# Package 'SynExtend'

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```
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     teny objects.
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```

2 Contents

# **Contents**

AAHitScoping
ApproximateBackground
BlastSeqs
BlockByRank
BlockExpansion
BlockReconciliation
BuiltInEnsembles
CheckAgainstReport
CIDist_NullDist
ClusterByK
CompetePairs
DecisionTree-class
dendrapply
DisjointSet
DPhyloStatistic
Endosymbionts_GeneCalls
Endosymbionts_LinkedFeatures
Endosymbionts_Pairs01
Endosymbionts_Pairs02
Endosymbionts Pairs03
Endosymbionts_Sets
Endosymbionts_Synteny
EstimateExoLabel
EstimRearrScen
EvoWeaver
EvoWeaver-GOPreds
EvoWeaver-PPPreds
EvoWeaver-PSPreds
EvoWeaver-SLPreds
EvoWeb
ExampleStreptomycesData
ExoLabel
ExpandDiagonal
ExtractBy
FastQFromSRR
FindSets
FitchParsimony
Generic
gffToDataFrame
HitConsensus
LinkedPairs
MakeBlastDb
NucleotideOverlap
OneSite
PairSummaries
PhyloDistance
PhyloDistance-CIDist
PhyloDistance-IRFDist 70

AAHitScoping 3

	PhyloDistance-KFDist	71
	PhyloDistance-RFDist	
	plot.EvoWeb	
	predict.EvoWeaver	
	PrepareSeqs	
	RandForest	
	RejectionBy	
	SelectByK	
	SequenceSimilarity	
	simMat	
	subset.dendrogram	
	SubSetPairs	
	SummarizePairs	
	SuperTree	
	SuperTreeEx	
	WithinSetCompetition	
Index	1	00
	tScoping Adjust the scope of kmer hits between feature and genome space.	_

# Description

This function is designed to work internally to functions within SynExtend so it works on relatively simple atomic vectors and has little overhead checking.

### Usage

```
AAHitScoping(hitlist,
fstrand1,
fstart1,
fstop1,
fstrand2,
fstart2,
fstop2)
```

# **Arguments**

hitlist	A list containing matrices produced by SearchIndex.
fstrand1	An integer vector of 0s and 1s describing the strand of features.
fstart1	Integer; a vector of left bounds of features.
fstop1	Integer; a vector of right bounds of features.
fstrand2	An integer vector of 0s and 1s describing the strand of features.
fstart2	Integer; a vector of left bounds of features.
fstop2	Integer; a vector of right bounds of features.

# **Details**

AAHitScoping converts the hits returned by SearchIndex from feature-to-feature context genome-to-genome context.

### Value

A list of matrices.

# Author(s)

Nicholas Cooley <npc19@pitt.edu>

#### See Also

 ${\tt NucleotideOverlap, SummarizePairs, WithinSetCompetition, RejectionBy}$ 

# **Examples**

#

 $\label{lem:approximate} \textit{Approximate background alignment score for a series of paired sequences}.$ 

# Description

This function is designed to work internally to SummarizePairs so it works on relatively simple atomic vectors and has little overhead checking.

# Usage

```
ApproximateBackground(p1, p2, code1, code2, mod1, mod2, aa1, aa2, nt1, nt2, register1, register2, aamat, ntmat)
```

# Arguments

p1	Integer; references positions within nt1 or aa1.
p2	Integer; references positions within nt2 or aa2.
code1	Logical; specifies whether the position referenced by p1 is reported as a coding sequence.
code2	Logical; specifies whether the position referenced by p2 is reported as a coding sequence.

mod1	Logical; specifies whether the position referenced by p1 can be translated without complaint by translate.
mod2	Logical; specifies whether the position referenced by p2 can be translated without complaint by translate.
aa1	AAStringSet.
aa2	AAStringSet.
nt1	DNAStringSet.
nt2	DNAStringSet.
register1	Integer; a vector that maps which positions in aa1 are the translations of that particular index in nt1. NAs identify positions that are not translated.
register2	Integer; a vector that maps which positions in aa2 are the translations of that particular index in nt2. NAs identify positions that are not translated.
aamat	A substitution matrix for amino acids.
ntmat	A substitution matrix for nucleotides.

#### **Details**

ApproximateBackground generates approximate background alignment scores for sets of sequences.

#### Value

A vector of numerics.

# Author(s)

Nicholas Cooley <npc19@pitt.edu>

### See Also

NucleotideOverlap, SummarizePairs, FindSynteny

6 BlastSeqs

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 from https://blast.ncbi.nlm.nih.gov/Bl

# Usage

### **Arguments**

seqs	Sequence(s) to run BLAST query on. This can be either an XStringSet or a path to a FASTA file.
BlastDB	Character; path to FASTA file in a pre-built BLAST Database. These can be built using either MakeBlastDb from R or the commandline makeblastdb function from BLAST+. For more information on building BLAST DBs, see here.
blastType	Character; type of BLAST query to run. See 'Details' for more information on available types.
extraArgs	Character; additional arguments to be passed to the BLAST query executed on the command line. This should be a single string. (Optional)
verbose	Logical; should output be displayed? (Optional, default TRUE)

#### **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

BlockByRank 7

- 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**

#

# Description

This function is designed to work internally to SummarizePairs so it works on relatively simple atomic vectors and has little overhead checking. All arguments must be the same length.

#### Usage

```
BlockByRank(index1,
partner1,
index2,
partner2)
```

# Arguments

index1	Integer; references the contigs containing candidate feature partners.
partner1	Integer; references the candidate feature partners by row position in the source DataFrame.
index2	Integer; references the contigs containing candidate feature partners.
partner2	Integer; references the candidate feature partners by row position in the source DataFrame.

8 BlockExpansion

#### **Details**

BlockByRank uses the diagonal rank to identify where runs of candidate features are present in sequential blocks. In cases where a candidate feature is part of two competing blocks it is assigned to the larger.

#### Value

A list with named elements absblocksize and blockidmap.

#### Author(s)

```
Nicholas Cooley <npc19@pitt.edu>
```

### See Also

```
NucleotideOverlap, SummarizePairs, FindSynteny
```

# **Examples**

BlockExpansion

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

# Description

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

### Usage

BlockExpansion 9

#### **Arguments**

Pairs An object of class PairSummaries.

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 FALSE 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 PairSummaries object with the new pairs

folded in.

DBPATH A file or connection pointing to the DECIPHER database supplied to FindSynteny

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

10 **BlockReconciliation** 

```
data("Endosymbionts_Pairs01", package = "SynExtend")
Pairs02 <- BlockExpansion(Pairs = Pairs,</pre>
                           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**

Pairs

A PairSummaries object.

ConservativeRejection

A logical defaulting to TRUE. By default only pairs that conflict within a syntenic block will be rejected. When FALSE any conflict will cause the rejection of the pair in the smaller block.

Precedent

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.

**PIDThreshold** 

Defaults to NULL, 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 PID >= PIDThreshold 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 >= SCOREThreshold will be retained.

Verbose

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

BlockReconciliation 11

#### **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 - frequences 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

12 CheckAgainstReport

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. Two groups of models are provided: 1. Models trained on the KEGG MODULES dataset 2. Models trained on the CORUM dataset

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")
```

#### **Format**

The data contain a named list of objects of class glm. This list currently has two entries: "KEGG" and "CORUM"

### **Examples**

CheckAgainstReport

Pull an assembly from the NCBI FTP site.

### Description

This function is designed to work internally to functions within SynExtend so it works on relatively simple atomic vectors and has little overhead checking.

# Usage

CIDist\_NullDist 13

#### **Arguments**

FTP\_ADDRESS Character; the ftp address of an ncbi assembly.

CHECK\_ADDRESS Character; the ftp address of an ncbi assembly report.

RETRY Integer; the number of times to retry an assembly download should it not pull

correctly.

#### **Details**

On occasion, readDNAStringSet fails to completely pull assemblies from the ncbi ftp site. It is not clear why, though it is infrequent but replicable at large scale. CheckAgainstReport checks the captured DNAStringSet against the reported assembly size and string widths.

#### Value

A DNAStringSet.

#### Author(s)

Nicholas Cooley <npc19@pitt.edu>

#### See Also

readDNAStringSet

#### **Examples**

#

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")
```

#### **Format**

A matrix CI\_DISTANCE\_INTERNAL with 197 columns and 13 rows.

#### **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 (respectively).

14 ClusterByK

#### 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

#### **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.

ClusterByK 15

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 "Cluster-Scalar" 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 suppled 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, FindSynteny, ExpandDiagonal

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

CompetePairs

CompetePairs

Find the best match pair in cases where ambiguity exists.

#### **Description**

A relatively simple routine for identifying a "best" pair in cases where many homologous are identified in a single genome-to-genome comparison. Selection is performed with a single collected measure, and can be performed with or without leveraging context of syntenic blocks.

#### Usage

#### **Arguments**

SynExtendObject

An object of class PairSummaries.

AllowCrossContigConflicts

A logical indicating where pair competition should take place between genomes

or contigs.

By A character vector of length 1 indicating which column in the PairSummaries

object to compete pairs with.

PollContext A logical indicating whether to include the context of block membership in the

competition.

NormalizeCompetition

A logical indicating whether or not to unit normalize the measure being used for

competition.

InflationParameter

A numeric of length 1 specifying an adjustment for how block context should

be penalized, greater than 1 or rewarded, less than 1.

Verbose Logical indicating whether or not to display a progress bar and print the time

difference upon completion.

### **Details**

CompetePairs uses a naive competition based approach to select a "true-est" ortholog in cases where many competing potential orthologs are present in a set of predicted pairs. The returned value is the previous object with two new attributes, "RetainByCompetition" is a vector of logicals specifying which pairs are retained post competition. A second new attribute named "Knockout" is a character vector that identifies –by rowname– the row which knocked out a removed pair.

#### Value

An object of class PairSummaries.

DecisionTree-class 17

#### Author(s)

```
Nicholas Cooley <npc19@pitt.edu>
```

#### See Also

```
SummarizePairs, NucleotideOverlap, FindSynteny, ExpandDiagonal, ClusterByK
```

#### Examples

```
data("Endosymbionts_Pairs01", package = "SynExtend")
Pairs02 <- CompetePairs(SynExtendObject = Endosymbionts_Pairs01)</pre>
```

DecisionTree-class

Decision Trees for Random Forests

### **Description**

DecisionTree objects comprising random forest models generated with RandForest.

#### Usage

```
## S3 method for class 'DecisionTree'
as.dendrogram(object, ...)
## S3 method for class 'DecisionTree'
plot(x, plotGain=FALSE, ...)
```

#### **Arguments**

object an object of class DecisionTree to convert to class dendrogram.

x an object of class DecisionTree to plot.

plotGain Logical; Determines if the Gini gain (for classification) or decrease in sum of

squared error (for regression) should be plotted for each decision point of the

tree. If FALSE, only plots the variable threshold for each decision point.

. For plot, further arguments passed to plot.dendrogram and text. Arguments

prefixed with "text." (e.g., text.cex) will be passed to text, and all other arguments are passed to plot.dendrogram.

For as.dendrogram, ... is further arguments for consistency with the generic

definition.

#### **Details**

These methods help work with DecisionTree objects, which are returned as part of RandForest. Coercion to dendrogram objects creates a 'dendrogram' corresponding to the structure of the decision tree. Each internal node possesses the standard attributes present in a 'dendrogram' object, along with the following extra attributes:

- variable: which variable was used to split at this node.
- thresh: cutoff for partitioning points; values less than thresh are assigned to the left node, and those greater than to the right node.

18 DecisionTree-class

• gain: change in the metric to maximize. For classification trees this is the Gini Gain, and for regression trees this is the decrease in sum of squared error.

Plotting allows for extra arguments to be passed to plot and text. Arguments prefixed with 'text' are passed to text, which controls the labeling of internal nodes. Common arguments used here are text.cex, text.adj, text.srt, and text.col. All other arguments are passed to plot.dendrogram. For example, col='blue' would change the dendrogram color to blue, whereas text.col='blue' would change the interior node labels to blue (but not the dendrogram itself).

### Value

as.dendrogram returns an object of class 'dendrogram'. plot returns NULL invisibly.

#### Warning

These functions can be quite slow for large decision trees. Usage is discouraged for trees with more than 100 internal nodes.

#### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

#### See Also

RandForest

```
set.seed(199L)
n_samp <- 100L
AA <- rnorm(n_samp, mean=1, sd=5)
BB <- rnorm(n_samp, mean=2, sd=3)
CC <- rgamma(n_samp, shape=1, rate=2)</pre>
err <- rnorm(n_samp, sd=0.5)</pre>
y <- AA + BB + 2*CC + err
d <- data.frame(AA,BB,CC,y)</pre>
train_i <- 1:90
test_i <- 91:100
train_data <- d[train_i,]</pre>
test_data <- d[test_i,]</pre>
rf_regr <- RandForest(y~., data=train_data, rf.mode="regression", max_depth=5L)
if(interactive()){
  # Visualize one of the decision trees
  plot(rf_regr[[1]])
dend <- as.dendrogram(rf_regr[[1]])</pre>
plot(dend)
```

dendrapply 19

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

#### **Arguments**

Χ	An object of class "dendrogram".
FUN	An R function to be applied to each dendrogram node, typically working on its attributes alone, returning an altered version of the same node.
	potential further arguments passed to FUN.
how	Character; one of c("pre.order", "post.order"), or an unambiguous abbreviation. Determines if nodes should be evaluated according to a 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 evaluted *prior to any* of its children (i.e., "top-down").

"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 (i.e., "bottom-up").

# 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.

20 dendrapply

#### 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.

```
require(graphics)
## a smallish simple dendrogram
dhc <- as.dendrogram(hc <- hclust(dist(USArrests), "ave"))</pre>
(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) {</pre>
      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))</pre>
      }
      n
  }
  mycols <- grDevices::rainbow(attr(dhc21, "members"))</pre>
  i <- 0
 })
dL <- dendrapply(dhc21, colLab)</pre>
op <- par(mfrow = 2:1)
 plot(dhc21)
 plot(dL) ## --> colored labels!
## Illustrating difference between pre.order and post.order
dend <- as.dendrogram(hclust(dist(seq_len(4L))))</pre>
f <- function(x){</pre>
  if(!is.null(attr(x, 'leaf'))){
    v <- as.character(attr(x, 'label'))</pre>
  } else {
    v \leftarrow paste0(attr(x[[1]], 'newattr'), attr(x[[2]], 'newattr'))
```

DisjointSet 21

```
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 \})</pre>
```

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

# 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

22 DPhyloStatistic

#### **Examples**

DPhyloStatistic

D-Statistic for Binary States on a Phylogeny

#### **Description**

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

# Usage

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

#### **Arguments**

dend An object of class dendrogram

PAProfile A vector representing presence/absence of binary traits. See Details for infor-

mation on supported input types.

NumIter Integer; 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 statstic 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 Value section or the original paper cited in References for more information.

The input parameter PAProfile 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.

DPhyloStatistic 23

#### Value

Returns a numerical value with the following cases:

• Value less than 0: the trait is more phylogenetically concentrated than expected by chance ("extremely clumped")

- Value close to 0: the trait is as phylogenetically concetrated as expected if it had evolved by Brownian motion
- Value close to 1: the trait is as phylogenetically concetrated as expected under a random distribution
- Value greater than 1: the trait is less phylogenetically concentrated than expected under a random distribution ("overdispersed")

#### 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.

```
### Replicating results from Table 1 in original paper ###
# creates a dendrogram with 16 leaves and branch lengths all 1
distMat <- suppressWarnings(matrix(seq_len(17L), nrow=16, ncol=16))</pre>
testDend <- as.dendrogram(hclust(as.dist(distMat)))</pre>
testDend <- dendrapply(testDend, \xspace \xs
                                                              attr(x, 'height') <- attr(x, 'height') / 2</pre>
                                                        })
attr(testDend[[1]], 'height') <- attr(testDend[[2]], 'height') <- 3</pre>
attr(testDend, 'height') <- 4</pre>
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 PAProfiles ###
```

```
allLabs <- as.character(labels(testDend))
# All these ways create a PAProfile 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]</pre>
```

Endosymbionts\_GeneCalls

Example genecalls

### **Description**

A named list of DataFrames.

### Usage

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

### **Format**

A named list.

### **Details**

Example genecalls.

### **Examples**

```
data(Endosymbionts_GeneCalls)
```

Endosymbionts\_LinkedFeatures

Example synteny links

### **Description**

An object of class LinkedPairs.

### Usage

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

#### **Format**

An object of class LinkedPairs.

### **Details**

An object of class LinkedPairs.

# **Examples**

data(Endosymbionts\_LinkedFeatures)

Endosymbionts\_Pairs01 Example predicted pairs

# Description

An object of class PairSummaries.

# Usage

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

### **Format**

An object of class PairSummaries.

# **Details**

An object of class PairSummaries.

# **Examples**

data(Endosymbionts\_Pairs01)

Endosymbionts\_Pairs02 Example predicted pairs

# Description

An object of class  ${\tt PairSummaries}$  where blocks have been expanded.

# Usage

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

### **Format**

An object of class PairSummaries.

26 Endosymbionts\_Sets

#### **Details**

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")
```

#### **Format**

An object of class PairSummaries.

#### **Details**

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")
```

#### **Format**

A named list of disjoint sets representing hypothetical COGs.

# **Details**

A named list of disjoint sets representing hypothetical COGs.

```
data(Endosymbionts_Sets)
```

Endosymbionts\_Synteny A synteny object

#### **Description**

An object of class Synteny.

#### Usage

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

#### **Format**

An object of class Synteny.

### **Details**

An object of class Synteny.

#### **Examples**

```
data(Endosymbionts_Synteny)
```

EstimateExoLabel

Estimate ExoLabel Disk Consumption

### **Description**

Estimate the total disk consumption for ExoLabel.

### Usage

# Arguments

num\_v Integer; approximate number of total unique nodes in the network.

avg\_degree Numeric; average degree of nodes in the network (i.e., the average number of

neighbors for each node)

is\_undirected Logical; indicates whether edges are undirected (TRUE) or directed (FALSE).

Undirected edges consume twice as much disk space internally because they

need to be recorded twice.

node\_name\_length

Integer; approximate average length of each node name, in characters.

28 EstimRearrScen

#### **Details**

This function provides a rough estimate of the total disk space required to run ExoLabel for a given input network. Only one of avg\_degree and num\_edges must be provided. The function prints out the estimated size of the original edgelist files, the estimated disk space and RAM 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, though it may impact the worst-case RAM consumption. Expected RAM consumption is determined by the average prefix length a random pair of vertex labels have in common, and should be closer to the minimum usage in most scenarios (see ExoLabel for more details).

#### Value

Invisibly returns a vector of length six, showing the estimated RAM consumption, estimated input edgelist file size, estimated disk consumption using in-place sort (use\_fast\_sort=FALSE), estimated disk consumption using fast sort (use\_fast\_sort=TRUE), estimated final file size, and ratio of the input file size to total ExoLabel disk usage. All values denote 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

Estimate Genome Rearrangement Scenarios with Double Cut and Join Operations

### **Description**

Take in a Synteny object and return predicted rearrangement events.

EstimRearrScen 29

#### Usage

```
EstimRearrScen(SyntenyObject, NumRuns = -1,

Mean = FALSE, MinBlockLength = -1,

Verbose = TRUE)
```

#### **Arguments**

SyntenyObject Synteny object, as obtained from running FindSynteny. Expected input is

unichromosomal sequences, though multichromosomal sequences are supported.

NumRuns Numeric; The number of scenarios to simulate. The default value of -1 cor-

responds to  $\sqrt{b}$  scenarios, where b is the number of unique breakpoints in the

Synteny object.

Mean Logical; Indicates whether to return the mean (TRUE) or minimum (FALSE) num-

ber of inversions and transpositions found across all runs.

MinBlockLength Numeric; Minimum size of syntenic blocks to use for analysis. The default

value of -1 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; If TRUE, displays a progress bar and prints 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 **events** rather than 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. The Mean parameter controls if the function returns the best found solution (Mean=FALSE) or the mean number of events from all solutions (Mean=TRUE).

30 EstimRearrScen

#### Value

An *NxN* 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, ..., N, and then have genome 2 numbers relative to that.

As an example, suppose genome 1 has elements ABE(r)G and genome 2 has elements EB(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

EvoWeaver 31

- 3. length: Length of block, in nucleotides
- 4. rel\_direction\_on\_2: 1 if the blocks have the same transcriptonal 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</pre>
```

EvoWeaver

EvoWeaver: Identifying Gene Functional Associations from Coevolutionary Signals

### **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)
```

32 **EvoWeaver** 

#### **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.

An object of class 'dendrogram' representing the overall species tree for the MySpeciesTree

list provided in ListOfData.

NoWarn Logical; If FALSE, displays warnings corresponding to which algorithms are

unavailable for given input data format (see Details for more information).

An object of class EvoWeaver. ew

Verbose Logical; If TRUE, displays output when calculating species tree.

Integer; The number of processors to use. Set to NULL to automatically use the **Processors** 

maximum amount of processors.

#### **Details**

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

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

- 2. ListOfData[[i]] = c('g1\_d1\_s1\_p1', 'g2\_d2\_s2\_p2', ..., 'gk\_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 (2) is the same as (1), just with the formatting of names slightly different. Each entry is of the form g\_d\_p, where g is the unique identifier for the genome, d is which chromosome the ortholog is located, s indicates whether the gene is on the forward or reverse strand, and p is what position the ortholog appears in on that chromosome. p must be a numeric. s 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. g,d can be any value as long as they don't contain an underscore ('\_').

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 (2). 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. 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') <- ....

EvoWeaver 33

#### Value

Returns a EvoWeaver object.

#### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

#### See Also

predict.EvoWeaver, ExampleStreptomycesData, BuiltInEnsembles, SuperTree

```
# 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):
1 <- list()</pre>
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(1)</pre>
## Constructing a EvoWeaver object according to (2):
## Here we need to add in the genome, chromosome, direction, and 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.
1 <- list()</pre>
l[['a']] \leftarrow c('a_1_0_1', 'c_1_1_2', 'd_1_0_1')
l[['b']] \leftarrow c('a_1_1_2', 'c_1_1_1')
1[['c']] \leftarrow c('a_1_1_3', 'b_1_0_2')
1[['d']] \leftarrow c('a_1_0_4', 'b_1_0_1')
l[['e']] <- c('b_1_0_3', 'c_1_0_3', 'd_1_0_2')
```

34 EvoWeaver-GOPreds

```
pwCase2 <- EvoWeaver(1)

## 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(...)
# where the same as the
## entries in Case 1.</pre>
```

EvoWeaver-GOPreds

Gene Organization Predictions for EvoWeaver

# **Description**

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

predict. EvoWeaver currently supports three Coloc methods:

- 'GeneDistance'
- 'MoransI'
- 'OrientationMI'

#### **Format**

None.

#### **Details**

All distance matrix methods require an EvoWeaver object initialized with gene locations using a four number code. See EvoWeaver for more information on input data types.

The built-in GeneDistance 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. If a given gene is found multiple times in the same genome, the maximal score across all possible pairings for that gene is used. The score for a pair of gene groups is the mean score of all gene pairings across the groups.

MoransI measures the extent to which gene distances are preserved across a phylogeny. This function uses the same initial scoring scheme as GeneDistance. The raw scores are passed into MoranI 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.

OrientationMI uses mutual information of the relative orientation of each pair of genes. Conservation of relative orientation 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  $\emptyset$  or 1, denoting whether the gene is on the forward or reverse strand. The mutual information is calculated as:

EvoWeaver-PPPreds 35

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

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.

#### 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 ten PP methods:

- 'ExtantJaccard'
- 'Hamming'
- 'GLMI'
- 'PAPV'
- 'CorrGL'
- 'ProfDCA'
- 'Behdenna'

- 'GLDistance'
- 'PAJaccard'
- 'PAOverlap'

#### **Format**

None.

#### **Details**

Most PP methods are compatible with a EvoWeaver object initialized with any input type. See EvoWeaver for more information on input data types.

When Method='Ensemble' or Method="PhylogeneticProfiling", EvoWeaver uses methods GLMI, GLDistance, PAJaccard, and PAOverlap.

These methods use presence/absence (P/A) 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 ExtantJaccard use Hamming and Jaccard distance (respectively) of P/A profiles to determine overall score.

GLMI uses mutual information of gain/loss (G/L) vectors to determine score, employing a weighting scheme such that concordant gains/losses give positive information, discordant gains/losses give negative information, and events that do not co-occur with a gain/loss in the other gene group give no information.

PAJaccard calculates the centered Jaccard index of P/A profiles, where each clade with identical extant patterns is collapsed to a single leaf.

PAOverlap calculates the proportion of time in the ancestry that both genes cooccur relative to the total time each individual gene occurs, based on ancestral states inferred with Fitch parsimony.

PAPV calculates a p-value for P/A 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 ExtantJaccard, Hamming, or GLMI 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 P/A profiles. This approach has been validated on P/A profiles in Fukunaga and Iwasaki (2022), though the implementation in EvoWeaver forsakes the persistent contrasive divergence method in favor of the 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-occurence 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.

GLDistance 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 GLDistance, then uses a Pearson's correlation coefficient weighted by p-value to infer similarity.

EvoWeaver-PSPreds 37

#### Author(s)

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#### References

Behdenna, A., et al., *Testing for Independence between Evolutionary Processes*. Systematic Biology, 2016. **65**(5): p. 812-823.

Chung, N.C, et al., *Jaccard/Tanimoto similarity test and estimation methods for biological presence-absence data*. BMC Bioinformatics, 2019. **20**(S15).

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Lokhov, A.Y., et al., *Optimal structure and parameter learning of Ising models*. Science advances, 2018. **4**(3): p. e1700791.

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:

- 'RPMirrorTree'
- 'RPContextTree'
- 'TreeDistance'

### **Format**

None.

38 EvoWeaver-PSPreds

#### **Details**

All distance matrix methods require a EvoWeaver object initialized with dendrogram objects. See EvoWeaver for more information on input data types.

The RPMirrorTree 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 Singular Value Decomposition (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 RPContextTree 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:

- "RF": Robinson-Foulds Distance
- "CI": Clustering Information 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.

# Author(s)

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# 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.

EvoWeaver-SLPreds 39

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:

- 'SequenceInfo'
- 'GeneVector'
- 'Ancestral'

#### **Format**

None.

#### **Details**

Sequence Level methods require a EvoWeaver object initialized with dendrogram objects and sequence information stored in the leaves. See EvoWeaver for more information on input data types.

When Method='Ensemble' or Method="SequenceLevel", EvoWeaver uses methods SequenceInfo and GeneVector. The argument useDNA switches between interpreting sequences as DNA or AA sequences.

The SequenceInfo 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.

40 EvoWeb

The GeneVector 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:

 $n_{AA}, n_{AC}, \ldots, r$ 

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 Cluster of Orthologous Genes (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.

### 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** 

EvoWeb

EvoWeb: Predictions from EvoWeaver

## **Description**

EvoWeb objects can be returned from predict. EvoWeaver.

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

### **Format**

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

### **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.

### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

### See Also

```
predict.EvoWeaver
simMat
plot.EvoWeb
```

### **Examples**

ExampleStreptomycesData

Example EvoWeaver Input Data from Streptomyces Species

### **Description**

Data from Streptomyces species to test EvoWeaver functionality.

# Usage

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

### **Format**

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.

#### **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 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.

### 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)</pre>
```

ExoLabel

ExoLabel: Out-of-Memory Fast Label Propagation

### **Description**

Detects communities in networks with Fast Label Propagation using disk space to drastically reduce memory overhead.

## Usage

## **Arguments**

edgelistfiles Character; vector of files to be processed. Each entry should be a machine-interpretable path to an edgelist file. See Details for expected format.

outfile Character; file to write final clusters to. Can be set to a vector of filepaths to run multiple clusterings (see "Multiple Clusterings").

mode

Character; specifies whether edges should be interpreted as undirected (default) or directed. If interpreted as directed, each edge V1 V2 is interpreted as  $V_1 \to V_2$ . Can be "undirected", "directed", or an unambiguous abbreviation.

add\_self\_loops

Logical or Numeric; determines if a self-loop cutoff should be added to the network. A self-loop cutoff of value w requires that at least one incoming edge has weight w in order to assign the node to that cluster (See "Self-Loops" for more information). If TRUE, adds self-loop cutoffs of weight 1.0 to all vertices. If set to numeric value w, adds self-loop cutoffs of weight w to all nodes. Can also be set to a vector when running multiple clusterings (see "Multiple Clusterings").

attenuation

Logical or Numeric; determines if label-hop attenuation should be used. If TRUE, uses attenuation to prevent single clusters from dominating results. Can also be set to a numeric to influence the strength of attenuation (larger values produce larger clusters). See "Attenuation" for more information on this parameter. Can also be set to a vector when running multiple clusterings (see "Multiple Clustering").

dist\_scaling

Logical or Numeric; further controls the scaling of label-hop attenuation. See "Attenuation" for more information on this parameter. Can also be set to a vector when running multiple clusterings (see "Multiple Clustering").

ignore\_weights

Logical; determines if weights should be ignored. If TRUE, all edges will be treated as an edge of weight 1. Must be set to TRUE if any of edgelistfiles are two-column tables (start->end only, lacking a weights column).

iterations

Integer; maximum number of times to process each node. If set to zero or NULL, automatically uses the square root of the max node degree. See "Algorithm Convergence" for more information.

return\_table

Logical; determines how the result of clustering is returned. If FALSE (default), returns a character vector corresponding to the path of outfile. If TRUE, parses outfile using read.table and returns the result (not recommended for very large graphs).

consensus\_cluster

Logical or Numeric; determines if consensus clustering should be used. **Currently disabled, but will be available in the next release.** If TRUE, runs the clustering algorithm nine times across varying parameters and forms a consensus clustering based on the agreement of each run. Can be set to a numeric vector to control the number of clusterings. See "Consensus Clustering" below for more information.

use\_fast\_sort

Logical; determines how files should be sorted. If FALSE, ExoLabel will perform file sorting functions in-place. If TRUE, ExoLabel will perform its file sorting functions using a second temporary file. This is much faster than the in-place sort, but consumes twice the amount of disk space. The relative disk consumption is about the same size as the input graph for use\_fast\_sort=FALSE, and about double the size of the input graph for use\_fast\_sort=TRUE (see "Memory Consumption" and the last paragraph of "Warning" below). Set to FALSE if you're worried about disk utilization.

verbose

Logical; determines if status messages (output, progress, etc.) should be displayed while running. Output messages are reduced if running in non-interactive mode.

sep

Character; expected character that separates entries on a line in each file in edgelistfiles. Defaults to tab, as would be expected in a .tsv formatted file. Set to ',' for a .csv file. Also determines the separator used in the output table.

tempfiledir

Character; vector corresponding to the location where temporary files used during execution should be stored. These temporary files are deleted after ExoLabel finishes running.

#### **Details**

ExoLabel identifies communities (clusters) in graph/network structures using a variant of Fast Label Propagation, as proposed by Traag and Subelj (2023).

However, 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. ExoLabel uses disk space for storing representations of graphs. While this is slower than computing on RAM, it allows ExoLabel to scale to graphs of enormous size while only using a comparatively small amount of memory. See "Memory Consumption" for details on the total disk/memory consumption of ExoLabel.

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

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 separator <sep> corresponds to the argument sep (defaulting to tab for .tsv format), and linesep is the newline value '\n'.

If ignore\_weight=TRUE, the file can be formatted as:

VERTEX1<sep>VERTEX2<linesep>

Note that the VERTEX1<sep>VERTEX2<sep>WEIGHT format is still accepted for ignore\_weight=FALSE, but the weights will be ignored. Also note that only positive weights are recorded; negative and zero-weighted edges are ignored.

### Value

Returns a list object with the parameters and result of the clustering. If using multiple clusterings, the return value is a list of lists, with each entry corresponding to the single-clustering case. This list has three entries, parameters, graph\_stats, and results.

parameters is a named vector with the values of add\_self\_loops, attenuation, dist\_scaling, and iterations used for the clustering.

graph\_stats is a named numeric vector containing the number of nodes and edges in the input graph.

results differs depending on the value of return\_table.

If return\_table=TRUE, results is 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, results is a character vector of length 1. This vector contains the path to the file to which the clusters were written. The file is formatted as a .tsv, with each line containing two tab separated columns (vertex name, assigned cluster). Clusters are numbered from one to the total number of clusters.

# **Self-Loops**

Label Propagation algorithms are susceptible to a large number of small weights outcompeting small numbers of strong edges. While self-loops can be added to mitigate this problem, they fail to scale to larger networks because noise can scale quadratically, whereas self-loops are constants.

The standard interpretation of self-loops adds a self-loop edge with fixed weight w to each node, essentially requiring any node's neighboring communities to have at least weight w to propagate. In a setting like orthology detection, spurious similarity scores will eventually outweigh both true similarities and the self-loop edges with increasing graph size.

To combat this, we treat self-loop values as a "self-loop cutoff" rather than a fixed value. Self-loop cutoffs are a value w' such that all neighboring communities must have at least one edge of weight w' in order to propagate. With this usage, even if a node has many neighbors in the same community with spurious similarities, it must have at least one neighbor in that community with a strong similarity in order for the node to join that community. This approach scales better with the size of graphs compared to the traditional usage of self-loops.

As an example, consider a node N not yet assigned to a community with 10 neighbors. Neighbors 1-9 are in community 1 with weight 0.1, and neighbor 10 is in community 2 with weight 0.8. Community 1 thus has total weight 0.9, and community 2 has weight 0.8. In the context of orthology detection, values below 0.2 are likely to be spurious. With a standard self-loop of 0.4, N would still be assigned to community 1, despite these being likely spurious. However, with a *self-loop cutoff* of 0.4, N would be assigned to community 2 because no edge in community 1 is at least 0.4.

### **Iterations**

One of the main issues of Label Propagation algorithms is that they can fail to converge. Consider an unweighted directed graph with four nodes connected in a loop. That is, A->B, B->C, C->D, D->A. If A, C are in cluster 1 and B, D are in cluster 2, this algorithm could keep processing all the nodes in a loop and never converge. To solve this issue, we introduce an additional measure for convergence controlled by iterations. If iterations=x, then we only allow the algorithm to process each node x times. Once a given node has been seen x times, it is no longer updated. This can be manually specified, but defaults to the square root of the largest node indegree.

### Attenuation

ExoLabel also incorporates label-hop attenuation to reduce the chance of a single massive cluster dominating results, as inspired by Leung et al. (2009). In short, as a particular label propagates to other nodes, its subsequent contribution diminishes. The farther a particular label is from its original source, the less its contribution. The degree to which its contribution diminishes scales dynamically based on the proportion of nodes that update on each cycle. Each node's attenuated weight is calculated as  $w' = w(1 - p^a d^s)$ , with w the node weight, p the proportion of nodes that changed label in the previous iteration, a the attenuation power (as controlled by attenuation), d the distance from the initial label, and s the distance scaling (as controlled by dist\_scaling).

Larger values of attenuation create larger clusters, whereas smaller values create smaller clusters. Passing a value of FALSE (equivalent to 0.0) disables attenuation entirely rather than returning all singleton clusters.

Larger values of dist\_scaling create smaller clusters by making the impact of attenuation more severe, whereas smaller values create larger clusters. Setting dist\_scaling to FALSE (equivalent to 0.0) will completely disable attenuation by making the algorithm ignore distances. **Note:** this parameter is somewhat experimental and its use is discouraged.

The default values of TRUE for both attenuation and dist\_scaling (equivalent to 1.0) recover the original implementation provided in Leung et al. (2009).

## **Multiple Clusterings**

Reading in the graph object takes a large portion of the processing time. This leads to a lot of duplicated effort when trying to cluster the same network under alternative parameter settings.

Multiple clusterings on the same network are supported by passing vectors of input to outfile and add\_self\_loops or attenuation. If the length of outfile is greater than 1, add\_self\_loops and attenuation can each be set to either a single value or a vector of the same length as outfile. For a single value, the same parameter value will be used across all clusterings. For multiple values, the corresponding value will be used in each clustering. See "Examples" for example usage.

Note that the order to process each node is randomly initialized, so multiple runs on the same parameters may produce different results if a random seed is not set.

### **Consensus Clustering**

Consensus clustering is not yet available, but will be enabled in the next release.

Consensus clustering runs ExoLabel on the input graph multiple times, transforming weight values according to the sigmoid function  $(1 + \exp(-s(w - \frac{1}{2}))^{-1})$ , where w is the original weight and s is the shape parameter.

By default, this runs nine times for shape parameters 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.

## 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 255 characters. This limitation is provided to decrease memory overhead and improve runtime. This behavior is controlled by the definition of MAX\_NODE\_NAME\_SIZE in src/OnDiskLP.c.

Second, nodes are indexed using 44-bit unsigned integers. This means that the maximum possible number of nodes available is  $2^{40}-1$ , which is about 17.5 trillion. This is because ExoLabel compresses weights and node labels into a single 64-bit integer to decrease disk consumption during sorting. Weights are rescaled with  $w'=log_2(w+1)$ , and the resulting value is transformed into a floating point number with a 16-bit mantissa and 4-bit exponent. This representation maintains a maximum error in precision of less than 0.05%, but does result in absolute errors getting larger as weights increase in size. For a point of reference, the error in representation is less than 0.00004 for weights in [0,1] and less than 10.5 for weights in [65,000, 70,000]. This error should be undetectable outside of extremely niche scenarios.

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. While there are safeguards in the code itself, unhandleable errors can occur when the OS runs out of space. Use <code>EstimateExoLabel</code> to estimate the disk consumption of your graph, and see "Memory Consumption" for more details on how the total disk/memory consumption is calculated. Note that using <code>use\_fast\_sort=TRUE</code> will double the maximal disk consumption of the algorithm.

#### **Memory Consumption**

Let v be the number of unique nodes, d the average indegree of nodes, and l the average length of node labels. Note that the number of edges e is equivalent to dv.

Specific calculations for memory/disk consumption are detailed below. In summary, the absolute worst case memory consumption is roughly (24l+46)v bytes, and the maximum disk consumption during computation is 16dv bytes (or 32dv bytes if use\_fast\_sort=TRUE). In practice, the RAM consumption is closer to 46v bytes. The final table consumes  $(2+l+\log_{10}v)v$  bytes on disk.

ExoLabel builds a trie to keep track of vertex names. Each internal node of the trie consumes 24 bytes, and each leaf node consumes 28 bytes. The lowest possible RAM consumption of the trie (if every label is length l and shares the same prefix of length l-1) is roughly 28v bytes, and the maximum RAM consumption (if no two node labels have any prefix in common) is (24l+28)v bytes. We can generalize this to estimate the total memory consumption as roughly (24(l-p)+28)v, where p is the average length of common prefix between any two node labels.

ExoLabel also uses a number of internal caches to speed up read/writes from files. These caches take around 200MB of RAM in total irrespective of graph size. Note that this calculation does not include the RAM required for R itself. It also uses an internal queue for processing nodes, which consumes roughly 10v bytes, and an internal index of size 8v bytes.

As for disk space, ExoLabel transforms the graph into a CSR-compressed network, which is split across two files: a neighbors list, and a weights list. CSR compressions also require an index, which is stored directly in the trie structure. The two files consume a total of 12 bytes per outgoing edge, for a total disk consumption of 12vd bytes. However, the initial reading of the edges requires 16 bytes per edge, resulting in a maximum disk consumption of 16dv. If use\_fast\_sort=TRUE, this edge reading maximally consumes 32 bytes per edge (a maximum disk consumption of 32dv). Note that undirected edges are stored as two directed edges, which doubles the disk consumption.

The final table returned contains vertex names and cluster numbers in human-readable format. Each line is of the format VERTEX<sep>CLUSTER, where <sep> is the argument passed to sep. Each line consumes at most  $l+2+\log_{10}v$  bytes. In the worst case, the number of clusters is equal to the number of vertices, which have at most  $\log_{10}v$  digits. The average number of digits is close to the number of digits of the largest number due to how the number of digits scales with numbers. The extra two bytes are for the sep and newline characters. Thus, the total size of the file is at most  $(2+l+\log_{10}v)v$  bytes. We remove all intermediate files prior to outputting clusters, so in practical cases this should be smaller than intermediate disk consumption.

### Author(s)

Aidan Lakshman < AHL27@pitt.edu>

#### References

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

Leung, X.Y.I., et al., *Towards real-time community detection in large networks*. Phys. Rev. E, 2009. **79**(066107). https://doi.org/10.1103/PhysRevE.79.066107

## See Also

EstimateExoLabel

48 ExpandDiagonal

```
if(file.exists(edgefile)) file.remove(edgefile)
writeLines(all_edges, edgefile)
## Run ExoLabel
res_file <- ExoLabel(edgefile)</pre>
clustering <- read.delim(res_file$result, header=FALSE)</pre>
colnames(clustering) <- c("Vertex", "Cluster")</pre>
clustering
## Can also return the result directly if the network is small enough
res <- ExoLabel(edgefile, return_table=TRUE)</pre>
print(res)
### Multiple Clustering ###
## Run with multiple add_self_loops values
tfs <- replicate(3, tempfile())</pre>
p2 <- ExoLabel(edgefile, tfs,</pre>
               add_self_loops=c(0,0.5,1),
               return_table = TRUE)
```

ExpandDiagonal

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

# Description

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

## Usage

# Arguments

SynExtendObject

An object of class PairSummaries.

DataBase01

A character string pointing to a SQLite database, or a connection to a DECIPHER database.

InheritConfidence

A logical indicating whether or not to inheret the user specified column-value pairs assigned to the input object.

ExpandDiagonal 49

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. To be retained, a pair evaluated

for expansion must be above all user specified confidences.

Processors An integer value indicating how many processors to supply to AlignPairs.

Supplying NULL will cause detection and use of all available cores.

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

```
library(RSQLite)
DBPATH <- system.file("extdata",</pre>
                       "Endosymbionts_v05a.sqlite",
                       package = "SynExtend")
tmp01 <- tempfile()</pre>
file.copy(from = DBPATH,
          to = tmp01)
DBCONN <- dbConnect(SQLite(), tmp01)</pre>
data("Endosymbionts_Pairs01", package = "SynExtend")
data("Endosymbionts_LinkedFeatures", package = "SynExtend")
# this will add segs to the DB
PrepareSeqs(SynExtendObject = Endosymbionts_LinkedFeatures,
            DataBase = tmp01,
            Verbose = TRUE)
ExpandedPairs <- ExpandDiagonal(SynExtendObject = Endosymbionts_Pairs01,</pre>
                                 DataBase01 = DBCONN,
                                  Verbose = TRUE)
dbDisconnect(DBCONN)
```

50 ExtractBy

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 DNAStingSet 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

## **Arguments**

х	A PairSummaries object, or if y is a DNAStringSet, a DFrame of gene calls such as one generated by gffToDataFrame.
у	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

## **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

FastQFromSRR 51

#### **Examples**

```
DBPATH <- system.file("extdata",</pre>
                       "Endosymbionts_v05a.sqlite",
                       package = "SynExtend")
data("Endosymbionts_Pairs03", package = "SynExtend")
data("Endosymbionts_Sets", package = "SynExtend")
# extract the first 10 disjoint sets
Sets <- ExtractBy(x = Endosymbionts_Pairs03,</pre>
                   y = DBPATH,
                   z = Endosymbionts_Sets[1:10],
                   Verbose = TRUE)
# extract just the pairs
Sets <- ExtractBy(x = Endosymbionts_Pairs03,</pre>
                   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 prefetch, fastq-dump, or fasterq-dump functions

in the SRAToolkit.

**ARGS** A list representing key and value sets used to construct the call to fastq-dump,

multi-argument values are passed to paste 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 fastq-dump. If FALSE - the default, they are removed and only the list of QualityScaledDNAStringSets returned by the

function are retained.

52 FindSets

#### **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 QualityScaledDNAStringSets. 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)</pre>
```

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

# **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.

FitchParsimony 53

### Author(s)

Nicholas Cooley <npc19@pitt.edu>

### See Also

**PairSummaries** 

# **Examples**

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

# Arguments

dend	An object of class 'dendrogram'
num_traits	Integer; The number of traits to inferred.
traits_list	A list of character vectors, where the $i$ 'th entry corresponds to the leaf labels that have the trait $i$ .
initial_state	Integer; The state assumed for the root node. Set to NULL to disable autofilling the root state. $\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$
fill_ambiguous	Logical; Determines if states that remain ambiguous after completion of the algorithm should be filled in randomly.

54 FitchParsimony

#### **Details**

Fitch Parismony 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.

### 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.

```
d <- as.dendrogram(hclust(dist(USArrests), "ave"))</pre>
labs <- labels(d)</pre>
# Defining some presence absence patterns
set.seed(123L)
pa_1 <- sample(labs, 15L)</pre>
pa_2 <- sample(labs, 20L)</pre>
# inferring ancestral states
fpd <- FitchParsimony(d, 2L, list(pa_1, pa_2))</pre>
# 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 \leftarrow dendrapply(fpd, \x){
  ai <- 1L
  s <- attr(x, 'FitchState')</pre>
  1 <- list()</pre>
  if(is.leaf(x)){
    # coloring tips based presence/absence
```

Generic 55

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

### Format

The format is an object of class "glm".

### **Details**

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

```
data(Generic)
```

56 gffToDataFrame

gffToDataFrame

Generate a DataFrame of gene calls from a gff3 file

### **Description**

Generate a DataFrame of gene calls from a gff3 file

### Usage

## **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 rtracklayer::import.

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>

HitConsensus 57

HitConsensus	Return a numeric measure of whether kmer hits linking two genomic
	features are in linearly similar locations in both features.

# Description

This function is designed to work internally to SummarizePairs so it works on relatively simple atomic vectors and has little overhead checking.

# Usage

```
HitConsensus(gene1left, gene2left, gene1right, gene2right, strand1, strand2, hit1left, hit1right, hit2left, hit2right)
```

# **Arguments**

gene1left	Integer; feature bound positions in nucleotide space.
gene2left	Integer; feature bound positions in nucleotide space.
gene1right	Integer; feature bound positions in nucleotide space.
gene2right	Integer; feature bound positions in nucleotide space.
strand1	Logical; is feature 1 on the positive or negative strand
strand2	Logical; is feature 2 on the positive or negative strand
hit1left	Integer; kmer hit bound positions in nucleotide space.
hit1right	Integer; kmer hit bound positions in nucleotide space.
hit2left	Integer; kmer hit bound positions in nucleotide space.
hit2right	Integer; kmer hit bound positions in nucleotide space.

## **Details**

HitConsensus calculates whether the distances between the bounds of a kmer hit and the feature bounds are different between the features linked by the kmer.

# Value

A vector of numerics.

## Author(s)

Nicholas Cooley <npc19@pitt.edu>

58 LinkedPairs

#### See Also

NucleotideOverlap, SummarizePairs, FindSynteny

#### **Examples**

#

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 overlayed on the locations of sequence features to clearly illustrate where exact sequence similarity is shared between pairs of sequence features.

### Usage

### **Arguments**

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

### **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.

MakeBlastDb 59

### 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

## **Arguments**

seqs	Sequence(s) to create a BLAST database from. This can be either an XStringSet or a path to a FASTA file.	
dbtype	Character; Either 'prot' for amino acid input, 'nucl' for nucleotide input, or an unambiguous abbreviation.	
dbname	Character; Name of the resulting database. If not provided, defaults to a random string prefixed by blastdb.	
dbpath	Character; Path where database should be created. If not provided, defaults to TMPDIR.	
extraArgs	Character; Additional arguments to be passed to the query executed on the command line. This should be a single string.	
createDirectory		
	Logical; Determines if a directory should be created for the database if it doesn't already exist. If FALSE, the function will throw an error instead of creating a directory.	
verbose	Logical; Determines if status messages should be displayed while running.	

## **Details**

MakeBlastDb is a barebones wrapper for makeblastdb from the BLAST+ commandline tools. It is set up for convenience purposes only and does not add any additional functionality. Requires a functioning installation of the BLAST+ commandline tools.

60 MoranI

#### 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**

#

MoranI

Moran's I Spatial Autocorrelation Index

## **Description**

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

## Usage

# **Arguments**

values Numeric; Vector containing signals for each point in space.

weights Numeric object of class dist with Size attribute equivalent to the length of

values, representing distances between each point in space.

alternative Character; determines how p-value should be calculated for hypothesis testing

against the null of no spatial correlation. 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:

$$I = \frac{N}{W} \frac{\sum_{i}^{N} \sum_{j}^{N} w_{ij} (x_{i} - \bar{x})(x_{j} - \bar{x})}{\sum_{i}^{N} (x_{i} - \bar{x})^{2}}$$

MoranI 61

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.

62 NucleotideOverlap

NormVec

Unit normalize a vector

# Description

This function is designed to work internally to functions within SynExtend so it works on relatively simple atomic vectors and has little overhead checking.

## Usage

```
NormVec(vec)
```

## **Arguments**

vec

A numeric or integer vector.

## **Details**

NormVec unit normalized a vector.

### Value

A numeric vector the same length as the input.

## Author(s)

Nicholas Cooley <npc19@pitt.edu>

# See Also

```
NucleotideOverlap, SummarizePairs, WithinSetCompetition, RejectionBy
```

# **Examples**

```
x \leftarrow NormVec(rnorm(n = 50, mean = 2, sd = 2))
```

NucleotideOverlap

Tabulating Pairs of Genomic Sequences

# Description

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

# Usage

NucleotideOverlap 63

### **Arguments**

SyntenyObject An object of class "Synteny" built from the FindSynteny in the package DECIPHER.

GeneCalls

A named list of objects of class "DFrame" built from gffToDataFrame, objects of class "GRanges" imported from rtracklayer::import, or objects of class "Genes" created from the DECIPHER function FindGenes. "DFrame"s built by "gffToDataFrame" 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 FindGenes function equivalently to those produced by gffToDataFrame. Using a "GRanges" object will force limit Index to TRUE.

ing a "GRanges" object will force LimitIndex to TRUE.

LimitIndex Logical indicating whether to limit which indices in a synteny object to query.

FALSE by default, when TRUE only the first sequence in all selected identifiers will be used. LimitIndex can be used to skip analysis of plasmids, or solely

query a single chromosome.

AcceptContigNames

Match names of contigs between gene calls object and synteny object. Where relevant, the first white space and everything following are removed from contig names. If "TRUE", NucleotideOverlap assumes that the contigs at each position in the synteny object and "GeneCalls" object are in the same order. Is automatically the "GeneCalls" object are in the same order.

ically 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

```
data("Endosymbionts_GeneCalls", package = "SynExtend")
data("Endosymbionts_Synteny", package = "SynExtend")
Links <- NucleotideOverlap(SyntenyObject = Endosymbionts_Synteny,</pre>
```

64 OneSite

```
GeneCalls = Endosymbionts_GeneCalls,
LimitIndex = FALSE,
Verbose = TRUE)
```

OneSite

Calculate a site on a right hyperbola.

## **Description**

This function is designed to work internally to functions within SynExtend so it works on relatively simple atomic vectors and has little overhead checking.

# Usage

# Arguments

X Numeric; an x coordinate value.Bmax Numeric; an asymptotic value.

Kd Numeric; the half-max of the right hyperbola.

### **Details**

OneSite calculates the Y-value for a given X-value on a right hyperbola.

#### Value

A numeric of length 1.

 $x \leftarrow OneSite(X = 3,$ 

## Author(s)

Nicholas Cooley <npc19@pitt.edu>

### See Also

NucleotideOverlap, SummarizePairs, WithinSetCompetition, RejectionBy

```
Bmax = 10,
Kd = 3)
```

```
\# plot(x = 1:10, y = vapply(X = 1:10, FUN = function(x) {OneSite(X = x, Bmax = 5, Kd = 2)}, FUN.VALUE = vector(model)
```

PairSummaries 65

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 ob-

ject was also required, but this object is now carried forward from NucleotideOverlap

 $inside \ the \ Linked Pairs \ object.$ 

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 consum-

ing, especially for large numbers of pairs. Default is FALSE.

Score Logical indicating whether to provide a length normalized score with DECI-

PHER's ScoreAlignment function. If TRUE all pairs will be aligned using DE-CIPHER'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 perform-

ing an alignment. By default this argument is "Generic" specifying a generic PID prediction model based on PIDs computed from a randomly selected set of

66 PairSummaries

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 synteny 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 synteny 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 - frequences between predicted pairs. "PIDType" provides a character vector with values of "NT" where either

PhyloDistance 67

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, NucleotideOverlap
```

# **Examples**

 ${\tt PhyloDistance}$ 

Calculate Distance between Unrooted Phylogenies

# Description

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

### Usage

## **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	Character; Method to use for calculating tree distances. The following values are supported: "CI", "RF", "KF", "JRF". See Details for more information.
RawScore	Logical; Determines if the function should return the distance between two trees (FALSE) or the component values used to calculate the distance (TRUE). 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".

68 PhyloDistance

#### **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 JRFExp=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=FALSE, or c(0, NA, NA) if RawScore=TRUE.

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 linked above.

### 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

```
# 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")</pre>
```

PhyloDistance-CIDist

```
# 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)</pre>
```

PhyloDistance-JRFDist Jaccard-Robinson-Foulds Distance and Nye Similarity

## **Description**

Calculate JRF distance between two unrooted phylogenies. Nye Similarity is a special case of JRF distance, obtained when the JRF exponent k is set to 1.

## **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 JRFExp=1, the distance is equivalent to the metric introduced in Nye et al. (2006). As JRFExp 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")</pre>
```

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")</pre>
```

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.

```
# 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")</pre>
```

74 plot.EvoWeb

```
# 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 can be returned 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 being targetting for additional functionality in later releases.

# Usage

# **Arguments**

x	A EvoWeb object. See EvoWeb
NumSims	Integer; Number of iterations to run the model for.
Gravity	Numeric; Strength of Gravity force. See 'Details'.
Coulomb	Numeric; Strength of Coulomb force. See 'Details'.
Connection	Numeric; Strength of Connective force. See 'Details'.
MoveRate	Numeric; Controls how far each point moves in each iteration.
Cutoff	Numeric; Cutoff value; if abs(val) < Cutoff, that Connection is shrunk to zero.
ColorPalette	Character; Color palette for graphing. Valid inputs are any palette available in palette.pals(). See palette for more info.
Verbose	Logical; Determines if status messages and progress bars should be displayed while running.
	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='ExtantJaccard'
evoweb <- predict(ew, Method='ExtantJaccard', Subset=1:50)

plot(evoweb)</pre>
```

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

#### **Arguments**

object A EvoWeaver object

Method Character; 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 Either a vector or a 2xN matrix representing the subset of data to predict on.

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).

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 specifed by name (character) or by index (numeric).

subset=rbind(c(1,2),c(1,3),c(2,3)) produces equivalent functionality to

subset=1:3.

Processors Integer; Number of cores to use for methods that support multithreaded execu-

tion. 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 Object of class dendrogram representing the phylogenetic relationship of all

genomes in the dataset. Required for Method=c('RPContextTree', 'GLDistance', 'CorrGL', 'MoransI', '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. The default value is "KEGG", corresponding to a built-in ensemble model trained on the KEGG MOD-ULE database. Alternative values allowed are "CORUM", for a built-in ensemble model trained on the CORUM database, or any user-trained model. See the examples for how to train an ensemble method to pass to PretrainedModel.

Has no effect if Method != 'Ensemble'.

NoPrediction Logical; determines if data should be returned prior to making prediction for

Method='Ensemble'.

If TRUE, this will instead return a data frame object with predictions from each algorithm for each pair. This dataframe is typically used to train an ensemble

If FALSE, EvoWeaver will return predictions for each pair (using user model if provided or a built-in otherwise).

ReturnDataFrame

Verbose

Logical; Determines if the function should return a data. frame object or a list of EvoWeb objects. Setting this parameter to FALSE is not recommended.

Logical; Determines if status messages and progress bars should be displayed

while running.

CombinePVal Logical; Determines if scores and p-values should be combined or returned as

separate values.

useDNA Logical; Determines whether to interpret sequences as DNA or AA (only used

for Sequence Level methods, see Details).

... 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. Common arguments to Method include:

- 'Ensemble': Ensemble prediction combining individual coevolutionary predictors. See Note below.
- 'PhylogeneticProfiling': All Phylogenetic Profiling Algorithms used in the EvoWeaver manuscript.
- 'PhylogeneticStructure': All EvoWeaver Phylogenetic Structure Methods
- 'GeneOrganization': All EvoWeaver Gene Organization Methods
- 'SequenceLevel': All EvoWeaver Sequence Level Methods used in the EvoWeaver manuscript.

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

The standard return type is a data. frame object with one column per predictor and an additional two columns specifying the genes in each pair. If ReturnDataFrame=FALSE, this returns a EvoWeb object. See EvoWeb for more information. Use of this parameter is discouraged.

By default, EvoWeaver weights scores by their p-value to correct for spurious correlations. The returned scores are raw\_score\*(1-p\_value). If CombinePVal=FALSE, EvoWeaver will instead return the raw score and the p-value separately. The resulting data.frame will have one column for the raw score (denoted METHOD.score) and one column for the p-value (denoted METHOD.pval). **Note:** p-values are recorded as (1-p). Not all methods support returning p-values separately from the score; in this case, only a METHOD.score column will be returned.

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.

Complete listing of all supported methods (asterisk denotes a method used in Ensemble, if possible):

- \* 'GLMI': MI of G/L profiles
- \* 'GLDistance': Score-based method based on distance between inferred ancestral Gain/Loss events
- \* 'PAJaccard': Centered Jaccard distance of P/A profiles with conserved clades collapsed
- \* 'PAOverlap': Conservation of ancestral states based on P/A profiles
- \* 'RPMirrorTree': MirrorTree using Random Projection for dimensionality reduction
- \* 'RPContextTree': MirrorTree with Random Projection correcting for species tree and P/A conservation
- \* 'GeneDistance': Co-localization analysis
- \* 'MoransI': Co-localization analysis using Moran's I for phylogenetic correction and significance

- \* 'OrientationMI': Mutual Information of Gene Relative Orientation
- \* 'GeneVector': Correlation of distribution of sequence level residues following Zhao et al. (2022)
- \* 'SequenceInfo': Mutual information of sites in multiple sequence alignment
- 'ExtantJaccard': Jaccard Index of Presence/Absence (P/A) profiles at extant leaves
- 'Hamming': Hamming similarity 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

#### Value

If ReturnDataFrame=TRUE, returns a data. frame object where each row corresponds to a single prediction for a pair of gene groups. The first two columns contain the gene group identifiers for each pair, and the remaining columns contain each prediction.

If ReturnDataFrame=FALSE, the return type is a list of EvoWeb objects. See EvoWeb for more info.

#### Note

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 potential issue where the R session can consume all available cores and then lose the ability to fork processes, with the only solution to restart the entire R session.

If ReturnDataFrame=FALSE and CombinePVal=FALSE, the resulting EvoWeb objects will contain values of type 'complex'. For each value, the real part denotes the raw score, and the imaginary part denotes 1-p, with p the p-value.

#### 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** 

PrepareSeqs 79

```
ew <- EvoWeaver(exData$Genes[1:50], MySpeciesTree=exData$Tree)</pre>
# Subset isn't necessary but is faster for a working example
evoweb1 <- predict(ew, Subset=1:2)</pre>
# print out results as an adjacency matrix
if(interactive()) print(evoweb1)
################
## Training own ensemble model
################
datavals <- evoweb1[,-c(1,2,10)]
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</pre>
myModel \leftarrow glm(y^{-}, datavals[,-c(1,2)], family='binomial')
testEvoWeaverObject <- EvoWeaver(exData$Genes[51:60], MySpeciesTree=exData$Tree)</pre>
evoweb2 <- predict(testEvoWeaverObject,</pre>
                      PretrainedModel=myModel)
# Print result as a data.frame of pairwise scores
if(interactive()) print(evoweb2)
```

PrepareSeqs

Add feature sequences to Decipher databases.

# Description

Given a SynExtend object with a GeneCalls attribute, and a DECIPHER database, add sequence tables named 'AAs' and 'NTs' to the database. The new tables contain all translatable sequences indicated by the genecalls, and all nucleotide feature sequences.

## Usage

#### **Arguments**

 ${\tt SynExtendObject}$ 

An object of class PairSummaries or of LinkedPairs. Object must have a GeneCalls attribute.

DataBase01

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.

Verbose Logical indicating whether or not to display a progress bar and print the time

difference upon completion.

#### **Details**

PrepareSeqs adds two tables to a DECIPHER database. One named 'AAs' that contains all translatable features, i.e. features with a coding length divisible by 3 and designated as coding. And another named 'NTs' which contains all features.

#### Value

An integer count of the number of feature sets added to the DECIPHER database.

#### Author(s)

Nicholas Cooley <npc19@pitt.edu>

#### See Also

SummarizePairs, NucleotideOverlap, FindSynteny

# **Examples**

RandForest

Classification and Regression with Random Forests

# **Description**

RandForest implements a version of Breiman's random forest algorithm for classification and regression.

#### Usage

```
RandForest(formula, data, subset, verbose=interactive(),
           weights, na.action,
           method='rf.fit',
           rf.mode=c('auto', 'classification', 'regression'),
           contrasts=NULL, ...)
## S3 method for class 'RandForest'
predict(object, newdata=NULL,
                na.action=na.pass, ...)
## Called internally by `RandForest`
RandForest.fit(x, y=NULL,
   verbose=interactive(), ntree=10,
   mtry=floor(sqrt(ncol(x))),
   weights=NULL, replace=TRUE,
   sampsize=if(replace) nrow(x) else ceiling(0.632*nrow(x)),
   nodesize=1L, max_depth=NULL,
   method=NULL,
    terms=NULL,...)
```

# **Arguments**

verbose

replace sampsize

ntree

mtry

O	
formula	an object of class "formula" (or one that can be coerced to that class): a symbolic description of the model to be fitted. See lm for more details.
data	An optional data frame, list, or environment (or object coercible by as.data.frame to a data frame) containing the variables in the model. If not found in data, the variables are taken from environment(formula), typically the environment from which RandForest is called.
subset	an optional vector specifying a subset of observations to be used in the fitting process.
weights	an optional vector of weights to be used in the fitting process. Should be NULL or a numeric vector.
na.action	a function which indicates what should happen when the data contain NAs. Currently experimental.
method	currently unused.
rf.mode	one of "auto", "classification", "regression" (or an unambiguous abbreviation), specifying the type of trees to build. If rf.mode="auto", the mode is inferred based on the type of the response variable.
contrasts	currently experimental; see 1m.
	further arguments passed to RandForest.fit.
object	an object of class 'RandForest' for prediction.
newdata	new data to predict on, typically provided as a data. frame object.

Logical; Determines if status messages should be displayed while running.

number of datapoints to sample for training each component decision tree.

logical; should data be sampled with replacement during training?

number of decision trees to grow. number of variables to try at each split.

number of datapoints to stop classification (see "Details")

max\_depth maximum depth of component decision trees.

x used internally by RandForest.fit

y used internally by RandForest.fit

terms used internally by RandForest.fit

## **Details**

RandForest implements a version of Breiman's original algorithm to train a random forest model for classification or regression. Random forests are comprised of a set of decision trees, each of which is trained on a subset of the available data. These trees are individually worse predictors than a single decision tree trained on the entire dataset. However, averaging predictions across the ensemble of trees forms a model that is often more accurate than single decision trees while being less susceptible to overfitting.

Random forests can either be trained for classification or regression. Classification forests are comprised of trees that assign inputs to a specific class. The output prediction is a vector comprised of the proportion of trees in the forest that assigned the datapoint to each available class. Regression forests are comprised of trees that assign each datapoint to a single continuous value, and the output prediction is comprised of the mean prediction across all component trees. When rf.mode="auto", the random forest will be trained in classification mode for response of type "factor", and in regression mode for response of type "numeric".

Several parameters exist to tune the behavior of random forests. The ntree argument controls how many decision trees are trained. At each decision point, the decision trees consider a random subset of available variables—the number of variables to sample is controlled by mtry. Each decision tree only sees a subset of available data to reduce its risk of overfitting. This subset is comprised of sampsize datapoints, which are sampled with or without replacement according to the replace argument.

Finally, the default behavior is to grow decision trees until they have fully classified all the data they see for training. However, this may lead to overfitting. Decision trees can be limited to smaller sizes by specifying the max\_depth or nodesize arguments. max\_depth refers to the depth of the decision tree. Setting this value to n means that every path from the root node to a leaf node will be at most length n. nodesize can be used to instead stop growing trees based on the size of the data to be partitioned at each decision tree node. If nodesize=n, then if a decision point receives less than n samples, it will stop trying to further split the data.

Classification forests are trained by maximizing the Gini Gain at each interior node. Split points are determined with exhaustive search for small data sizes, or simulated annealing for larger sizes. Regression forests are trained by maximizing the decrease in sum of squared error (SSE) if all points in each partition are assigned their mean output value. Nodes stop classification when either no partition improves the maximization metric (Gini Gain or decrease in SSE) or when the criteria specified by nodesize / max\_depth are met.

Some of the arguments provided are for consistency with the base 1m function. Use caution changing any values referred to as "Experimental" above. NA values may cause unintended behavior.

## Value

An object of class 'RandForest', which itself contains a number of objects of class 'DecisionTree' which can be used for prediction with predict.RandForest

#### Note

Generating a single decision tree model is possible by setting ntree=1 and sampsize=nrow(data). 'DecisionTree' objects do not currently support prediction.

#### Author(s)

Aidan Lakshman <ahl27@pitt.edu>

#### References

Breiman, L. (2001), Random Forests, Machine Learning 45(1), 5-32.

#### See Also

DecisionTree class

```
set.seed(199L)
n_samp <- 100L
AA <- rnorm(n_samp, mean=1, sd=5)
BB <- rnorm(n_samp, mean=2, sd=3)
CC <- rgamma(n_samp, shape=1, rate=2)</pre>
err <- rnorm(n_samp, sd=0.5)</pre>
y \leftarrow AA + BB + 2*CC + err
d <- data.frame(AA,BB,CC,y)</pre>
train_i <- 1:90
test_i <- 91:100
train_data <- d[train_i,]</pre>
test_data <- d[test_i,]</pre>
rf_regr <- RandForest(y~., data=train_data, rf.mode="regression", max_depth=5L)</pre>
if(interactive()){
  # Visualize one of the decision trees
  plot(rf_regr[[1]])
}
## classification
y1 < -y < -5
y2 <- y < 0 & y >= -5
y3 \leftarrow y < 5 \& y >= 0
y4 <- y >= 5
y_cl <- rep(0L, length(y))</pre>
y[y1] <- 1L
y[y2] \leftarrow 2L
y[y3] <- 3L
y[y4] \leftarrow 4L
d$y <- as.factor(y)
train_data <- d[train_i,]</pre>
test_data <- d[test_i,]</pre>
rf_classif <- RandForest(y~., data=train_data, rf.mode="classification", max_depth=5L)
if(interactive()){
  # Visualize one of the decision trees for classification
  plot(rf_classif[[1]])
```

84 RejectionBy

}

RejectionBy

Given an object of candidate pairs, reject false positives.

## **Description**

This function is designed to work internally to functions within SynExtend so it works on relatively simple atomic vectors and has little overhead checking.

# Usage

```
RejectionBy(input,
            criteria = list("fdr" = 1e-5,
                             "centroidthreshold" = list("globalpid" = 0.3),
                             "glmforbiddencolumns" = c("alitype"),
                             "lmforbiddencolumns" = c("response",
                                                       "alitype"),
                             "kargs" = list("max" = 15,
                                            "scalar" = 4,
                                            "unitnorm" = TRUE)),
            rankby = "rawscore",
            method = "direct",
            supportedcolumns = c("consensus",
                                  "kmerdist"
                                  "featurediff",
                                  "localpid"
                                  "globalpid",
                                  "matchcoverage",
                                  "localscore",
                                  "deltabackground",
                                  "rawscore",
                                  "response"),
            dropinappropriate = FALSE)
```

# **Arguments**

method

input A data.frame; currently set up to take in an internal representation of the columns eventually printed by SummarizePairs. Supported column names are enumerated in the supportedcolumns argument.

criteria A list of named objects that control the nobs of various rejection routines.

rankby A colname in the the input data.frame which will be used for the identification

of false positives.

Character; identify a method by which to reject false positives, currently sup-

ported methods include: glm, lm, kmeans, and direct.

supportedcolumns

Character; a vector of column names to select internal variables for candidate pair evaluation.

SelectByK 85

dropinappropriate

Logical; FALSE by default. If TRUE, should a method imply that it is incapable of logically separating true positives from false positives, no candidates are returned. If FALSE, all candidates are returned. Only really applicable in cases where very few initial candidates are identified.

#### **Details**

RejectionBy is yet another attempt at building a logical but simple routine for rejecting false positive candidate pairs in a scenario where it is difficult to proxy a distribution of appropriate false-positives.

#### Value

A value.

#### Author(s)

Nicholas Cooley <npc19@pitt.edu>

#### See Also

 ${\tt NucleotideOverlap, SummarizePairs, WithinSetCompetition, RejectionBy }$ 

# **Examples**

#

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)
```

86 SelectByK

## **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.

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

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

SequenceSimilarity 87

SequenceSimilarity

Return a numeric value that represents the similarity between two aligned sequences as determined by a provided substitution matrix.

# **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

# **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.

88 simMat

#### Value

Returns a single numeric.

#### Author(s)

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

#### See Also

```
AlignSeqs, AlignProfiles, AlignTranslation, DistanceMatrix
```

## **Examples**

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'
```

simMat 89

```
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; Determines if the diagonal is included in the data. If FALSE, the constructor generates 1s for the diagonal.
х	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.

90 simMat

#### 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>

```
## Creating a blank simMat object initialized to zeros
s <- simMat(0, nelem=20)</pre>
## Print out 5 rows instead of 10
print(s, n=5)
## Create a simMat object with 5 entries from a vector
vec <- 1:(dimn*(dimn-1) / 2)</pre>
s1 <- as.simMat(vec, DIAG=FALSE)</pre>
s1
## Here we include the diagonal
vec <- 1:(dimn*(dimn+1) / 2)</pre>
s2 <- as.simMat(vec, DIAG=TRUE)</pre>
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
## Get/set diagonal
Diag(s1)
Diag(s1) < -5
s1
```

subset.dendrogram 91

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.dendogram, 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 'dendogram'
    subset Character; A vector of labels to keep (see invert).
    invert Logical; If TRUE, subsets to the leaves not in subset.
    ... Additional arguments for consistency with generic.
```

#### Value

An object of class 'dendrogram' corresponding to the subset of the 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

```
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)</pre>
```

92 **SubSetPairs** 

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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.

SummarizePairs 93

#### Author(s)

Nicholas Cooley <npc19@pitt.edu>

#### See Also

PairSummaries NucleotideOverlap

#### **Examples**

SummarizePairs

Provide summaries of hypothetical orthologs.

# Description

Given a LinkedPairs object 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

94 SummarizePairs

#### **Arguments**

SynExtendObject

An object of class LinkedPairs-class.

DataBase01 A character string pointing to a SQLite database, or a connection to a DECIPHER

database.

AlignmentFun Character of length 1; a character string of length one specifying a link{DECIPHER}

alignment function. Currently only supports AlignPairs.

DefaultTranslationTable

Character of length 1; an identifier that can be recognized by getGeneticCode to use as the translation table for translating coding sequences in the case that

one is missing from supplied genecalls.

KmerSize Integer of length 1; Specify the kmer size for assessing kmer distance in nu-

cleotide space between two candidate pairs.

Verbose Logical of length 1; if TRUE progress bar and function timing will be displayed.

ShowPlot Logical of length 1; if TRUE provide some plots describing candidate pairs. Cur-

rently not implemented.

Processors Integer of length 1; specify the number of processors available to SummarizePairs

for multithreaded applications. If NULL all available detectable cores will be re-

quested.

Storage Numeric of length 1; a soft limit on the memory alloted to SummarizePairs for

the storage of sequence data from the supplied database. In Gb.

IndexParams A named list of arguments to be passed to IndexSeqs. Must be compliant with

do. call's expectation for its args argument.

SearchParams A named list of arguments to be passed to SearchIndex. Must be compliant

with do.call's expectation for its args argument.

SearchScheme Character of length 1; currently supported arguments include; "spike" indicating

to 'spike' in a population of background candidates by searching one set of codings sequences against the reverse of another, "standard" which will only search coding sequences from one genome against the other in the forward direction, and "reciprocal" which will perform a search strategy similar to Reciprocal Best

Hits.

RejectBy Character of length 1; currently supported arguments include; "glm" and "lm"

which use the eponymous functions to model the data within a set of candidate pairs and reject candidate pairs below a particular False Discovery Rate as determined from a set of known negatives generated when a "spike" search scheme is used. "kmeans" is a supported method that will run a naive kmeans based routine to cluster candidates within the set and reject candidates below a user supplied threshold. Lastly, "direct" will simply rank all candidate pairs by the user supplied attribute and drop all candidates below a user supplied FDR

threshold.

RetainInternal Logical of length 1; if TRUE internal values used for candidate pair rejection will

be attached to the returned object.

... Additional arguments to pass to interior functions. Currently not implemented.

#### **Details**

SummarizePairs collects features describing each linked feature pair. These features include:

• p1: a character identifier for the candidate pair partner in the supplied query.

SummarizePairs 95

- p2: a character identifier for the candidate pair partner in the supplied subject.
- Consensus: a numeric value calculated by HitConsensus describing whether relative locations of linking hits are in linearly similar positions in both candidate pair partners.
- p1featurelength: length of candidate query feature in nucleotides.
- p2featurelength: length of candidate subject feature in nucleotides.
- blocksize: integer value indicating the number of shared features blocked together.
- KDist: numeric value of the euclidean distance between candidate pairs in kmer space.
- TotalMatch: integer value indicating total nucleotides shared between candidates pairs in the original searches.
- MaxMatch: integer value indicating the largest kmer shared between candidate pairs in the original searches.
- UniqueMatches: integer value indicating the number of kmers shared between candidate pair partners.
- Local\_PID: numeric value of the local PID for the alignment of the candidate pair.
- Local\_Score: numeric value of the local alignment score for the candidate pair.
- Approx\_Global\_PID: approximate global PID for the alignment of the candidate pair.
- Approx\_Global\_Score: approximate global score for the alignment of the candidate pair.
- Block\_UID: integer value giving an identifier number to the feature block that that candidate pair is part of.
- Delta\_Background: the approximate global score of the alignment modified by the background of the sequences.

#### Value

An object of class PairSummaries.

#### Author(s)

Nicholas Cooley <npc19@pitt.edu>

#### See Also

PrepareSeqs, NucleotideOverlap, FindSynteny, LinkedPairs-class

DataBase01 = DBCONN,
Verbose = TRUE)

dbDisconnect(DBCONN)

SuperTree Create a Species Tree from Gene Trees

#### **Description**

Given a set of unrooted gene trees, creates a species tree. While this function also works for rooted gene trees, the resulting root may not be accurately placed.

# 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 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 Logical; Determines if status messages and progress bars should be displayed

while running.

Processors Integer; 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.

SuperTreeEx 97

#### Author(s)

Aidan Lakshman <ahl27@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]])
if(interactive()) print(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)</pre>
```

SuperTreeEx

Example Dendrograms

## **Description**

A set of four dendrograms for use in SuperTree examples.

# Usage

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

#### **Format**

A list with four 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")
```

 ${\tt WithinSetCompetition}$ 

Pare down candidate pairs to one-to-one sets.

# **Description**

This function is a work in progress, please be patient.

# Usage

#### **Arguments**

SynExtendObject

A PairSummaries object created by SummarizePairs.

AllowCrossContigConflicts

Logical; return only one candidate per per disjoint set for each contig to contig

pair, or for each genome to genome pair.

CompeteBy Character; a column name from the PairSummaries object.

PollContext Logical; when competing candidate pairs, consider block membership.

 ${\tt ContextInflation}$ 

Numeric; a value to adjust block membership strength. Lower values increase

the strength of block membership.

Verbose Logical; print a progress bar and timings.

# Details

For each assembly to assembly comparison, or each contig to contig comparison, all disjoint sets are collected for candidate pairs. In cases where there are more than 2 nodes, i.e. features, in a set, the connecting edges are competed against each other, and only the strongest edges – and their resulting nodes – are retained.

# Value

A PairSummaries object.

## Author(s)

Nicholas Cooley <npc19@pitt.edu>

# See Also

SummarizePairs

WithinSetCompetition 99

```
data("Endosymbionts_Pairs01", package = "SynExtend")
x <- WithinSetCompetition(Endosymbionts_Pairs01)</pre>
```

# Index

* GeneCalls	CIDist (PhyloDistance-CIDist), 69			
gffToDataFrame, 56	CIDist_NullDist, 13			
* datasets	ClusterByK, 14, 17			
BuiltInEnsembles, 12	Clustering Information Distance, 13, 38,			
CIDist_NullDist, 13	68			
<pre>Endosymbionts_GeneCalls, 24</pre>	CompetePairs, 16			
Endosymbionts_LinkedFeatures, 24	CorrGL.EvoWeaver(EvoWeaver-PPPreds), 35			
Endosymbionts_Pairs01, 25				
Endosymbionts_Pairs02, 25	data.frame, 7, 44, 76			
Endosymbionts_Pairs03, 26	DecisionTree class, 83			
<pre>Endosymbionts_Sets, 26</pre>	DecisionTree-class, 17			
<pre>Endosymbionts_Synteny, 27</pre>	dendrapply, 19, 68, 69, 71–73			
ExampleStreptomycesData, 41	dendrogram, 17, 19, 20, 22, 76, 96, 97			
Generic, 55	Diag(simMat), 88			
SuperTreeEx, 97	Diag<- (simMat), 88			
[.LinkedPairs (LinkedPairs), 58	DisjointSet, 21, 50, 96			
'DecisionTree', 82	dist, 60, 88			
	DistanceMatrix, 88			
AAHitScoping, 3	do.call, <i>94</i>			
AlignPairs, <i>49</i> , <i>94</i>	DPhyloStatistic, 22			
AlignProfiles, 88				
AlignSeqs, 88	Endosymbionts_GeneCalls, 24			
AlignTranslation, 88	Endosymbionts_LinkedFeatures, 24			
Ancestral.EvoWeaver	Endosymbionts_Pairs01, 25			
(EvoWeaver-SLPreds), 39	Endosymbionts_Pairs02, 25			
ApproximateBackground, 4	Endosymbionts_Pairs03, 26			
as.data.frame,81	Endosymbionts_Sets, 26			
as.data.frame.simMat(simMat),88	Endosymbionts_Synteny, 27			
as.dendrogram, 20	EstimateExoLabel, 27, 46, 47			
as.dendrogram.DecisionTree	EstimateRearrangementScenarios			
(DecisionTree-class), 17	(EstimRearrScen), 28			
as.matrix.simMat(simMat),88	EstimRearrScen, 28			
as.simMat(simMat),88	EvoWeaver, 31, <i>34–42</i> , <i>75</i> , <i>77</i> , <i>78</i>			
attributes, 19	EvoWeaver Gene Organization Methods, 77			
	EvoWeaver Gene Organization			
Behdenna.EvoWeaver (EvoWeaver-PPPreds),	Predictors, <i>37</i> , <i>39</i> , <i>40</i> , <i>78</i>			
35	EvoWeaver Phylogenetic Profiling			
BlastSeqs, 6, 60	Methods, 77			
BlockByRank, 7	EvoWeaver Phylogenetic Profiling			
BlockExpansion, 8	Predictors, 35, 39, 40, 78			
BlockReconciliation, 10	EvoWeaver Phylogenetic Structure			
BuiltInEnsembles, 12, 33	Methods, 77			
	EvoWeaver Phylogenetic Structure			
CheckAgainstReport, 12	Predictors, <i>35</i> , <i>37</i> , <i>40</i> , <i>78</i>			

INDEX 101

EvoWeaver Sequence Level Methods, 77	MakeBlastDb, 6, 7, 59			
EvoWeaver Sequence Level Predictors,	Moran's I, 77			
35, 37, 39, 78	MoranI, <i>34</i> , 60			
EvoWeaver-class (EvoWeaver), 31	MoransI.EvoWeaver (EvoWeaver-GOPreds),			
EvoWeaver-GOPreds, 34	34			
EvoWeaver-PPPreds, 35				
EvoWeaver-PSPreds, 37	NormVec, 62			
EvoWeaver-SLPreds, 39	NucleotideOverlap, 4, 5, 8, 9, 15, 17, 49, 58			
EvoWeaver-utils (EvoWeaver), 31	62, 62, 64, 67, 80, 85, 86, 93, 95			
EvoWeb, 40, 74, 75, 77, 78	Nye Similarity, 38			
ExampleStreptomycesData, 33, 41				
ExoLabel, 27, 28, 42	OneSite, 64			
	OrientationMI.EvoWeaver			
ExpandDiagonal, 15, 17, 48	(EvoWeaver-GOPreds), 34			
ExtantJaccard.EvoWeaver	(Evolicavel Gol Fedg), 3 T			
(EvoWeaver-PPPreds), 35	PairSummaries, 9, 11, 21, 49, 50, 53, 65, 86,			
ExtractBy, 50	93			
FastQFromSRR, 51	PAJaccard.EvoWeaver			
FindSets, 21, 52	(EvoWeaver-PPPreds), 35			
FindSynteny, 5, 8, 9, 11, 15, 17, 21, 29, 31,	palette, 74			
	PAOverlap.EvoWeaver			
49, 50, 58, 63, 67, 80, 86, 95	(EvoWeaver-PPPreds), 35			
FitchParsimony, 53	PhyloDistance, 38, 39, 67, 69, 70, 72, 73			
formula,81	PhyloDistance-CI			
	(PhyloDistance-CIDist), 69			
GeneDistance.EvoWeaver	, -			
(EvoWeaver-GOPreds), 34	PhyloDistance-CIDist, 69			
Generic, 55	PhyloDistance-JRF			
GeneVector.EvoWeaver	(PhyloDistance-JRFDist), 70			
(EvoWeaver-SLPreds), 39	PhyloDistance-JRFDist, 70			
getGeneticCode,94	PhyloDistance-KF			
gffToDataFrame, 56	(PhyloDistance-KFDist), 71			
GLDistance.EvoWeaver	PhyloDistance-KFDist, 71			
(EvoWeaver-PPPreds), 35	PhyloDistance-RF			
glm, <i>12</i>	(PhyloDistance-RFDist), 72			
GLMI.EvoWeaver (EvoWeaver-PPPreds), 35	PhyloDistance-RFDist, 72			
	Phylogenetic Profiling Algorithms, 77			
Hamming.EvoWeaver(EvoWeaver-PPPreds),	plot.DecisionTree (DecisionTree-class)			
35	17			
HitConsensus, 57, 95	plot Grand 17			
T   0 04	plot. EvoWeb, <i>41</i> , 74			
IndexSeqs, 94	predict.EvoWeaver, 31–33, 35, 37, 39–41, 74, 75, 75			
Jaccard-Robinson-Foulds Distance, 38, 68	predict.RandForest, 82			
JRFDist(PhyloDistance-JRFDist), 70	predict.RandForest (RandForest), 80			
	PrepareSeqs, 79, 95			
KFDist (PhyloDistance-KFDist), 71	print.LinkedPairs(LinkedPairs), 58			
Kuhner-Felsenstein Distance, 38,68	print.simMat(simMat), 88			
, ,	ProfDCA.EvoWeaver (EvoWeaver-PPPreds),			
lapply, 20	35			
LinkedPairs, 58				
LinkedPairs-class (LinkedPairs), 58	RandForest, 17, 18, 80			
list, 61	rapply, 19, 20			
lm, 81, 82	read.table, 43			
±111, UZ, UZ	. cuu. cubic, <i>fo</i>			

INDEX

```
readDNAStringSet, 13
RejectionBy, 4, 62, 64, 84, 85
RFDist (PhyloDistance-RFDist), 72
Robinson-Foulds Distance, 38, 68
RPContextTree.EvoWeaver
        (EvoWeaver-PSPreds), 37
RPMirrorTree.EvoWeaver
        (EvoWeaver-PSPreds), 37
SearchIndex, 3, 94
SelectByK, 85
SequenceInfo.EvoWeaver
        (EvoWeaver-SLPreds), 39
SequenceSimilarity, 87
simMat, 40, 41, 88
simMat-class(simMat), 88
SpeciesTree (EvoWeaver), 31
subset, 91
subset.dendrogram, 91
SubSetPairs, 92
SummarizePairs, 4, 5, 7, 8, 15, 17, 57, 58, 62,
        64, 80, 84, 85, 93, 98
SuperTree, 32–34, 36, 96, 97
SuperTreeEx, 97, 97
Synteny, 28, 29, 31
text, 17
TMPDIR, 59
translate, 5
TreeDistance.EvoWeaver
        (EvoWeaver-PSPreds), 37
TreeLine, 97
WithinSetCompetition, 4, 62, 64, 85, 98
XStringSet, 6, 59
```