# Package: EnvNJ (via r-universe)

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Type Package

Title Whole Genome Phylogenies Using Sequence Environments

Version 0.1.3

Description Contains utilities for the analysis of protein sequences in a phylogenetic context. Allows the generation of phylogenetic trees base on protein sequences in an alignment-independent way. Two different methods have been implemented. One approach is based on the frequency analysis of n-grams, previously described in Stuart et al. (2002) [<doi:10.1093/bioinformatics/18.1.100>](https://doi.org/10.1093/bioinformatics/18.1.100). The other approach is based on the species-specific neighborhood preference around amino acids. Features include the conversion of a protein set into a vector reflecting these neighborhood preferences, pairwise distances (dissimilarity) between these vectors, and the generation of trees based on these distance matrices.

License GPL  $(>= 2)$ 

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Suggests testthat

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```
aa.at
```
Residue Found at the Requested Position

## $\begin{minipage}[c]{0.4\linewidth} \textbf{Description} \end{minipage} \vspace{-0.3cm}$

Returns the residue found at the requested position.

## **Usage**

aa.at(at, target)

## **Arguments**



#### <span id="page-2-0"></span>aa.comp 3

## Value

Returns a single character representing the residue found at the indicated position in the indicated protein.

## See Also

aa.comp()

## Examples

aa.at(2, 'MFSQQQRCVE')

aa.comp *Amino Acid Composition*

## Description

Returns a table with the amino acid composition of the target protein.

## Usage

```
aa.comp(target, uniprot = TRUE)
```
## Arguments



## Value

Returns a dataframe with the absolute frequency of each type of residue found in the target peptide.

## Examples

```
aa.comp('MPSSVSWGILLLAGLCCLVPVSLAEDPQGDAAQK', uniprot = FALSE)
```
Computes the frequency of each amino acid in each species.

#### Usage

aaf(data)

## Arguments

data input data must be a dataframe (see details).

## Details

Input data must be a dataframe where each row corresponds to an individual protein, and each column identifies a species. Therefore, the columns' names of this dataframe must be coherent with the names of the OTUs being analyzed.

## Value

A dataframe providing amino acid frequencies en the set of species. Rows correspond amino acids and columns to species.

#### See Also

env.sp(), otu.vector(), otu.space()

#### Examples

aaf(bovids)

bovids *13 orthologous mtDNA-encoded proteins of 11 bovine species.*

## Description

A dataset containing the sequences of mtDNA-encoded proteins from different bovids

#### Usage

bovids

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#### <span id="page-4-0"></span>cos2dis 5

## Format

A data frame with 13 rows (one per protein) and 11 variables (one per species)

## Source

<https://www.ncbi.nlm.nih.gov/genome/organelle/>

cos2dis *Convert Cosines Between Vectors into Pairwise Dissimilarities*

## Description

Converts cosines values into dissimilarities values.

#### Usage

cos2dis(cos)

#### Arguments

 $\cos$  a square upper triangular matrix where  $\cos(i, j)$  is the cosine between the vector i and j.

#### Details

Cosines are standard measure of vector similarity, and can be converted into distance by dij = -log(  $(1 + \cos(i, j))$  /2).

## Value

A triangular matrix with the distances.

## See Also

vcos()

## Examples

```
data(bovids)
vectors = otu.space(bovids[, 7:11])
cosData = vcos(vectors)
disData = cos2dis(cosData)
```
<span id="page-5-0"></span>

Converts a phylip distance matrix into a either an R dataFrame or matrix.

## Usage

```
d.phy2df(phyfile, as = 'matrix')
```
## Arguments



## Value

Either a dataframe or a matrix containing the distances read from the phy file.

#### See Also

d.df2pny()

## Examples

## Not run: d.phy2df(phyfile = "./data\_t/d\_dummy.txt")

df2fasta *Convert Dataframe into Fasta File*

## Description

Converts a dataframe into a fasta file.

## Usage

df2fasta(df, out.file)

## Arguments



#### <span id="page-6-0"></span>env.extract 7

## Details

The format of the df should be as follows. Each row represents a protein sequence and each column a species.

## Value

A fasta file that is saved in the specified path.

## See Also

fastaconc()

#### Examples

```
## Not run: df2fasta(df = bovids, out.file = "./example.fasta")
```
env.extract *Sequence Environment Around a Given Position*

## Description

Extracts the sequence environment around a given position.

## Usage

env.extract(seq, c, r)

## Arguments



## Value

Returns a a strings with the extracted environment sequence.

## References

Aledo et al. Sci Rep. 2015; 5: 16955. (PMID: 26597773)

## See Also

env.matrices(), env.sp()

## Examples

```
env.extract('ARGGQQQCATSYV', c = 8, r = 2)
```
<span id="page-7-0"></span>

Builds trees based on the environment around the indicated amino acid(s).

## Usage

env.fasta(file,  $r = 10$ , aa = 'all', out.file = 'any')

## Arguments



#### Details

This function builds alignment-independent phylogenetic trees. The input data is a fasta file. When an out.file path is provided, the environment sequences of each species and the vector representing each species are saved in the path provided.

#### Value

A list with two objects, the first one is an inter-species distance matrix. The second one is an object of class 'phylo'.

## See Also

```
envnj(), fastaconc()
```
## Examples

```
## Not run: env.fasta(file = "./data_t/sample5.fasta")
```
<span id="page-8-0"></span>

Provides the frequencies of each amino acid within the environment.

## Usage

env.matrices(env)

## Arguments

env a character string vector containing the environments.

## Value

Returns a list of two dataframes. The first, shown the environment in matrix form. The second provides the frequencies of each amino acid within the environments.

## References

Aledo et al. Sci Rep. 2015; 5: 16955. (PMID: 26597773)

## See Also

env.extract(), otu.vector()

## Examples

env.matrices(c('ANQRmCTPQ', 'LYPPmQTPC', 'XXGSmSGXX'))

env.sp *Extract the Sequence Environments*

#### Description

Extracts the sequence environments around the selected amino acid(s) in the chosen species.

#### Usage

```
env.sp(data, sp, r = 10, aa = 'all', silent = TRUE)
```
## <span id="page-9-0"></span>Arguments



## Details

Input data must be a dataframe where each row corresponds to an individual protein. The columns contain the sequence of the protein corresponding to the row in each species. Therefore, the columns' names of this dataframe must be coherent with the names of the OTUs being analyzed.

## Value

A list of environment sequences. Each element from the list is a vector with the environment sequences around an amino acid. So, the length list is the same as the length of aa.

## See Also

otu.vector(), otu.space()

#### Examples

data(bovids) env.sp(data = bovids, sp = "Bos\_taurus",  $r = 2$ )

## envfascpp *Convert Fasta Files into Environment Vectors*

## Description

Converts fasta files into environment vectors

#### Usage

```
envfascpp(path, r = 10, exefile, outfile)
```
## Arguments



#### <span id="page-10-0"></span>envnj 11

## Details

This function builds and write vectors representing the species' proteome. To use this function, you must first download the source code envfas.cpp (https://bitbucket.org/jcaledo/envnj/src/master/AncillaryCode/envfas.cpp) and compile it.

## Value

A txt file per fasta file analyzed. Each txt file can be read as a vector. Thus the number of lines gives the dimension of the vector.

## See Also

envnj(), fastaconc()

## Examples

```
## Not run: envfastacpp("./data_t/list.txt", 10, ".", "./MyResults")
```


#### Description

Builds trees based on the environment around the indicated amino acid(s).

#### Usage

```
envnj(data, r = 10, aa = 'all', metric = "cosine", clustering = "nj", outgroup = 'any')
```
#### Arguments



#### Details

This function builds alignment-independent phylogenetic trees.

#### <span id="page-11-0"></span>Value

A list with two objects, the first one is an inter-species distance matrix. The second one is an object of class 'phylo'.

## See Also

otu.space(), metrics()

#### Examples

```
data(bovids)
envnj(bovids[, 7:11], aa = "all", outgroup = "Pseudoryx_nghetinhensis")
```
fastaconc *Concatenate Fasta Files in a Single Multispecies Fasta File*

## Description

Concatenate fasta files from different species in a single multispecies fasta file.

## Usage

```
fastaconc(otus, inputdir = ".", out.file = "./concatenated_multispecies.fasta")
```
#### Arguments



## Details

When we have fasta files (extension should be '.fasta'), each one for a species containing different sequences of the given species, this function concatenate the different sequences of the same species and writes it as a single sequence in a single multispecies fasta file. If the individual fasta files are found in the working directory, the inputdir argument don't need to be passed. The names of the individual fasta files must match the otus' names.

## Value

A single multispecies fasta file with the sequences of each species spliced in a single sequence.

## See Also

df2fasta()

#### <span id="page-12-0"></span>metrics 13

#### Examples

```
## Not run: fastaconc(otus = c('Glis_glis', 'Ovis_aries', 'Sus_scrofa'))
```
#### metrics *Pairwise Vector Dissimilarities*

## Description

Computes the dissimilarity between n-dimensional vectors.

#### Usage

metrics(vset, method = 'euclidean',  $p = 2$ )

## **Arguments**



#### Details

Although many of the offered methods compute a proper distance, that is not always the case. For instance, for a non null vector, v, the 'cosine' method gives  $d(v, 2v) = 0$ , violating the coincidence axiom. For that reason we prefer to use the term dissimilarity instead of distance. The methods offered can be grouped into families.

#### L\_p family::

('euclidean', 'manhattan', 'minkowski', 'chebyshev') Euclidean = sqrt( sum  $|P_i - Q_i|^{2}$ ) Manhattan = sum  $|P_i - Q_i|$ Minkowski =  $(\text{sum} P_i - Q_i |P_p)$ <sup>1</sup>/p  $Chebyshev = max | P_i - Q_i |$ 

## L\_1 family::

('sorensen', 'soergel', 'lorentzian', 'kulczynski', 'canberra') Sorensen = sum  $|P_i - Q_i| / \text{sum}(P_i + Q_i)$ Soergel = sum  $|P_i - Q_i|$  / sum max $(P_i, Q_i)$ Lorentzian = sum  $ln(1 + |P_i - Q_i|)$ Kulczynski = sum  $|P_i - Q_i| / \text{sum min}(P_i, Q_i)$ Canberra = sum  $|P_i - Q_i| / (P_i + Q_i)$ 

#### Intersection family::

('non-intersection', 'wavehedges', 'czekanowski', 'motyka') Non-intersection = 1 - sum min(P i , Q i) Wave-Hedges = sum  $|P_i - Q_i| / max(P_i, Q_i)$  $Czekanowski = sum | P_i - Q_i | / sum | P_i + Q_i |$ Motyka = sum max $(P_i, Q_i) /$  sum  $(P_i, Q_i)$ 

#### Inner product family::

('cosine', 'jaccard') Cosine = -  $ln(0.5 (1 + (P_i Q_i) / sqrt(sum P_i^2))$  sqrt(sum  $Q_i^2)$ )) Jaccard = 1 - sum  $(P_i Q_i) / (sum P_i^2 + sum Q_i^2 - sum (P_i Q_i))$ 

#### Squared-chord family::

('bhattacharyya', 'squared\_chord') Bhattacharyya = - ln sum sqrt $(P_i Q_i)$ Squared-chord = sum ( $sqrt(P_i)$  - sqrt $(Q_i)$ )<sup>^2</sup>

#### Squared Chi family::

('squared\_chi') Squared-Chi = sum (  $(P_i - Q_i)$   $\frac{2}{7}$  /  $(P_i + Q_i)$  )

#### Shannon's entropy family::

('kullback-leibler', 'jeffreys', 'jensen-shannon', 'jensen\_difference') Kullback-Leibler = sum  $P_i * log(P_i / Q_i)$ Jeffreys = sum (P\_i - Q\_i) \* log(P\_i / Q\_i) Jensen-Shannon =  $0.5(\text{sum P_i i} / (P_i + Q_i)) + \text{sum Q_i i} (Q_i / (P_i + Q_i)))$ Jensen difference = sum  $(0.5(P_i i log(P_i) + Q_i i log(Q_i))) - 0.5(P_i i + Q_i i) ln(0.5(P_i + Q_i))$ 

#### Mismatch family::

('hamming', 'mismatch', 'mismatchZero', 'binary') Hamming =  $(\#$  coordinates where P i != Q i) / n Mismatch =  $\#$  coordinates where that P\_i != Q\_i MismatchZero = Same as mismatch but after removing the coordinates where both vectors have zero.

Binary  $=$  (# coordinates where a vector has 0 and the other has a non-zero value)  $/$  n.

#### Combinations family::

('taneja', 'kumar-johnson', 'avg') Taneja = sum ( $P_i + Q_i / 2$ ) log( $P_i + Q_i / (2$  sqrt( $P_i * Q_i$ ))) Kumar-Johnson = sum (P\_i^2 - Q\_i^2)^2 / 2 (P\_i Q\_i)^1.5  $Avg = 0.5$  (sum  $|P_i - Q_i| + max |P_i - Q_i|$ )

## Value

A matrix with the computed dissimilarity values.

## <span id="page-14-0"></span>msa.merge 15

## References

Sung-Hyuk Cha (2007). International Journal of Mathematical Models and Methods in Applied Sciences. Issue 4, vol. 1

Luczac et al. (2019). Briefings in Bioinformatics 20: 1222-1237.

https://r-snippets.readthedocs.io/en/latest/real\_analysis/metrics.html

#### See Also

vcos(), vdis()

## Examples

metrics(matrix(1:9, ncol =3), 'cosine')

msa.merge *Carry Out a MSA of a Set of Different Orthologous Proteins*

## Description

Carries out a MSA of a set of different orthologous proteins in different species.

#### Usage

msa.merge(data, outfile = 'any')

#### Arguments



#### Details

The input data has the same format that the input data used for EnvNJ or SVD-n-Gram methods. Thus, the name of columns must correspond to that of species.

#### Value

A dataframe containing the MSA (species x position).

## See Also

msa.tree

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## Examples

## Not run: data(bovids) msa.merge(bovids) ## End(Not run)

## msa.tree *Infer a tree based on a MSA*

## Description

Infers a tree base on a MSA.

#### Usage

msa.tree(data, outgroup = 'any')

#### Arguments



## Details

The input data has the same format that the input data used for EnvNJ or SVD-n-Gram methods. Thus, the name of columns must correspond to that of species.

#### Value

A list containing the (i) MSA, (ii) the distance matrix and (iii) the tree.

## See Also

msa.merge

## Examples

## Not run: data(bovids) msa.tree(bovids) ## End(Not run)

<span id="page-15-0"></span>

<span id="page-16-0"></span>

Computes normalized compression distances.

## Usage

ncd(seq1, seq2)

#### Arguments



## Details

The two fasta files must be in the working directory. This function use zpaq to compress files. Thus, the zpaq software must be installed on your system and in the search path for executables if you wish to use this function. NCD =  $(Z(xy)$  - min $(Z(x), Z(y))$  / max $(Z(x), Z(y))$  Where  $Z(x), Z(y)$  and  $Z(xy)$  are the lengths of the compressed versions of seq1, seq2 and the concatenated sequences 1 and 2, respectively.

## Value

A non-negative real value reflecting the dissimilarity between seq1 and seq2.

## See Also

ncdnj()

## Examples

 $try(ncd(seq1 = "./A.fasta", seq2 = "./B.fasta"))$ 

<span id="page-17-0"></span>

Computes a distance matrix using normalized compression distance.

#### Usage

ncdnj(wd)

#### Arguments

wd character string indicating the path to the directory where the input files can be found (see details).

## Details

The input files, which must be found at the wd provided, consist of a file named 'list.txt' containing the names of the fasta files to be analyzed (one per line). The referred fasta files also must be found at the provided wd. This function use zpaq to compress files. Thus, the zpaq software must be installed on your system and in the search path for executables if you wish to use this function.

## Value

A list where the first element is a symmetric distance matrix and the second one is a phylogenetic tree build using NJ.

#### See Also

ncd()

## Examples

try(ncdnj("./data\_t"))

ngram *Compute n-Gram Frequencies Vector*

#### Description

Computes the n-gram frequencies vector for a given protein.

#### Usage

 $ngram(prot, k = 4)$ 

## <span id="page-18-0"></span>ngraMatrix 19

#### Arguments



## Details

The one letter code for amino acids is used (capital).

## Value

A dataframe with two columns, the first one given the peptides and the second one the corresponding absolute frequency.

## References

Stuart et al. Bioinformatics 2002; 18:100-108.

## See Also

```
ngraMatrix(), ffp(), svdgram()
```
## Examples

ngram(bovids\$Bos\_taurus[1], k = 3)

ngraMatrix *Compute n-Gram Frequencies Dataframe*

## Description

Computes the n-gram frequencies dataframe for the protein and species provides.

#### Usage

```
ngraMatrix(data, k = 4, silent = FALSE)
```
#### Arguments



## Details

The argument prot can be obtained using orth() and orth.seq().

#### Value

A list with two dataframes. The first one with nsp \* npr columns (nsp: number of species, npr: number of proteins per species) and npe rows (npe: number of peptides, 20 for  $n = 1$ , 400 for  $n = 2$ , 8000 for  $n = 3$  and 160000 for  $n = 4$ ). The entries of the dataframe are the number of times that the indicated peptide has been counted in the given protein. Orthologous proteins are in consecutive columns, thus the first nsp columns are the orthologous of protein 1 and so on. The second dataframe contains the Species Vector Sums (each vector describes one species).

## References

Stuart et al. Bioinformatics 2002; 18:100-108.

#### See Also

ngram(), svdgram()

#### Examples

ngraMatrix(bovids[,1:3], k = 2)

otu.space *Compute the Matrix Representing the Species Vector Subspace*

#### **Description**

Computes the matrix representing the species vector subspace.

#### Usage

otu.space(data,  $r = 10$ , aa = "all", silent = TRUE)

#### Arguments



#### Details

Input data must be a dataframe where each row corresponds to an individual protein, and each column identifies a species. Therefore, the columns' names of this dataframe must be coherent with the names of the OTUs being analyzed. The dimension of the vector representing each species will depend on the settings. For instance, if we choose a single amino acid and a radius of 10 for the sequence environment, then we will get a vector of dimension 400 (20 amino acids x 20 positions). If we opt for the 20 amino acids and  $r = 10$ , then the vector will be of dimension 8000 (400 for each amino acid \* 20 amino acids). Please, note that r is selected in the function env.sp() that will provide the input dataframe for the current function.

<span id="page-19-0"></span>

#### <span id="page-20-0"></span>otu.vector 21

## Value

A matrix representing the species vector subspace.

#### See Also

env.sp(), otu.vector()

#### Examples

```
data(bovids)
otu.space(bovids[, 1:5], r = 2)
```
otu.vector *Convert a Set of Sequence Environments into a Vector*

## Description

Converts a set of sequence environments into a vector.

#### Usage

otu.vector(envl, sp = "", aa = "all", silent = TRUE)

#### **Arguments**



#### Details

The dimension of the vector representing the species will depend on the settings. For instance, if we choose a single amino acid and a radius of 10 for the sequence environment, then we will get a vector of dimension 400 (20 amino acids x 20 positions). If we opt for the 20 amino acids and  $r =$ 10, then the vector will be of dimension 8000 (400 for each amino acid \* 20 amino acids). Please, note that r is selected in the function env.sp() that will provide the input dataframe for the current function.

## Value

A matrix representing the species. This matrix can be converted into a vector representing the target species just typing as.vector(matrix). Each coordinate is the frequency of a given amino acid at a certain position from the environment (see details).

#### 22 svdgram i Svetske konstantine i Svetske konstantine i Svetske konstantine i Svetske konstantine i Svetske k

## See Also

env.sp(), otu.space()

#### Examples

data(bovids) cow = env.sp(bovids, "Bos\_taurus") otu.vector(cow)

reyes *13 orthologous mtDNA-encoded proteins of 34 mammalian species.*

## Description

A dataset containing the sequences of mtDNA-encoded proteins from different mammalian species (Reyes et al. 1996, Mol.Biol. Evol. 17:979)

#### Usage

reyes

## Format

A data frame with 13 rows (one per protein) and 34 variables (one per species)

#### Source

<https://www.ncbi.nlm.nih.gov/genome/organelle/>

svdgram *Compute Phylogenetic Trees Using an n-Gram and SVD Approach*

## Description

Computes phylogenetic trees using an n-gram and SVD approach.

#### Usage

```
svdgram(matrix, rank, species, SVS = TRUE)
```
<span id="page-21-0"></span>

#### <span id="page-22-0"></span> $\cos$  23

#### Arguments



## Details

When the matrix passed as argument is a matrix of peptide-protein, the function implement the method described by Stuart et al. 2002 (see references).

## Value

An object of class multiPhylo containing a tree for each rank value required.

## References

Stuart et al. Bioinformatics 2002; 18:100-108.

## See Also

ngraMatrix()

## Examples

```
a \leq ngraMatrix(bovids[, 1:4], k = 2)[[2]][, -1]
species \leq names(a)
svdgram(matrix = a, rank = 4, species = species, SVS = FALSE)
```


s **Compute Pairwise Cosines of the Angles Between Vectors** 

## Description

Computes pairwise cosines of the angles between vectors.

#### Usage

```
vcos(vectors, silent = TRUE, digits = 3)
```
#### <span id="page-23-0"></span>**Arguments**



#### Details

Cosines are standard measure of vector similarity. If the angle between two vectors in n-dimensional space is small, then the individual elements of their vectors must be very similar to each other in value, and the calculated cosine derived from these values is near one. If the vectors point in opposite directions, then the individual elements of their vectors must be very dissimilar in value, an the calculated cosine is near minus one.

## Value

A triangular matrix with the cosines of the angles formed between the given vectors.

#### See Also

vdis()

#### Examples

vcos(otu.space(bovids[, 1:4]))

vdis *Compute Pairwise Distances Between Vectors*

## Description

Computes pairwise distances between vectors.

## Usage

vdis(cos)

#### Arguments

 $\cos$  a square upper triangular matrix where  $\cos(i,j)$  is the cosine between the vector i and j.

## Details

Cosines are standard measure of vector similarity, and can be converted into distance by dij = -log(  $(1 + \cos(i, j))$  /2).

#### <span id="page-24-0"></span>vect2tree 25

## Value

A triangular matrix with the distances.

## See Also

vcos()

## Examples

```
data(bovids)
vectors = otu.space(bovids[, 7:11])
cosData = vcos(vectors)
disData = suppressWarnings(vdis(cosData))
```
vect2tree *Convert a Set of Vectors into a Tree*

## Description

Converts a set of vectors into a tree.

#### Usage

```
vect2tree(path, metric = "cosine", clustering = "nj")
```
## Arguments



## Details

This function computes the distance matrix and builds the corresponding tree.

#### Value

a list with two elements: a distance matrix and a tree.

#### See Also

envnj(), fastaconc(), envfascpp()

## Examples

## Not run: vec2tree("./data\_t")

<span id="page-25-0"></span>

Builds a tree when species are encoded by n-dim vectors.

## Usage

```
vtree(matrix, outgroup = 'any')
```
## Arguments



## Details

The method is based on a distance matrix obtained after converting the cos between vector (similarity measurement) in a dissimilarity measurement.

## Value

A list with two objects, the first one is an inter-species distance matrix. The second one is an object of class 'phylo'.

#### See Also

svdgram

## Examples

```
data(bovids)
mymatrix <- ngraMatrix(bovids[, 6:11], k = 2)[[2]][, 2:7]
vtree(mymatrix, outgroup = "Pseudoryx_nghetinhensis")
```
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