

# Package ‘ModCon’

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**Type** Package

**Title** Modifying splice site usage by changing the mRNP code, while maintaining the genetic code

**Version** 1.17.0

**Description** Collection of functions to calculate a nucleotide sequence surrounding for splice donors sites to either activate or repress donor usage. The proposed alternative nucleotide sequence encodes the same amino acid and could be applied e.g. in reporter systems to silence or activate cryptic splice donor sites.

**License** GPL-3 + file LICENSE

**Encoding** UTF-8

**LazyData** true

**VignetteBuilder** knitr

**Depends** data.table, parallel, utils, stats, R (>= 4.1)

**Suggests** testthat, knitr, rmarkdown, dplyr, shinycssloaders, shiny, shinyFiles, shinydashboard, shinyjs

**SystemRequirements** Perl

**biocViews** FunctionalGenomics, AlternativeSplicing

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---

|                  |                                                       |
|------------------|-------------------------------------------------------|
| calculateHZEIint | <i>Calculate HZEI integral of nucleotide sequence</i> |
|------------------|-------------------------------------------------------|

---

## Description

This function calculates the HZEI integral of a nucleotide sequence.

## Usage

```
calculateHZEIint(ntSequence)
```

## Arguments

|            |                                                                                                                                                               |
|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ntSequence | Character value of nucleotide sequence whose HZEI integral will be calculated.<br>It should be at least 11 nt long and only contain bases 'A', 'G', 'C', 'T'. |
|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|

## Value

Integer value stating the HZEI integral of the given sequence ntSequence

## Examples

```
## Example to increase HZEI integral for a given coding sequence
x <- calculateHZEIint('ATACCAGCCAGCTATTACATTT')
```

---

`calculateMaxEntScanScore`*Calculate MaxEntScan score of a splice site sequence*

---

**Description**

This function calculates the MaxEntScan score of either splice donor (SD) or acceptor sequences (SA).

**Usage**

```
calculateMaxEntScanScore(seqVector, ssType)
```

**Arguments**

|           |                                                                                                                                                                                                                                 |
|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| seqVector | Character value of nucleotide sequence of a splice site sequence. SA sequences should be 23nt long (20 intronic, 3 exonic) and SD sequences should be 9nt long (3 exonic, 6 intronic). Only bases 'A', 'G', 'C', 'T' permitted. |
| ssType    | Numeric value which indicates the type of splice site. Either '3' for an SA or '5' for an SD.                                                                                                                                   |

**Value**

Numeric vector stating the MaxEntScan score per splice site sequence entered with seqVector

**Examples**

```
calculateMaxEntScanScore('TTCCAAACGAACTTTTGTAGGGA', 3)
calculateMaxEntScanScore('GAGGTAAGT', 5)
```

---

`cds`*CDS of firefly luciferase*

---

**Description**

Character string of the nucleotide sequence encoding the firefly luciferase.

**Usage**

```
cds
```

**Format**

character string

**Examples**

```
cds
```

---

changeSequenceHZEI      *Adjust HZEI integral of nucleotide sequence*

---

### Description

Adjust the HZEI integral of a nucleotide sequence (min. 24nt long)

### Usage

```
changeSequenceHZEI(inSeq, increaseHZEI=TRUE, nGenerations=50, parentSize=300,
startParentSize=1000, bestRate=50, semiLuckyRate=20, luckyRate=5, mutationRate=1e-04,
optiRate=100, sdMaximalHBS=10, acMaximalMaxent=4, nCores=-1)
```

### Arguments

|                 |                                                                                                                                              |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| inSeq           | Character value of nucleotide sequence (min 24nt long, only bases A, G, T or C)                                                              |
| increaseHZEI    | Logical value if HZEI integral should be increased or decreased during SD degradation. If TRUE, function aims to increase HZEI integral.     |
| nGenerations    | Numeric value setting maximal number of generations                                                                                          |
| parentSize      | Numeric value setting size of parent generations, generated from previous generations                                                        |
| startParentSize | Numeric value setting size of initiated parent generation of sequences                                                                       |
| bestRate        | Numeric value setting percentage how many of the fittest sequences are used to produce the next generation                                   |
| semiLuckyRate   | Numeric value setting percentage of sequences which are selected for breeding with a probability based on the respective HZEI-score integral |
| luckyRate       | Numeric value setting percentage of sequences which are randomly selected for breeding                                                       |
| mutationRate    | Numeric value setting chance of each codon, to mutate randomly within a child sequence                                                       |
| optiRate        | Numeric value setting level of HZEI integral optimization                                                                                    |
| sdMaximalHBS    | Numeric value of minimal HBS of SDs which should be tried to be degraded in their intrinsic strength                                         |
| acMaximalMaxent | Numeric value of minimal MaxEntScan score of SAs which should be tried to be degraded in their intrinsic strength                            |
| nCores          | Numeric value setting number of cores which should be used for parallel computations. If set to '-1' all available cores are selected.       |

### Value

Character value of a nucleotide sequence encoding the same amino acid sequence as inSeq, but an increased HZEI integral, due to alternative codon selection.

**Examples**

```
## Load R packages
library('parallel')
library('utils')
library('data.table')

## Set parameters for genetic algorithm
inSeq <- 'ATGGAAGACGCCAAAAACATAAAGAAAGCCCGGCCATTCTATCCGCTGGAAGATGGAACC'

## Increase HZEI integral
res <- changeSequenceHZEI(inSeq)

## Setting additional parameters
res <- changeSequenceHZEI(inSeq, increaseHZEI=TRUE, nGenerations=50, parentSize=300,
startParentSize=1000, bestRate=50, semiLuckyRate=20, luckyRate=5, mutationRate=1e-04,
optiRate=100, sdMaximalHBS=10, acMaximalMaxent=4, nCores=1)

## Access sequence with highest generated HZEI integral
res[[3]]
```

---

Codons*Table of codons and encoded amino acids*

---

**Description**

Table of codons and encoded amino acids

**Usage**

Codons

**Format**

A data frame with columns:

**ndiff** Indicator, how many codons encode the same amino acid

**AA** Amino acid three-lettred code

**name** Amino acid full name

**seq** Codon sequence

**Examples**

Codons

---

|                   |                                                            |
|-------------------|------------------------------------------------------------|
| createCodonMatrix | <i>Create codon matrix from coding nucleotide sequence</i> |
|-------------------|------------------------------------------------------------|

---

### Description

This function creates a codon matrix with 2 rows and as many columns as codons within the sequence.

### Usage

```
createCodonMatrix(cds)
```

### Arguments

|     |                                                                                                                                                                                           |
|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| cds | Character value of nucleotide sequence whose HZEI integral will be calculated. It should be at least 3 nt long and only contain bases 'A', 'G', 'C', 'T'. Length must be a multiple of 3. |
|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

### Value

Character matrix holding the encoded codon sequence in both rows.

### Examples

```
## Example to create codon matrix
createCodonMatrix("ATGAATGATCAAAGCTAGCC")
```

---

|                                |                                                |
|--------------------------------|------------------------------------------------|
| createFilialSequencePopulation | <i>Generate new sequences by recombination</i> |
|--------------------------------|------------------------------------------------|

---

### Description

This function generates new sequences from set of parental sequences through recombination.

### Usage

```
createFilialSequencePopulation(sequenceVector, generateNrecombinedSequences)
```

### Arguments

|                              |                                                                                                            |
|------------------------------|------------------------------------------------------------------------------------------------------------|
| sequenceVector               | Character vector of nucleotide sequences which will be used to create new sequences through recombination. |
| generateNrecombinedSequences | Numeric value setting number of recombined sequences which will be generated                               |

**Value**

Character vector of nucleotide sequences, generated by recombination from the entered sequenceVector, holding as much filial sequences as stated in generateNrecombinedSequences. Modes of recombination are cross-over, insertion and random.

**Examples**

```
createFilialSequencePopulation(c('AAABBBCCDDDEEEFFF', 'GGGHHIIJJJKKLLLL'), 3)
```

**decreaseGTsiteStrength**

*Remove or degrade intrinsic strength of specific GT site while keeping the HZEI integral neutral.*

**Description**

Degrade or remove specific GT site from a coding sequence by codon selection keeping the HZEI integral near zero.

**Usage**

```
decreaseGTsiteStrength(cds, sdSeqStartPosition)
```

**Arguments**

**cds** Character value of a coding nucleotide sequence which holds the splice site of interest. Sequence length must be dividable by 3 and only contain bases 'A', 'G', 'C', 'T'.

**sdSeqStartPosition** Numeric value of position of the first nucleotide of the splice donor of interest

**Value**

Character vector of a nucleotide sequence encoding the same amino acid as the entered cds, but the intrinsic strength of a specific GT site within the CDS is degraded as much as possible.

**Examples**

```
library(data.table)
cds <- paste0('ATGGAAGACGCCAAAAACATAAGAAAGGCCGCGCCATTCTATCCGCTGGAAGATGGAACCGCTGGAGAGCAACTGCA',
' TAAGGCTATGAAGAGATACGCCCTGGTTCTGGAACAATTGCTTTTACAGATGCACATATCGAGGTGGACATCACTTACGCTGAGTACTTCGAAA',
' TGTCCGTTTCGGTTGGCAGAAGCTATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAACTCTCTTCAATTCTTTAT',
' GCCGGTGTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGCAACGACATTTATAATGAACGTGAATTGCTCAACAGTATGGGCATTTCG',
' CAGCCTACCGTGGTGTTCGTTTCCAAAAAGGGTTGCAAAAAATTTGAACGTGCAAAAAAGCTCCCAATCATCAAAAAATTATTATCATGG',
' ATTCATAAACGGATTACCAGGGATTTCAGTCGATGTACACGTTTCGTACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGCCAGAG',
' GTCCTTCGATAGGGACAAGACAATTGCACTGATCATGAACCTCTGGATCTACTGGTCTGCCTAAAGGTGTCGCTCTGCCTCATAGAACTGCC',
' TGCCTGAGATTCTCGCATGCCAGAGATCCTATTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTGTTCCATTCCATCACGGTT',
' TTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTATAGATTGAAGAAGAGCTGTTTCTGAGGAGCCTTCA',
' GGATTACAAGATTCAAAGTGCCTGCTGGTGCCAACCTATTCTCCTTCTCGCCAAAGCACTCTGATTGACAAATACGATTTATCTAATTTA',
' CACGAAATTGCTTCTGGTGGCGCTCCCTCTCTAAGGAAGTCGGGAAGCGGTTGCCAAGAGGTTCCATCTGCCAGGTATCAGGCAAGGATATG',
```

```
'GGCTCACTGAGACTACATCAGCTATTCTGATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGGTAAAGTTGTTCCATTTTTGAAGCGAA',
'GGTTGTGGATCTGGATACCGGAAAAACGCTGGGCGTTAATCAAAGAGGCGAACTGTGTGTGAGAGGTCCATGATTATGTCCGGTTATGTAAAC',
'AATCCGGAAGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTGGGACGAAGACGAACACTTCTTCATCG',
'TTGACCGCTGAAGTCTCTGATTAAGTACAAAGGCTATCAGGTGGCTCCCGCTGAATTGGAATCCATCTTGCTCCAACACCCCAACATCTTCGA',
'CGCAGGTGTCGCAGGTCTTCCCGACGATGACGCCGTTGAACTTCCCGCCGCCGTTGTTGTTTGGAGCACGGAAGACGATGACGGAAAAAGAG',
'ATCGTGGATTACGTGCCAGTCAAGTAACAACCGCGAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCTTACCGAA',
'AACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGGAAGATCGCCGTG')

sdSeqStartPosition <- 1001
cdsNew <- decreaseGtsiteStrength(cds, sdSeqStartPosition)
print(cdsNew)
```

---

|            |                                                                                                |
|------------|------------------------------------------------------------------------------------------------|
| degradeSAs | <i>Remove or degrade intrinsic strength of splice acceptors while adjusting HZEI integral.</i> |
|------------|------------------------------------------------------------------------------------------------|

---

## Description

Degrade or remove splice acceptor sites of certain intrinsic strength (in MaxEntScan score) from a coding sequence by codon selection while keeping the HZEI integral up.

## Usage

```
degradeSAs(fanFunc, maxhbs=10, maxME=4, increaseHZEI=TRUE)
```

## Arguments

|              |                                                                                                                                          |
|--------------|------------------------------------------------------------------------------------------------------------------------------------------|
| fanFunc      | codon matrix with two rows (see example below)                                                                                           |
| maxhbs       | Numeric threshold which strength of internal donor sites should be degraded (in HBS)                                                     |
| maxME        | Numeric threshold which strength of internal acceptor sites should be degraded (in MaxEntScan score)                                     |
| increaseHZEI | Logical value if HZEI integral should be increased or decreased during SD degradation. If TRUE, function aims to increase HZEI integral. |

## Value

Character value of a nucleotide sequence encoding the same amino acid as the entered codon matrix fan, but the intrinsic strength of all present splice acceptor (SA) sites is degraded as much as possible, in case they exceed the given threshold maxME. Additionally, splice donor site strengths greater maxhbs are avoided, during SA degradation.

## Examples

```
library(data.table)
sdMaximalHBS <- 10
acMaximalMaxent <- 4
increaseHZEI <- TRUE
## Initiating the Codons matrix plus corresponding amino acids
ntSequence <- 'TTTGTCTTTTCTGTGTGGCAGTGGGATTAGCCTCCTATCGATCTATGCGATA'
## Create Codon Matrix by splitting up the sequence by 3nt
fanFunc <- createCodonMatrix(ntSequence)
degradeSAs(fanFunc, maxhbs=sdMaximalHBS, maxME=acMaximalMaxent, increaseHZEI=increaseHZEI)
```

---

|            |                                                                                             |
|------------|---------------------------------------------------------------------------------------------|
| degradeSDs | <i>Remove or degrade intrinsic strength of splice donors while adjusting HZEI integral.</i> |
|------------|---------------------------------------------------------------------------------------------|

---

### Description

Degrade or remove splice donor sites of certain intrinsic strength (in HBS) from a coding sequence by codon selection.

### Usage

```
degradeSDs(fanFunc, maxhbs=10, increaseHZEI=TRUE)
```

### Arguments

|              |                                                                                                                                          |
|--------------|------------------------------------------------------------------------------------------------------------------------------------------|
| fanFunc      | Codon matrix with two rows (see example below)                                                                                           |
| maxhbs       | Numeric threshold which strength of internal donor sites should be degraded                                                              |
| increaseHZEI | Logical value of HZEI integral should be increased or decreased during SD degradation. If TRUE, function aims to increase HZEI integral. |

### Value

Character value of a nucleotide sequence encoding the same amino acid as the entered codon matrix fanFunc, but the intrinsic strength of all present splice donors (SD) sites is degraded as much as possible, in case they exceed the given threshold maxhbs.

### Examples

```
library(data.table)
## Initiating the Codons matrix plus corresponding amino acids
ntSequence <- 'TTTTCGATCGGGATTAGCCTCCAGGTAAGTATCTATCGATCTATGCGATAG'
## Create Codon Matrix by splitting up the sequence by 3nt
fanFunc <- createCodonMatrix(ntSequence)
degradeSDs(fanFunc, maxhbs=10, increaseHZEI=TRUE)
```

---

|                           |                                                            |
|---------------------------|------------------------------------------------------------|
| generateRandomCodonsPerAA | <i>Randomly choose Codon to encode amino acid sequence</i> |
|---------------------------|------------------------------------------------------------|

---

### Description

Encode amino acid sequence by random codon selection

### Usage

```
generateRandomCodonsPerAA(aaVector)
```

### Arguments

|          |                                                                 |
|----------|-----------------------------------------------------------------|
| aaVector | Character vector of amino acids in three letter code (e.g. Met) |
|----------|-----------------------------------------------------------------|

**Value**

Character value of a nucleotide sequence encoding the same amino acid as the entered by aaVector by random Codon selection.

**Examples**

```
generateRandomCodonsPerAA(c('Lys', 'Lys'))
```

---

```
getOverlappingVectorsFromVector
```

*Create overlapping subvectors*

---

**Description**

Create overlapping subvectors from large vector

**Usage**

```
getOverlappingVectorsFromVector(largeVector, subvectorLength, subvectorOverlap )
```

**Arguments**

largeVector      Large character vector to break down into overlapping subvectors

subvectorLength  
                  Numeric value of length of smaller subvectors

subvectorOverlap  
                  Numeric value of length of subvector overlap

**Value**

Creates a list of overlapping subvectors from an input vector largeVector. The length of these overlapping subvectors is stated by subvectorLength and the overlap of the resulting subvectors is stated by subvectorOverlap.

**Examples**

```
getOverlappingVectorsFromVector(c(1,2,3,4), 2, 1)
```

---

|     |                                      |
|-----|--------------------------------------|
| hbg | <i>Donor sequences and their HBS</i> |
|-----|--------------------------------------|

---

**Description**

Donor sequences and their HBS

**Usage**

hbg

**Format**

A data frame with columns:

**seq** 11nt long donor sequence

**hbs** HBS of the donor sequence

**special\_seq** Shorter version of the donor sequence

**Examples**

hbg

---

|     |                              |
|-----|------------------------------|
| hex | <i>Hexamers and Z scores</i> |
|-----|------------------------------|

---

**Description**

Hexamers and Z scores

**Usage**

hex

**Format**

A data frame with columns:

**seq** Sequence of the hexamer.

**value** ZEI-score of the hexamer from HEXplorer.

**first** First codon within the hexamer.

**second** Second codon within the hexamer.

**first\_AA** First encoded amino acid within the hexamer (three letter code).

**second\_AA** Second encoded amino acid within the hexamer (three letter code).

**AA** Both encoded amino acid within the hexamer

**Examples**

hex

---

increaseGTsiteStrength

*Increasing intrinsic strength of specific GT site while keeping the HZEI integral neutral.*

---

## Description

Increasing intrinsic strength specific GT site from a coding sequence by codon selection keeping the HZEI integral near zero.

## Usage

```
increaseGTsiteStrength(cds, sdSeqStartPosition)
```

## Arguments

|                    |                                                                                   |
|--------------------|-----------------------------------------------------------------------------------|
| cds                | Coding nucleotide sequence which holds the splice site of interest                |
| sdSeqStartPosition | Numeric value of position of the first nucleotide of the splice donor of interest |

## Value

Character vector of a nucleotide sequence encoding the same amino acid as the entered cds, but the intrinsic strength of a specific GT site within the CDS is enhanced as much as possible.

## Examples

```
library(data.table)
cds <- paste0('ATGGAAGACGCCAAAAACATAAAGAAAGGCCGCGCCATTCTATCCGCTGGAAGATGGAACCGCTGGAGAGCAACTGCA',
' TAAGGCTATGAAGAGATACGCCCTGGTTCTTGAACAATTGCTTTTACAGATGCACATATCGAGGTGGACATCACTTACGCTGAGTACTTCGAAA',
' TGTCCGTTTCGGTTGGCAGAAGCTATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACCTCTTCAATTCTTTAT',
' GCCGGTGTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGGAACGACATTTATAATGAACGTGAATTGCTCAACAGTATGGGCATTTTCG',
' CAGCTACCGTGGTGTTCGTTTCCAAAAAGGGTTGCAAAAAATTTTGAACGTCAAAAAAAGCTCCCAATCATCAAAAAATTATTATCATGG',
' ATTCTAAAACGGATTACCAGGGATTTCACTCGATGTACACGTTTCGTACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTGCCAGA',
' GTCCTTCGATAGGGACAAGACAATTGCACTGATCATGAACCTCTGGATCTACTGGTCTGCCTAAAGGTGTCGCTCTGCCTCATAGAACTGCC',
' TGCCTGAGATTCTCGCATGCCAGAGATCCTATTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTGTTCCATTCCATCACGGTT',
' TTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTATAGATTGAAGAAGAGCTGTTTCTGAGGAGCCTTCA',
' GGATTACAAGATTCAAAGTGCCTGCTGGTGCCAACCTATTCTCTTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTTATCTAATTTA',
' CACGAAATTGCTTCTGGTGGCGCTCCCTCTCTAAGGAAGTCGGGAAGCGGTTGCCAAGAGGTTCCATCTGCCAGGTATCAGGCAAGGATATG',
' GGCTCACTGAGACTACATCAGCTATTCTGATTACACCCGAGGGGATGATAAACCGGCGCGGTCGGTAAAGTTGTTCCATTTTTGAAGCGAA',
' GGTGTGGATCTGGATACCGGAAAAACGCTGGGCGTTAATCAAAGAGGCGAACTGTGTGTGAGAGGTCTATGATTATGTCCGGTTATGTAAAC',
' AATCCGGAAGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTGGGACGAAGACGAACACTTCTTCATCG',
' TTGACCGCTGAAGTCTCTGATTAAGTACAAAGGCTATCAGTGGCTCCCGCTGAATTGGAATCCATCTTGCTCCAACACCCCAACATCTTCGA',
' CGCAGGTGTCGAGGTCTTCCGACGATGACGCGGTGAACCTCCCGCCGCGTTGTTGTTTGGAGCACGGAAGACGATGACGAAAAAGAG',
' ATCGTGGATTACGTCGCCAGTCAAGTAACAACCGCAAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCTTACCGAA',
' AACTCGACGAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGGAAGATCGCCGTG')

sdSeqStartPosition <- 1001
cdsNew <- increaseGTsiteStrength(cds, sdSeqStartPosition)
print(cdsNew)
```

---

|        |               |
|--------|---------------|
| ModCon | <i>ModCon</i> |
|--------|---------------|

---

### Description

Execute ModCon on a donor site within a coding sequence either increasing or decreasing its HZEI weight.

### Usage

```
ModCon(cds, sdSeqStartPosition, upChangeCodonsIn=16, downChangeCodonsIn=16,
optimizeContext=TRUE, sdMaximalHBS=10, acMaximalMaxent=4, optiRate=100,
nGenerations=50, parentSize=300, startParentSize=1000, bestRate=40,
semiLuckyRate=20, luckyRate=5, mutationRate=1e-04, nCores=-1)
```

### Arguments

|                    |                                                                                                                                                                                       |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| cds                | Character value of coding nucleotide sequence which holds the splice site of interest                                                                                                 |
| sdSeqStartPosition | Numeric value of the position of the first nucleotide of the splice donor of interest                                                                                                 |
| upChangeCodonsIn   | Numeric value of number of codons to change upstream of the donor site of interest                                                                                                    |
| downChangeCodonsIn | Numeric value of number of codons to change downstream of the donor site of interest                                                                                                  |
| optimizeContext    | Character value which determines, if TRUE (the default) the donor context will be adjusted to increase the splice site HEXplorer weight (SSHW), if FALSE, the SSHW will be decreased. |
| sdMaximalHBS       | Numeric value of minimal HBS of SDs which should be tried to be degraded in their intrinsic strength                                                                                  |
| acMaximalMaxent    | Numeric value of minimal MaxEntScan score of SAs which should be tried to be degraded in their intrinsic strength                                                                     |
| optiRate           | Numeric value setting level of HZEI integral optimization                                                                                                                             |
| nGenerations       | Numeric value setting maximal number of generations                                                                                                                                   |
| parentSize         | Numeric value setting size of parent generations, generated from previous generations                                                                                                 |
| startParentSize    | Numeric value setting size of initiated parent generation of sequences                                                                                                                |
| bestRate           | Numeric value setting percentage how many of the fittest sequences are used to produce the next generation                                                                            |
| semiLuckyRate      | Numeric value setting percentage of sequences which are selected for breeding with a probability based on the respective HZEI-score integral                                          |
| luckyRate          | Numeric value setting percentage of sequences which are randomly selected for breeding                                                                                                |

|              |                                                                                                                                        |
|--------------|----------------------------------------------------------------------------------------------------------------------------------------|
| mutationRate | Numeric value setting chance of each codon, to mutate randomly within a child sequence                                                 |
| nCores       | Numeric value setting number of cores which should be used for parallel computations. If set to '-1' all available cores are selected. |

### Value

Creates a character value of a coding nucleotide sequence encoding the same amino acid sequence as the entered cds, but with an alternative nucleotide surrounding around the splice donor (SD) sequence position, stated with sdSeqStartPosition. Depending on the entered optimizeContext, the SD surrounding is either adjusted aiming to enhance or decrease the splice site HEXplorer wheighth.

### Examples

```
## Load R packages
library('parallel')
library('utils')
library('data.table')

## Set parameters for simplest use of ModCon (optimizing to 100%)
cds <- paste0('ATGGAAGACGCCAAAAACATAAAGAAAGGCCCGGCCATTCTATCCGCTGGAAGATGGAACCGCTGGAGAGCAACTGCA',

'TAAGGCTATGAAGAGATACGCCCTGGTTCTGGAACAATTGCTTTTACAGATGCACATATCGAGGTGGACATCACTTACGCTGAGTACTTCGAAA',
'TGTCCGTTTCGGTTGGCAGAAGCTATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACCTCTTCAATTCTTTAT',
'GCCGGTGTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGGAACGACATTTATAATGAACGTGAATTGCTCAACAGTATGGGCATTTCG',
'CAGCCTACCGTGGTGTTCGTTTCCAAAAAGGGTTGCAAAAAATTTGAACGTGCAAAAAAGCTCCCAATCATCAAAAAATTATTATCATGG',
'ATTCTAAAACGGATTACCAGGGATTTCAATCGATGTACACGTTTCGTACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTGCCAGA',
'GTCCTTCGATAGGGACAAGACAATTGCACTGATCATGAACCTCTGATCTACTGGTCTGCCTAAAGGTGTCGCTCTGCCTCATAGAACTGCC',
'TGCGTGAGATTCTCGCATGCCAGAGATCCTATTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAAGTGTGTTCCATTCCATCACGGTT',
'TTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTATAGATTGAAGAAGAGCTGTTTCTGAGGAGCCTTCA',
'GGATTACAAGATTCAAAGTGCCTGCTGGTGCCAACCTATTCTCCTTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTTATCTAATTTA',
'CACGAAATTGCTTCTGGTGGCGCTCCCTCTCTAAGGAAGTCGGGAAGCGGTTGCCAAGAGGTTCCATCTGCCAGGTATCAGGCAAGGATATG',
'GGCTCACTGAGACTACATCAGCTATTCTGATTACACCGAGGGGATGATAAACCGGGCGCGGTGCGTAAAGTTGTTCCATTTTTGAAGCGAA',
'GGTTGTGGATCTGGATACCGGAAAACGCTGGCGTTAATCAAAGAGGCGAAGCTGTGTGTGAGAGGTCCTATGATTATGTCCGGTTATGTAAAC',
'AATCCGGAAGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTGGGACGAAGACGAACACTTCTTCATCG',
'TTGACCGCTGAAGTCTCTGATTAAGTACAAAGGCTATCAGGTGGCTCCCGCTGAATTGGAATCCATCTTGCTCCAACCCCAACATCTTCGA',
'CGCAGGTGTCGCGAGTCTTCCCGACGATGACGCCGTGAACCTCCCGCCCGGTTGTTGTTTGGAGCACGGAAGACGATGACGAAAAAGAG',
'ATCGTGGATTACGTCGCCAGTCAAGTAACAACCGCGAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCTTACCGGAA',
'AACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGCGGAAGATCGCCGTG')

## Execute ModCon
finalSequence <- ModCon(cds, 1001)

## Print final cds sequence with the alternative SD nucleotide surrounding
print(finalSequence)

## More parameters can be set for use of ModCon when not optimizing to 100% (e.g. 50%)

## Execute ModCon
finalSequence <- ModCon(cds, 1001, upChangeCodonsIn=16, downChangeCodonsIn=16,
optimizeContext=FALSE, sdMaximalHBS=10, acMaximalMaxent=4,
optiRate=50, nGenerations=5, parentSize=200, startParentSize=800,
```

```
bestRate=50, semiLuckyRate=10, luckyRate=5, mutationRate=1e-03, nCores=1)

## Print final cds sequence with the alternative SD nucleotide surrounding
print(finalSequence)
```

---

|                  |                                                            |
|------------------|------------------------------------------------------------|
| mutatePopulation | <i>Randomly exchange codons within a set of sequences.</i> |
|------------------|------------------------------------------------------------|

---

### Description

For every codon within a set of nucleotide sequences randomly exchange the codon encoding the same amino acid to a certain chance.

### Usage

```
mutatePopulation(sequenceVector, codonReplacementChance)
```

### Arguments

**sequenceVector** Character vector of nucleotide sequences (at least 3 nt long)

**codonReplacementChance** Numeric value of chance of a codons within the sequences to get exchanged to another codon encoding the same amino acid

### Value

Creates a character vector of coding nucleotide sequences encoding the same amino acid sequence as the entered sequenceVector. By a mutation rate stated in codonReplacementChance, codons are randomly exchanged, by alternative codons encoding the same amino acid.

### Examples

```
mutatePopulation(c("CGCGATACGCTAAGCGCTACCGATAGTGGA", "TGGGATATTTTAAGCGCTGACGATAGTGGA"), 0.1)
```

---

|                       |                                                                  |
|-----------------------|------------------------------------------------------------------|
| recombineTwoSequences | <i>Generate new sequence from recombination of two sequences</i> |
|-----------------------|------------------------------------------------------------------|

---

### Description

This function generates a new sequences through recombination of two parental sequences using 3 modi of recombination. Either random combination of codons, crossover recombination or insertion.

### Usage

```
recombineTwoSequences(ntSequence1, ntSequence2, preferenceVector)
```

**Arguments**

|                  |                                                                                                                                                                                                                                                                                                       |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ntSequence1      | Character value of a nucleotide sequence                                                                                                                                                                                                                                                              |
| ntSequence2      | Character value of a nucleotide sequence                                                                                                                                                                                                                                                              |
| preferenceVector | Numeric vector of length three which indicates which modus of recombination should be preferred. The first number states the chance of random recombination, the second number indicates the chance of cross-over recombination and the third number indicates the chance of insertion recombination. |

**Value**

Character value of a nucleotide sequence, generated by recombination from the entered ntSequence1 and ntSequence2. Modes of recombination are cross-over, insertion and random and mode preferences can be stated by preferenceVector.

**Examples**

```
recombineTwoSequences("AGGGCCTGGAGGAGGCTT", "TAAGGCAAGCCTGGACCC", c(1, 3, 2))
```

---

|                   |                                  |
|-------------------|----------------------------------|
| selectBestAndMean | <i>Select best HZEI and mean</i> |
|-------------------|----------------------------------|

---

**Description**

From all sequences of a generation report highest HZEI integral and mean HZEI integral of all.

**Usage**

```
selectBestAndMean(sequenceVector, clusterName, increaseHZEI=TRUE)
```

**Arguments**

|                |                                                                                                                                          |
|----------------|------------------------------------------------------------------------------------------------------------------------------------------|
| sequenceVector | Character vector of nucleotide sequences                                                                                                 |
| clusterName    | Name of cluster generated with package parallel                                                                                          |
| increaseHZEI   | Logical value if HZEI integral should be increased or decreased during SD degradation. If TRUE, function aims to increase HZEI integral. |

**Value**

Numeric vector of length 2 stating the best HZEI integral and the mean HZEI integral of a nucleotide sequence vector sequenceVector. Depending on the increaseHZEI mode, the best HZEI integral value is either the highest (for increaseHZEI==TRUE) or lowest (for increaseHZEI==FALSE).

## Examples

```
## Setup cluster
library(parallel)
nCores <- 1
clust <- makeCluster(nCores)
clusterExport(clust, list('getOverlappingVectorsFromVector', 'hex',
  'calculateHZEIint'), envir = environment())
selectBestAndMean(c('CGCGATACGCTAAGCGCTACCGATAGTGGA', 'TGGGATATTTTAAGCGCTGACGATAGTGGA'),
  clust, increaseHZEI=TRUE)
```

---

```
selectMatingIndividuals
```

*Selecting mating sequences from a pool of sequences*

---

## Description

Selecting sequences from a pool of nucleotide sequences based in chance and their HZEI integral.

## Usage

```
selectMatingIndividuals(inputGeneration, whoMatesBestPercent=40, whoMatesSemiRandom=20,
  whoMatesLuckily=5, clust, increaseHZEI=TRUE)
```

## Arguments

|                     |                                                                                                                                          |
|---------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| inputGeneration     | Character vector of nucleotide sequences                                                                                                 |
| whoMatesBestPercent | Numeric value e.g. 20 (which would mean that sequences with the top 20 percent highest HZEI integral are selected for mating)            |
| whoMatesSemiRandom  | Numeric value (is always lower than total number of sequences in input_generation)                                                       |
| whoMatesLuckily     | Numeric value (is always lower than total number of sequences in input_generation)                                                       |
| clust               | Name of cluster generated with package parallel                                                                                          |
| increaseHZEI        | Logical value of HZEI integral should be increased or decreased during SD degradation. If TRUE, function aims to increase HZEI integral. |

## Value

Character vector of nucleotide sequences which are selected from an entered vector of nucleotide sequences inputGeneration for creation of filial sequences by recombination. Sequences are selected by different criteria stated by whoMatesBestPercent, whoMatesSemiRandom, whoMatesLuckily and increaseHZEI.

**Examples**

```
## Setup cluster
library(parallel)
nCores <- 1
clust <- makeCluster(nCores)
clusterExport(clust, list('getOverlappingVectorsFromVector',
'hex'), envir=environment())
selectMatingIndividuals(c('CGCGATACGCGCGATACG', 'CGCGATACGTGGGATATT',
'CTAAGCGCTCGCGATACG', 'CGCGATACGTTAAGCGCT', 'GACGATAGTCGCGATACG'),
whoMatesBestPercent=40, whoMatesSemiRandom=1, whoMatesLuckily=1, clust, increaseHZEI=TRUE)
```

---

slidingWindowHZEImanipulation

*Quickly manipulate HZEI integral of nucleotide sequence*


---

**Description**

Quickly manipulate HZEI integral of nucleotide sequence (min. 21nt long)

**Usage**

```
slidingWindowHZEImanipulation(inSeq, increaseHZEI=TRUE)
```

**Arguments**

|              |                                                                                                                                          |
|--------------|------------------------------------------------------------------------------------------------------------------------------------------|
| inSeq        | Character value of nucleotide sequence (min 21nt long, only bases 'A', 'G', 'T' or 'C')                                                  |
| increaseHZEI | Logical value if HZEI integral should be increased or decreased during SD degradation. If TRUE, function aims to increase HZEI integral. |

**Value**

Character value of a nucleotide sequence encoding the same amino acid sequence as inSeq, but an increased HZEI integral, due to alternative codon selection, accomplished through sliding window optimization.

**Examples**

```
# Load R packages
library('parallel')
library('utils')
library('data.table')

# Set parameters for genetic algorithm
inSeq <- 'ATGGAAGACGCCAAAAACATAAAGAAAGCAGGCTAAGCCTAGCTTGCCATTGCCCGGCGCCATTCTATCCGCTGGAAGATGGAATT'

maximizedHZEIseq <- slidingWindowHZEImanipulation(inSeq, increaseHZEI=TRUE)
minimizedHZEIseq <- slidingWindowHZEImanipulation(inSeq, increaseHZEI=FALSE)

#Access sequence with maximized HZEI intregral
maximizedHZEIseq
```

```
#Access sequence with minimized HZEI integral  
minimizedHZEIseq
```

---

|                |                             |
|----------------|-----------------------------|
| startModConApp | <i>Start GUI of VarCon.</i> |
|----------------|-----------------------------|

---

**Description**

Start graphical user interface for the ModCon application.

**Usage**

```
startModConApp()
```

**Value**

Shiny app

**Examples**

```
startModConApp()
```

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