuperTree(exData, NAMEFUN=namefun)
```

---

SuperTreeEx

*Example Dendrograms*

---

### Description

A set of 20 dendrograms for use in [SuperTree](#) examples.

### Usage

```
data("SuperTreeEx")
```

### Value

A list with 20 elements, where each is a object of type [dendrogram](#) corresponding to a gene tree constructed from a set of 301 *Streptomyces* genomes. Each leaf node is labeled in the form A\_B\_C, where A is a number identifying the genome, B is a number identifying the contig, and C is a number identifying the gene. Altogether, each label uniquely identifies a gene.

### Examples

```
data(SuperTreeEx, package="SynExtend")
```

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