

Package ‘immApex’

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Title Tools for Adaptive Immune Receptor Sequence-Based Machine and Deep Learning

Version 1.1.0

Description A set of tools to build tensorflow/keras3-based models in R from amino acid and nucleotide sequences focusing on adaptive immune receptors. The package includes pre-processing of sequences, unifying gene nomenclature usage, encoding sequences, and combining models. This package will serve as the basis of future immune receptor sequence functions/packages/models compatible with the scRepertoire ecosystem.

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Contents

immApex-package	2
adjacencyMatrix	3
formatGenes	4
generateSequences	5
geometricEncoder	6
getIMGT	7
getIR	8
immapex_AA.data	8
immapex_blosum.pam.matrices	9
immapex_example.data	10
immapex_gene.list	10
inferCDR	11
mutateSequences	12
onehotEncoder	13
positionalEncoder	14
probabilityMatrix	15
propertyEncoder	16
sequenceDecoder	17
tokenizeSequences	18
variationalSequences	19
Index	22

immApex-package	<i>immApex: Tools for Adaptive Immune Receptor Sequence-Based Keras3 Modeling</i>
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Description

A set of tools to build tensorflow/keras3-based models in R from amino acid and nucleotide sequences focusing on adaptive immune receptors. The package includes pre-processing of sequences, unifying gene nomenclature usage, encoding sequences, and combining models. This package will serve as the basis of future immune receptor sequence functions/packages/models compatible with the scRepertoire ecosystem.

Author(s)

Maintainer: Nick Borchering <ncborch@gmail.com>

See Also

Useful links:

- <https://github.com/BorchLab/immApex/>
- Report bugs at <https://github.com/BorchLab/immApex/issues>

adjacencyMatrix	<i>Adjacency matrix from amino acid or nucleotide sequences</i>
-----------------	---

Description

Calculate frequency of adjacency between residues along a set of biological sequences.

Usage

```
adjacencyMatrix(  
  input.sequences = NULL,  
  normalize = TRUE,  
  sequence.dictionary = amino.acids  
)
```

Arguments

input.sequences	The amino acid or nucleotide sequences to use
normalize	Return the values as a function of total number of residues (TRUE) or frequencies (FALSE)
sequence.dictionary	The letters to use in sequence generation (default are all amino acids)

Value

Adjacency matrix based on input.sequences.

Examples

```
new.sequences <- generateSequences(prefix.motif = "CAS",  
  suffix.motif = "YF",  
  number.of.sequences = 100,  
  min.length = 8,  
  max.length = 16)  
  
adj.matrix <- adjacencyMatrix(new.sequences,  
  normalize = TRUE)
```

`formatGenes`*Ensure clean gene nomenclature using IMGT annotations*

Description

This function will format the genes into a clean nomenclature using the IMGT conventions.

Usage

```
formatGenes(  
  input.data,  
  region = "v",  
  technology = NULL,  
  species = "human",  
  simplify.format = TRUE  
)
```

Arguments

<code>input.data</code>	Data frame of sequencing data or scRepertoire outputs
<code>region</code>	Sequence gene loci to access - "v", "d", "j", or "c" or a combination using c("v", "d", "j")
<code>technology</code>	The sequencing technology employed - 'TenX' , 'Adaptive' , or 'AIRR'
<code>species</code>	One or two word designation of species. Currently supporting: "human", "mouse", "rat", "rabbit", "rhesus monkey", "sheep", "pig", "platypus", "alpaca", "dog", "chicken", and "ferret"
<code>simplify.format</code>	If applicable, remove the allelic designation (TRUE) or retain all information (FALSE)

Value

A data frame with the new columns of formatted genes added.

Examples

```
data(immapex_example.data)  
formatGenes(immapex_example.data[["TenX"]],  
  region = "v",  
  technology = "TenX")
```

generateSequences	<i>Randomly Generate Amino Acid Sequences</i>
-------------------	---

Description

Use this to make synthetic amino acid sequences for purposes of testing code, training models, or noise.

Usage

```
generateSequences(  
  prefix.motif = NULL,  
  suffix.motif = NULL,  
  number.of.sequences = 100,  
  min.length = 1,  
  max.length = 10,  
  sequence.dictionary = amino.acids  
)
```

Arguments

prefix.motif	Add defined amino acid/nucleotide sequence to the start of the generated sequences.
suffix.motif	Add defined amino acid/nucleotide sequence to the end of the generated sequences
number.of.sequences	Number of sequences to generate
min.length	Minimum length of the final sequence. The min.length may be adjusted if incongruent with prefix.motif/suffix.motif lengths
max.length	Maximum length of the final sequence
sequence.dictionary	The letters to use in sequence generation (default are all amino acids)

Value

A vector of generated sequences

Examples

```
generateSequences(prefix.motif = "CAS",  
  suffix.motif = "YF",  
  number.of.sequences = 100,  
  min.length = 8,  
  max.length = 16)
```

geometricEncoder *Geometric Encoder from Amino Acid Strings*

Description

Use this to transform amino acid sequences into a geometric encoding of the sequence.

Usage

```
geometricEncoder(  
  input.sequences,  
  method.to.use = "BLOSUM62",  
  theta = pi/3,  
  verbose = TRUE  
)
```

Arguments

input.sequences	The set of amino acid sequences
method.to.use	The method or approach for the conversion: <ul style="list-style-type: none">• BLOcks SUBstitution Matrices: BLOSUM45, BLOSUM50, BLOSUM62, BLOSUM80, BLOSUM100• Point Accepted Mutation Matrices: PAM30, PAM40, PAM70, PAM120, PAM250
theta	The angle for geometric transformation
verbose	Print messages corresponding to the processing step

Value

Geometric encoded amino acid sequences in a matrix

Examples

```
new.sequences <- generateSequences(prefix.motif = "CAS",  
                                  suffix.motif = "YF",  
                                  number.of.sequences = 100,  
                                  min.length = 8,  
                                  max.length = 16)  
  
sequence.matrix <- geometricEncoder(new.sequences,  
                                    method.to.use = "BLOSUM62",  
                                    theta = pi/3)
```

`getIMGT`*Get IMGT Sequences for Specific Loci*

Description

Use this to access the ImMunoGeneTics (IMGT) sequences for a specific species and gene loci. More information on IMGT can be found at imgt.org.

Usage

```
getIMGT(  
  species = "human",  
  chain = "TRB",  
  sequence.type = "aa",  
  frame = "inframe",  
  region = "v",  
  max.retries = 3,  
  verbose = TRUE  
)
```

Arguments

<code>species</code>	One or two-word common designation of species.
<code>chain</code>	Sequence chain to access, e.g., TRB or IGH .
<code>sequence.type</code>	Type of sequence - aa (amino acid) or nt (nucleotide).
<code>frame</code>	Designation for all , inframe , or inframe+gap .
<code>region</code>	Gene loci to access.
<code>max.retries</code>	Number of attempts to fetch data in case of failure.
<code>verbose</code>	Print messages corresponding to the processing step.

Value

A list of allele sequences.

Examples

```
TRBV_aa <- getIMGT(species = "human",  
  chain = "TRB",  
  frame = "inframe",  
  region = "v",  
  sequence.type = "aa",  
  max.retries = 3)
```

getIR	<i>Extract Immune Receptor Sequences</i>
-------	--

Description

Use this to extract immune receptor sequences from a Single-Cell Object or the output of [combineTCR](#) and [combineBCR](#).

Usage

```
getIR(input.data, chains, sequence.type = "aa")
```

Arguments

input.data	Single-cell object or the output of combineTCR and combineBCR from scReper-toire
chains	Immune Receptor chain to use - TRA , TRB , IGH , or IGL
sequence.type	Extract amino acid (aa) or nucleotide (nt) sequences

Value

A data frame of nucleotide or amino acid sequences

immapex_AA.data	<i>A list of amino acid properties</i>
-----------------	--

Description

A list of amino acid properties that are used for [propertyEncoder](#) function.

This includes:

- atchleyFactors
- crucianiProperties
- FASGAI
- kideraFactors
- MSWHIM
- ProtFP
- stScales
- tScales
- VHSE
- zScales

Usage

```
data("immapex_AA.data")
```

Value

List of 10 amino acid properties for 20 amino acids

`immapex_blosum.pam.matrices`

List of amino acid substitution matrices

Description

A list of amino acid substitution matrices, using the Point Accepted Matrix (PAM) and BLOck SUBstitution Matrix (BLOSUM) approaches. A discussion and comparison of these matrices are available at [PMID: 21356840](#).

- BLOSUM45
- BLOSUM50
- BLOSUM62
- BLOSUM80
- BLOSUM100
- PAM30
- PAM40
- PAM70
- PAM120
- PAM250

Usage

```
data("immapex_blosum.pam.matrices")
```

Value

List of 10 substitution matrices

immapex_example.data *Example contig data for Apex*

Description

Contains a collection of bulk or paired TCR sequences in the respective formats in the form of a list from the following sources:

- TenX: 10k_Human_DTC_Melanoma_5p_nextgem_Multiplex from [10x Website](#).
- AIRR: Human_colon_16S8157851 from [PMID: 37055623](#).
- Adaptive: Adaptive_2283_D0 from [PMID: 36220826](#).

More information on the data formats are available: [AIRR](#), [Adaptive](#), and [TenX](#).

Usage

```
data("immapex_example.data")
```

Value

List of 3 example data sets for 10x, AIRR and Adaptive contigs.

immapex_gene.list *A list of IMGT gene names by genes, loci, and species*

Description

A list of regularized gene nomenclature to use for converting for data for uniformity. Data is organized by gene region, loci and species. Not all species are represented in the data and pseudogenes have not been removed.

Usage

```
data("immapex_gene.list")
```

Value

List of gene nomenclature by region, loci, and species.

`inferCDR`*Infer portions of the CDR Loop from Vgene data*

Description

Use this isolate sequences from the CDR loop using the V gene annotation. When there are multiple V gene matches for a single gene, the first allelic sequence is used.

Usage

```
inferCDR(  
  input.data,  
  reference = NULL,  
  chain = "TRB",  
  technology = NULL,  
  sequence.type = "aa",  
  sequences = c("CDR1", "CDR2")  
)
```

Arguments

<code>input.data</code>	Data frame output of formatGenes
<code>reference</code>	IMGT reference sequences from getIMGT
<code>chain</code>	Sequence chain to access, like TRB or IGH
<code>technology</code>	The sequencing technology employed - TenX , Adaptive , AIRR , or Omniscope
<code>sequence.type</code>	Type of sequence - aa for amino acid or nt for nucleotide
<code>sequences</code>	The specific regions of the CDR loop to get from the data, such as CDR1 .

Value

A data frame with the new columns of CDR sequences added.

Examples

```
# Getting the Sequence Reference  
data(immapex_example.data)  
TRBV_aa <- getIMGT(species = "human",  
  chain = "TRB",  
  frame = "inframe",  
  region = "v",  
  sequence.type = "aa")  
  
# Ensuring sequences are formatted to IMGT  
TenX_formatted <- formatGenes(immapex_example.data[["TenX"]],  
  region = "v",  
  technology = "TenX")
```

```
# Inferring CDR loop elements
TenX_formatted <- inferCDR(TenX_formatted,
                           chain = "TRB",
                           reference = TRBV_aa,
                           technology = "TenX",
                           sequence.type = "aa",
                           sequences = c("CDR1", "CDR2"))
```

mutateSequences	<i>Randomly Mutate Sequences of Amino Acids</i>
-----------------	---

Description

Use this to mutate or mask sequences for purposes of testing code, training models, or noise.

Usage

```
mutateSequences(
  input.sequences,
  n.sequences = 1,
  mutation.rate = 0.01,
  position.start = NULL,
  position.end = NULL,
  sequence.dictionary = amino.acids
)
```

Arguments

input.sequences	The amino acid or nucleotide sequences to use
n.sequences	The number of mutated sequences to return
mutation.rate	The rate of mutations to introduce into sequences
position.start	The starting position to mutate along the sequence Default = NULL will start the random mutations at position 1
position.end	The ending position to mutate along the sequence Default = NULL will end the random mutations at the last position
sequence.dictionary	The letters to use in sequence mutation (default are all amino acids)

Value

A vector of mutated sequences

Examples

```

sequences <- generateSequences(prefix.motif = "CAS",
                              suffix.motif = "YF",
                              number.of.sequences = 100,
                              min.length = 8,
                              max.length = 16)

mutated_sequences <- mutateSequences(sequences,
                                     n.sequence = 1,
                                     position.start = 3,
                                     position.end = 8)

```

onehotEncoder

One Hot Encoder from Amino Acid or Nucleotide Strings

Description

Use this to transform amino acid or nucleotide sequences into a one hot encoding of the sequence.

Usage

```

onehotEncoder(
  input.sequences,
  max.length = NULL,
  motif.length = 1,
  convert.to.matrix = TRUE,
  sequence.dictionary = amino.acids,
  padding.symbol = ".",
  verbose = TRUE
)

```

Arguments

input.sequences	The amino acid or nucleotide sequences to use
max.length	Additional length to pad, NULL will pad sequences to the max length of input.sequences
motif.length	The length of the amino acid residues to encode - a motif.length = 1 produces single amino acid encodings
convert.to.matrix	Return a matrix (TRUE) or a 3D array (FALSE)
sequence.dictionary	The letters to use in sequence generation (default are all amino acids). This will be overrode if using a motif approach (motif.length > 1)
padding.symbol	Symbol to use for padding at the end of sequences
verbose	Print messages corresponding to the processing step

Value

One hot encoded sequences in a matrix or 3D array

Examples

```
new.sequences <- generateSequences(prefix.motif = "CAS",
                                  suffix.motif = "YF",
                                  number.of.sequences = 100,
                                  min.length = 8,
                                  max.length = 16)

if(reticulate::py_module_available("numpy")) {
  sequence.matrix <- onehotEncoder(new.sequences,
                                  convert.to.matrix = TRUE)
}
```

positionalEncoder

Adding Position-Specific Information to Sequences

Description

Use this calculate positional encoding for recurrent neural networks using sin/cos and position information.

Usage

```
positionalEncoder(number.of.sequences, latent.dims = NULL)
```

Arguments

`number.of.sequences` The number of sequences to generate position information

`latent.dims` The number of latent dimensions.

Value

A matrix of values

Examples

```
position.info <- positionalEncoder(number.of.sequences = 1000,
                                   latent.dims = 64)
```

probabilityMatrix	<i>Position Probability Matrix for Amino Acid or Nucleotide Sequences</i>
-------------------	---

Description

Use this to generate a position-probability or weight matrix for a set of given sequences.

Usage

```
probabilityMatrix(  
  input.sequences,  
  max.length = NULL,  
  convert.PWM = FALSE,  
  background.frequencies = NULL,  
  sequence.dictionary = amino.acids,  
  padding.symbol = ".",  
  verbose = TRUE  
)
```

Arguments

input.sequences	The amino acid or nucleotide sequences to use
max.length	Additional length to pad, NULL will pad sequences to the max length of input.sequences
convert.PWM	Convert the matrix into a positional weight matrix using log likelihood
background.frequencies	Provide amino acid or nucleotide frequencies for the positional weight matrix. If NULL, assumes uniform likelihood.
sequence.dictionary	The letters to use in sequence generation (default are all amino acids)
padding.symbol	Symbol to use for padding at the end of sequences
verbose	Print messages corresponding to the processing step

Value

A matrix with position specific probabilities or weights

Examples

```
new.sequences <- generateSequences(prefix.motif = "CAS",  
                                  suffix.motif = "YF",  
                                  number.of.sequences = 100,  
                                  min.length = 8,  
                                  max.length = 16)
```

```
PPM.matrix <- probabilityMatrix(new.sequences)
```

propertyEncoder *Encoder from Amino Acid String by Properties*

Description

Use this to transform amino acid sequences a a matrix by amino acid properties derived from dimensional reduction strategies

Usage

```
propertyEncoder(  
  input.sequences,  
  max.length = NULL,  
  method.to.use = NULL,  
  convert.to.matrix = TRUE,  
  summary.function = NULL,  
  padding.symbol = ".",  
  verbose = TRUE  
)
```

Arguments

input.sequences	The amino acid sequences to use
max.length	Additional length to pad, NULL will pad sequences to the max length of input.sequences
method.to.use	The method or approach to use for the conversion: <ul style="list-style-type: none">• Individual sets: atchleyFactors, crucianiProperties, FASGAI, kideraFactors, MSWHIM, ProtFP, stScales, tScales, VHSE, zScales"• Multiple Sets: c("atchleyFactors", "VHSE")
convert.to.matrix	Return a matrix (TRUE) or a 3D array (FALSE)
summary.function	Return a matrix that summarize the amino acid method/property Available summaries include: "median", "mean", "sum", variance ("vars"), or Median Absolute Deviation ("mads")
padding.symbol	Symbol to use for padding at the end of sequences
verbose	Print messages corresponding to the processing step

Value

Converted amino acid sequences by property in a matrix or 3D array

Examples

```

new.sequences <- generateSequences(prefix.motif = "CAS",
                                  suffix.motif = "YF",
                                  number.of.sequences = 100,
                                  min.length = 8,
                                  max.length = 16)

if(reticulate::py_module_available("numpy")) {
sequence.matrix <- propertyEncoder(new.sequences,
                                   method.to.use = "VHSE",
                                   convert.to.matrix = TRUE)
}

```

sequenceDecoder

One Hot Decoder from One Hot Encoded Matrix or 3D Array

Description

Use this to transform one hot encoded sequences back into amino acid or nucleotide sequences.

Usage

```

sequenceDecoder(
  sequence.matrix,
  encoder = "onehotEncoder",
  aa.method.to.use = NULL,
  call.threshold = 0.5,
  sequence.dictionary = amino.acids,
  padding.symbol = ".",
  remove.padding = TRUE
)

```

Arguments

sequence.matrix	The encoded sequences to decode in an array or matrix
encoder	The method to prepare the sequencing information - "onehotEncoder" or "propertyEncoder"
aa.method.to.use	The method or approach to use for the conversion: <ul style="list-style-type: none"> • Individual sets: atchleyFactors, crucianiProperties, FASGAI, kideraFactors, MSWHIM, ProtFP, stScales, tScales, VHSE, zScales" • Multiple Sets: c("atchleyFactors", "VHSE")
call.threshold	The relative strictness of sequence calling with higher values being more stringent

`sequence.dictionary` The letters to use in sequence generation (default are all amino acids)
`padding.symbol` Symbol to use for padding at the end of sequences
`remove.padding` Remove the additional symbol from the end of decoded sequences

Value

Decoded amino acid or nucleotide sequences

Examples

```
new.sequences <- generateSequences(prefix.motif = "CAS",
                                  suffix.motif = "YF",
                                  number.of.sequences = 100,
                                  min.length = 8,
                                  max.length = 16)
if(reticulate::py_module_available("numpy")) {
  sequence.matrix <- onehotEncoder(new.sequences,
                                   convert.to.matrix = TRUE)

  decoded.sequences <- sequenceDecoder(sequence.matrix,
                                       padding.symbol = ".")
}
```

`tokenizeSequences` *Generate Tokenized Sequences from Amino Acid String*

Description

Use this to transform amino acid sequences into tokens in preparing for deep learning models.

Usage

```
tokenizeSequences(
  input.sequences,
  add.startstop = TRUE,
  start.token = "!",
  stop.token = "^",
  max.length = NULL,
  convert.to.matrix = TRUE,
  verbose = TRUE
)
```

Arguments

input.sequences	The amino acid or nucleotide sequences to use
add.startstop	Add start and stop tokens to the sequence
start.token	The character to use for the start token
stop.token	The character to use for the stop token
max.length	Additional length to pad, NULL will pad sequences to the max length of input.sequences
convert.to.matrix	Return a matrix (TRUE) or a vector (FALSE)
verbose	Print messages corresponding to the processing step

Value

Tokenize sequences in a matrix or vector

Examples

```
new.sequences <- generateSequences(prefix.motif = "CAS",
                                  suffix.motif = "YF",
                                  number.of.sequences = 100,
                                  min.length = 8,
                                  max.length = 16)

sequence.matrix <- tokenizeSequences(new.sequences,
                                     add.startstop = TRUE,
                                     start.token = "!",
                                     stop.token = "^",
                                     convert.to.matrix = TRUE)
```

variationalSequences *Generate Similar Sequences using Variational Autoencoder*

Description

Use this to simulate sequences using a variational autoencoder (VAE) and perturbation of the probability distributions.

Usage

```
variationalSequences(  
  input.sequences,  
  encoder.function = "onehotEncoder",  
  aa.method.to.use = NULL,  
  number.of.sequences = 100,
```

```

encoder.hidden.dim = c(128, 64),
decoder.hidden.dim = NULL,
latent.dim = 16,
batch.size = 16,
epochs = 50,
learning.rate = 0.001,
epsilon.std = 1,
call.threshold = 0.2,
activation.function = "relu",
optimizer = "adam",
disable.eager.execution = FALSE,
sequence.dictionary = amino.acids,
verbose = TRUE
)

```

Arguments

<code>input.sequences</code>	The amino acid or nucleotide sequences to use
<code>encoder.function</code>	The method to prepare the sequencing information - "onehotEncoder" or "propertyEncoder"
<code>aa.method.to.use</code>	The method or approach to use for the conversion: <ul style="list-style-type: none"> • Individual sets: atchleyFactors, crucianiProperties, FASGAI, kideraFactors, MSWHIM, ProtFP, stScales, tScales, VHSE, zScales" • Multiple Sets: c("atchleyFactors", "VHSE")
<code>number.of.sequences</code>	Number of sequences to generate
<code>encoder.hidden.dim</code>	A vector of the neurons to use in the hidden layers for the encoder portion of the model
<code>decoder.hidden.dim</code>	A vector of the neurons to use in the hidden layers for the decoder portion of the model. If NULL assumes symmetric autoencoder
<code>latent.dim</code>	The size of the latent dimensions
<code>batch.size</code>	The batch size to use for VAE training
<code>epochs</code>	The number of epochs to use in VAE training
<code>learning.rate</code>	The learning rate to use in VAE training
<code>epsilon.std</code>	The epsilon to use in VAE training
<code>call.threshold</code>	The relative strictness of sequence calling with higher values being more stringent
<code>activation.function</code>	The activation for the dense connected layers
<code>optimizer</code>	The optimizer to use in VAE training

Index

* **internal**

immApex-package, [2](#)

adjacencyMatrix, [3](#)

combineBCR, [8](#)

combineTCR, [8](#)

formatGenes, [4](#), [11](#)

generateSequences, [5](#)

geometricEncoder, [6](#)

getIMGT, [7](#), [11](#)

getIR, [8](#)

immApex (immApex-package), [2](#)

immApex-package, [2](#)

immapex_AA.data, [8](#)

immapex_blosum.pam.matrices, [9](#)

immapex_example.data, [10](#)

immapex_gene.list, [10](#)

inferCDR, [11](#)

mutateSequences, [12](#)

onehotEncoder, [13](#)

positionalEncoder, [14](#)

probabilityMatrix, [15](#)

propertyEncoder, [8](#), [16](#)

sequenceDecoder, [17](#)

tokenizeSequences, [18](#)

variationalSequences, [19](#)