Package 'AnaCoDa'

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Type Package

Title Analysis of Codon Data under Stationarity using a Bayesian Framework

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URL https://github.com/clandere/AnaCoDa

VignetteBuilder knitr

NeedsCompilation yes

Depends R (>= 3.3.0), Rcpp (>= 0.11.3), VGAM, methods, mvtnorm

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RcppModules Test_mod, Trace_mod, CovarianceMatrix_mod, MCMCAlgorithm_mod, Model_mod, Parameter_mod, Genome_mod, Gene_mod, SequenceSummary_mod

Description Is a collection of models to analyze genome scale codon data using a Bayesian framework. Provides visualization routines and checkpointing for model fittings. Currently published models to analyze gene data for selection on codon usage based on Ribosome Overhead Cost (ROC) are: ROC (Gilchrist et al. (2015) <doi:10.1093/gbe/evv087>), and ROC with phi (Wallace & Drummond (2013) <doi:10.1093/molbev/mst051>). In addition 'AnaCoDa' contains three currently unpublished models. The FONSE (First order approximation On NonSense Error) model analyzes gene data for selection on codon usage against of nonsense error rates. The PA (PAusing time) and PANSE (PAusing time + NonSense Error) models use ribosome footprinting data to analyze estimate ribosome pausing times with and without nonsense error rate from ribosome footprinting data.

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LinkingTo Rcpp

LazyLoad yes

LazyData yes

RoxygenNote 7.1.1

Repository CRAN

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Contents

AAToCodon *Amino Acid to codon set*

Description

Converts one character amino acid code to the set of codon encoding that amino acid

Usage

```
AAToCodon(aa, focal = FALSE)
```

Arguments

aa	Amino acid in single character notation
focal	logical, Include the alphabetically last (focal) codon

Value

Returns the names of the codon encoding the give amino acid

See Also

codonToAA

acfCSP *Plots ACF for codon specific parameter traces*

Description

The function calculates and by defaults plots the acf and estimates the autocorrelation in the trace

Usage

```
acfCSP(
  parameter,
  csp = "Mutation",
  numMixtures = 1,
  samples = NULL,
  lag.max = 40,
  plot = TRUE
)
```

Arguments

parameter	object of class Parameter
csp	indicates which parameter to calculate the autocorrelation. Must be Mutation (the default, ROC, FONSE), Selection (ROC, FONSE), Alpha (PA, PANSE), LambdaPrime (PA, PANSE), NSERate (PA, PANSE)"
numMixtures	indicates the number of CSP mixtures used
samples	number of samples at the end of the trace used to calculate the acf
lag.max	Maximum amount of lag to calculate acf. Default is 10*log10(N), where N i the number of observations.
plot	logical. If TRUE (default) a plot of the acf is created

See Also

acfMCMC

---

acfMCMC *Autocorrelation function for the likelihood or posterior trace*

Description

The function calculates and by defaults plots the acf and estimates the autocorrelation in the trace.

Usage

```
acfMCMC(mcmc, type = "LogPosterior", samples = NULL, lag.max = 40, plot = TRUE)
```

Arguments

mcmc	object of class MCMC
type	"LogPosterior" or "LogLikelihood", defaults to "LogPosterior"
samples	number of samples at the end of the trace used to calculate the acf
lag.max	Maximum amount of lag to calculate acf. Default is 10*log10(N), where N i the number of observations.
plot	logical. If TRUE (default) a plot of the acf is created

See Also

acfCSP

addObservedSynthesisRateSet *Add gene observed synthesis rates*

Description

addObservedSynthesisRateSet returns the observed synthesis rates of the genes within the genome specified.

Usage

```
addObservedSynthesisRateSet(
  genome,
  observed.expression.file,
  match.expression.by.id = TRUE
)
```

Arguments

genome	A genome object initialized with initializeGenomeObject to add observed expression data.
observed.expression.file	A string containing the location of a file containing empirical expression rates (optional).
match.expression.by.id	If TRUE (default) observed expression values will be assigned by matching sequence identifier. If FALSE observed expression values will be assigned by order

Value

Returns the genome after adding the new gene expression values

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")
expression_file <- system.file("extdata", "expression.csv", package = "AnaCoDa")
## reading genome
genome <- initializeGenomeObject(file = genome_file)


## add expression values after the genome was initiallized,
## or adding an additional set of expression values
genome <- addObservedSynthesisRateSet(genome = genome,
                  observed.expression.file = expression_file)
```

aminoAcids *Amino acids*

Description

Returns a vector of all amino acids

Usage

```
aminoAcids()
```

Value

Returns a vector of all amino acids

See Also

codons

calculateMarginalLogLikelihood *Calculates the marginal log-likelihood for a set of parameters*

Description

initializes the model object.

Usage

```
calculateMarginalLogLikelihood(
  parameter,
  mcmc,
  mixture,
  n.samples,
  divisor,
  warnings = TRUE
)
```

Arguments

parameter	An object created with initializeParameterObject.
mcmc	An object created with initializeMCMCObject
mixture	determines for which mixture the marginal log-likelihood should be calculated
n.samples	How many samples should be used for the calculation
divisor	A value > 1 in order to scale down the tails of the importance distribution
warnings	Print warnings such as when the variance of a parameter is 0, which might occur when parameter is fixed

Details

calculateMarginalLogLikelihood Calculate marginal log-likelihood for calculation of the Bayes factor using a generalized harmonix mean estimator of the marginal likelihood. See Gronau et al. (2017) for details

Value

This function returns the model object created.

Examples

```
## Not run:
# Calculate the log-marginal likelihood
parameter <- loadParameterObject("parameter.Rda")
mcmc <- loadMCMCObject("mcmc.Rda")
calculate_marginal_likelihood(parameter, mcmc, mixture = 1,
samples = 500, scaling = 1.5)

# Calculate the Bayes factor for two models
parameter1 <- loadParameterObject("parameter1.Rda")
parameter2 <- loadParameterObject("parameter2.Rda")
mcmc1 <- loadMCMCObject("mcmc1.Rda")
mcmc2 <- loadMCMCObject("mcmc2.Rda")
mll1 <- calculate_marginal_likelihood(parameter1, mcmc1, mixture = 1,
samples = 500, scaling = 1.5)
mll2 <- calculate_marginal_likelihood(parameter2, mcmc2, mixture = 1,
samples = 500, scaling = 1.5)
cat("Bayes factor: ", mll1 - mll2, "\n")

## End(Not run)
```

---

calculateSCUO *calculates the synonymous codon usage order (SCUO)*

Description

calculateSCUO calulates the SCUO value for each gene in genome. Note that if a codon is absent, this will be treated as NA and will be skipped in final calculation

Usage

```
calculateSCUO(genome)
```

Arguments

genome	A genome object initialized with initializeGenomeObject.

Value

returns the SCUO value for each gene in genome

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

## reading genome
genome <- initializeGenomeObject(file = genome_file)
scuo <- calculateSCUO(genome)
```

---

codons *Codons*

Description

Returns a vector of all codons

Usage

```
codons()
```

Value

Returns a vector of all codons

See Also

aminoAcids

---

codonToAA *translates codon to amino acid*

Description

Translates a given codon into the amino acid encoded by it.

Usage

```
codonToAA(codon)
```

Arguments

codon	character, codon to translate

Value

Returns the amino acid encoded by the given codon as character

See Also

AAToCodon

`convergence.test` *Convergence Test*

Description

Convergence Test

Usage

```
convergence.test(
  object,
  samples = 10,
  frac1 = 0.1,
  frac2 = 0.5,
  thin = 1,
  plot = FALSE,
  what = "Mutation",
  mixture = 1
)
```

Arguments

`object`	an object of either class Trace or MCMC
`samples`	number of samples at the end of the trace used to determine convergence (< length of trace). Will use as starting point of convergence test. If the MCMC trace is of length x, then starting point for convergence test will be x - samples.
`frac1`	fraction to use from beginning of samples
`frac2`	fraction to use from end of samples
`thin`	the thinning interval between consecutive observations, which is used in creating a coda::mcmc object (according to the Coda documentation, users should specify if a MCMC chain has already been thinned using a the thin parameter). This does not further thin the data.
`plot`	(logical) plot result instead of returning an object
`what`	(for Trace Object only) which parameter to calculate convergence.test – current options are Selection, Mutation, MixtureProbability, Sphi, Mphi, ExpectedPhi, and AcceptanceCSP
`mixture`	(for Trace Object only) mixture for which to calculate convergence.test

Details

Be aware that convergence.test for Trace objects works primarily for Trace objects from the ROC parameter class. Future updates will adapt this function to work for parameters from other models and expression traces

Value

Geweke score object evaluating whether means of two fractions (frac1 and frac2) differ. Convergence occurs when they don't differ significantly, i.e. pnorm(abs(convergence.test(mcmcObj)$a, ,lower.tail=FALSE)*2 > 0.05

Examples

```
## check for convergence after a run:

genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)
sphi_init <- c(1,1)
numMixtures <- 2
geneAssignment <- c(rep(1,floor(length(genome)/2)),rep(2,ceiling(length(genome)/2)))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
                                       gene.assignment = geneAssignment,
                                       mixture.definition = "allUnique")
samples <- 2500
thinning <- 50
adaptiveWidth <- 25
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning,
                             adaptive.width=adaptiveWidth, est.expression=TRUE,
                             est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)
divergence.iteration <- 10
## Not run:
runMCMC(mcmc = mcmc, genome = genome, model = model,
        ncores = 4, divergence.iteration = divergence.iteration)
# check if posterior trace has converged
convergence.test(object = mcmc, samples = 500, plot = TRUE)

trace <- getTrace(parameter)
# check if Mutation trace has converged
convergence.test(object = trace, samples = 500, plot = TRUE, what = "Mutation")
# check if Sphi trace has converged
convergence.test(object = trace, samples = 500, plot = TRUE, what = "Sphi")
# check if ExpectedPhi trace has converged
convergence.test(object = trace, samples = 500, plot = TRUE, what = "ExpectedPhi")

## End(Not run)
```

`findOptimalCodon` *Find and return list of optimal codons*

Description

`findOptimalCodon` extracrs the optimal codon for each amino acid.

Usage

```
findOptimalCodon(csp)
```

Arguments

`csp`	a `data.frame` as returned by `getCSPEstimates`.

Value

A named list with with optimal codons for each amino acid.

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)
sphi_init <- 1
numMixtures <- 1
geneAssignment <- rep(1, length(genome))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
                                       gene.assignment = geneAssignment,
                                       mixture.definition = "allUnique")
model <- initializeModelObject(parameter = parameter, model = "ROC")
samples <- 2500
thinning <- 50
adaptiveWidth <- 25
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning,
                             adaptive.width=adaptiveWidth, est.expression=TRUE,
                             est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)
divergence.iteration <- 10
## Not run:
runMCMC(mcmc = mcmc, genome = genome, model = model,
        ncores = 4, divergence.iteration = divergence.iteration)

csp_mat <- getCSPEstimates(parameter, CSP="Selection")
opt_codons <- findOptimalCodon(csp_mat)

## End(Not run)
```

fixDEta *fixDEta*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Fix the value of selection its current value

fixDM *fixDM*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Fix the value of mutation its current value

fixSphi *fixSphi*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Fix the value of s_phi (standard deviation of lognormal for synthesis rates) at its current value

geomMean *Take the geometric mean of a vector*

Description

geomMean will calculate the geometric mean of a list of numerical values.

Usage

```
geomMean(x, rm.invalid = TRUE, default = 1e-05)
```

Arguments

x	A vector of numerical .
rm.invalid	Boolean value for handling 0, negative, or NA values in the vector. Default is TRUE and will not include these values in the calculation. If FALSE, these values will be replaced by the value give to default and will be included in the calculation.
default	Numerical value that serves as the value to replace 0, negative, or NA values in the calculation when rm.invalid is FALSE. Default is 1e-5.

Details

This function is a special version of the geometric mean specifically for AnaCoda. Most models in Anacoda assume a log normal distribution for phi values, thus all values in x are expectd to be positive. geomMean returns the geometric mean of a vector and can handle 0, negative, or NA values.

Value

Returns the geometric mean of a vector.

Examples

```
x <- c(1, 2, 3, 4)
geomMean(x)

y<- c(1, NA, 3, 4, 0, -1)
# Only take the mean of non-Na values greater than 0
geomMean(y)

# Replace values <= 0 or NAs with a default value 0.001 and then take the mean
geomMean(y, rm.invalid = FALSE, default = 0.001)
```

---

getAdaptiveWidth *getAdaptiveWidth*

Description

Return sample adaptiveWidth value, which is the number of samples (not iterations) between adapting parameter proposal widths

Value

number of sample steps between adapting proposal widths

getCAI *Calculate the Codon Adaptation Index*

Description

getCAI returns the Codon Adaptation Index for a genome based on a provided reference.

Usage

```
getCAI(referenceGenome, testGenome, default.weight = 0.5)
```

Arguments

referenceGenome	A genome object initialized with initializeGenomeObject. Serves as reference set to calculate the necessary codon weights.
testGenome	A genome object initialized with initializeGenomeObject. The genome for which the CAI is supposed to be calculated
default.weight	Default weight to use if codon is missing from referenceGenome

Value

Returns a named vector with the CAI for each gene

Examples

```
genome_file1 <- system.file("extdata", "more_genes.fasta", package = "AnaCoDa")
genome_file2 <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

## reading genome
referenceGenome <- initializeGenomeObject(file = genome_file1)
testGenome <- initializeGenomeObject(file = genome_file2)

cai <- getCAI(referenceGenome, testGenome)
```

getCAIweights *Calculate the CAI codon weigths for a reference genome*

Description

getCAIweights returns the weights for the Codon Adaptation Index based on a reference genome.

Usage

```
getCAIweights(referenceGenome, default.weight = 0.5)
```

Arguments

referenceGenome	A genome object initialized with initializeGenomeObject.
default.weight	Set default weight for any codon not observed in the reference genome

Value

Returns a named vector with the CAI weights for each codon

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

## reading genome
referenceGenome <- initializeGenomeObject(file = genome_file)

wi <- getCAIweights(referenceGenome)
```

---

getCodonCounts *Get Codon Counts For all Amino Acids*

Description

provides the codon counts for a fiven amino acid across all genes

Usage

```
getCodonCounts(genome)
```

Arguments

genome	A genome object from which the counts of each codon can be obtained.

Details

The returned matrix containes a row for each gene and a column for each synonymous codon of aa.

Value

Returns a data.frame storing the codon counts for each amino acid.

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

## reading genome
genome <- initializeGenomeObject(file = genome_file)
counts <- getCodonCounts(genome)
```

getCodonCountsForAA *Get Codon Counts For a specific Amino Acid*

Description

provides the codon counts for a fiven amino acid across all genes

Usage

```
getCodonCountsForAA(aa, genome)
```

Arguments

aa	One letter code of the amino acid for which the codon counts should be returned
genome	A genome object from which the counts of each codon can be obtained.

Details

The returned matrix containes a row for each gene and a coloumn for each synonymous codon of aa.

Value

Returns a data.frame storing the codon counts for the specified amino acid.

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

## reading genome
genome <- initializeGenomeObject(file = genome_file)
counts <- getCodonCountsForAA("A", genome)
```

getCodonSpecificPosteriorMeanForCodon
getCodonSpecificPosteriorMeanForCodon

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Calculate codon-specific parameter (CSP) posterior mean

Arguments

mixtureElement	mixture to calculate CSP posterior mean. Should be between 1 and n, where n is number of mixtures.
samples	number of samples to use for calculating posterior mean
codon	codon to calculate CSP
paramType	CSP to calculate posterior mean for. 0: Mutation (ROC,FONSE) or Alpha (PA, PANSE). 1: Selection (ROC,FONSE), Lambda (PANSE), Lambda^prime (PA). 2: NSERate (PANSE)
withoutReference	If model uses reference codon, then ignore this codon (fixed at 0). Should be TRUE for ROC and FONSE. Should be FALSE for PA and PANSE.
log_scale	If true, calculate posterior mean on log scale. Should only be used for PA and PANSE.

Value

posterior mean value for CSP

---

getCodonSpecificPosteriorVarianceForCodon
getCodonSpecificPosteriorVarianceForCodon

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Calculate codon-specific parameter (CSP) variance

Arguments

mixtureElement	mixture to calculate CSP variance. Should be between 1 and n, where n is number of mixtures.
samples	number of samples to use for calculating variance
codon	codon to calculate CSP
paramType	CSP to calculate variance for. 0: Mutation (ROC,FONSE) or Alpha (PA, PANSE). 1: Selection (ROC,FONSE), Lambda (PANSE), Lambda^prime (PA). 2: NSERate (PANSE)
unbiased	If TRUE, should calculate variance using unbiased (N-1). Otherwise, used biased (N) correction
withoutReference	If model uses reference codon, then ignore this codon (fixed at 0). Should be TRUE for ROC and FONSE. Should be FALSE for PA and PANSE.
log_scale	If true, calculate posterior mean on log scale. Should only be used for PA and PANSE.

Value

variance over trace for CSP

`getCodonSpecificQuantilesForCodon` *getCodonSpecificQuantilesForCodon*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Calculate quantiles of CSP traces

Arguments

`mixtureElement`	mixture to calculate CSP variance. Should be between 1 and n, where n is number of mixtures.
`samples`	number of samples to use for calculating variance
`codon`	codon to calculate CSP
`paramType`	CSP to calculate variance for. 0: Mutation (ROC,FONSE) or Alpha (PA, PANSE). 1: Selection (ROC,FONSE), Lambda (PANSE), Lambda^prime (PA). 2: NSERate (PANSE)
`probs`	vector of two doubles between 0 and 1 indicating range over which to calculate quantiles. <0.0275, 0.975> would give 95% quantiles.
`withoutReference`	If model uses reference codon, then ignore this codon (fixed at 0). Should be TRUE for ROC and FONSE. Should be FALSE for PA and PANSE.
`log_scale`	If true, calculate posterior mean on log scale. Should only be used for PA and PANSE.

Value

vector representing lower and upper bound of quantile

`getCSPEstimates` *Return Codon Specific Paramters (or write to csv) estimates as data.frame*

Description

`getCSPEstimates` returns the codon specific parameter estimates for a given parameter and mixture or write it to a csv file.

Usage

```
getCSPEstimates(
  parameter,
  filename = NULL,
  mixture = 1,
  samples = 10,
  relative.to.optimal.codon = T,
  report.original.ref = T,
  log.scale = F
)
```

Arguments

parameter	parameter an object created by `initializeParameterObject`.
filename	Posterior estimates will be written to file (format: csv). Filename will be in the format <parameter_name>_<filename>.csv.
mixture	estimates for which mixture should be returned
samples	The number of samples used for the posterior estimates.
relative.to.optimal.codon	Boolean determining if parameters should be relative to the preferred codon or the alphabetically last codon (Default=TRUE). Only applies to ROC and FONSE models
report.original.ref	Include the original reference codon (Default = TRUE). Note this is only included for the purposes of simulations, which expect the input parameter file to be in a specific format. Later version of AnaCoDa will remove this.
log.scale	Calculate posterior means, standard deviation, and posterior probability intervals on the natural log scale. Should be used for PA and PANSE models only.

Value

returns a list data.frame with the posterior estimates of the models codon specific parameters or writes it directly to a csv file if `filename` is specified

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)
sphi_init <- c(1,1)
numMixtures <- 2
geneAssignment <- c(rep(1,floor(length(genome)/2)),rep(2,ceiling(length(genome)/2)))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
                                       gene.assignment = geneAssignment,
                                       mixture.definition = "allUnique")
model <- initializeModelObject(parameter = parameter, model = "ROC")
samples <- 2500
```

```
thinning <- 50
adaptiveWidth <- 25
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning,
                             adaptive.width=adaptiveWidth, est.expression=TRUE,
                             est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)
divergence.iteration <- 10
## Not run:
runMCMC(mcmc = mcmc, genome = genome, model = model,
        ncores = 4, divergence.iteration = divergence.iteration)

## return estimates for codon specific parameters
csp_mat <- getCSPEstimates(parameter)

# write the result directly to the filesystem as a csv file. No values are returned
getCSPEstimates(parameter, filename=file.path(tempdir(), "test.csv"))


## End(Not run)
```

`getEstimatedMixtureAssignmentForGene` *getEstimatedMixtureAssignmentForGene*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Get estimated mixture assignment for gene

Arguments

`samples`	number of samples over which to calculate mixture assignment
`geneIndex`	corresponding index of gene in genome. Should be a number between 1 and length(genome).

Value

returns value between 1 and n, where n is number of mixtures

`getEstimatedMixtureAssignmentProbabilitiesForGene` *getEstimatedMixtureAssignmentProbabilitiesForGene*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Get estimated mixture assignment probabilities for gene

Arguments

samples	number of samples over which to calculate mixture assignment probabilities
geneIndex	corresponding index of gene in genome. Should be a number between 1 and length(genome).

Value

returns vector of probabilities representing mixture probabilities for gene

---

getExpressionEstimates

Returns the estimated phi posterior for a gene

Description

Posterior estimates for the phi value of specified genes

Usage

```
getExpressionEstimates(
  parameter,
  gene.index,
  samples,
  quantiles = c(0.025, 0.975),
  genome = NULL
)
```

Arguments

parameter	on object created by `initializeParameterObject`.
gene.index	a integer or vector of integers representing the gene(s) of interesst.
samples	number of samples for the posterior estimate
quantiles	vector of quantiles, (default: c(0.025, 0.975))
genome	if genome is given, then will include gene ids in output (default is NULL)

Details

The returned vector is unnamed as gene ids are only stored in the `genome` object, but the `gene.index` vector can be used to match the assignment to the genome.

Value

returns a vector with the mixture assignment of each gene corresbonding to `gene.index` in the same order as the genome.

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)
sphi_init <- c(1,1)
numMixtures <- 2
geneAssignment <- c(rep(1,floor(length(genome)/2)),rep(2,ceiling(length(genome)/2)))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
                                       gene.assignment = geneAssignment,
                                       mixture.definition = "allUnique")
model <- initializeModelObject(parameter = parameter, model = "ROC")
samples <- 2500
thinning <- 50
adaptiveWidth <- 25
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning,
                             adaptive.width=adaptiveWidth, est.expression=TRUE,
                             est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)
divergence.iteration <- 10
## Not run:
runMCMC(mcmc = mcmc, genome = genome, model = model,
        ncores = 4, divergence.iteration = divergence.iteration)

# get the estimated expression values for all genes based on the mixture
# they are assigned to at each step
estimatedExpression <- getExpressionEstimates(parameter, 1:length(genome), 1000)

## End(Not run)
```

`getGroupList` *getGroupList*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Get amino acids (ROC, FONSE) or codons (PA, PANSE) for which parameters will be estimated

Value

returns list of amino acids or codons

`getLogLikelihoodTrace` *getLogLikelihoodTrace*

Description

Method of MCMC class (access via mcmc$<function name>, where mcmc is an object initialized by initializeMCMCObject). Returns the logLikelihood trace

Value

vector representing logLikelihood trace

`getLogPosteriorMean` *getLogPosteriorMean*

Description

Method of MCMC class (access via mcmc$<function name>, where mcmc is an object initialized by initializeMCMCObject). Calculate the mean log posterior probability over the last n samples

Arguments

`samples`	postive value less than total length of the MCMC trace

Value

mean logPosterior

`getLogPosteriorTrace` *getLogPosteriorTrace*

Description

Method of MCMC class (access via mcmc$<function name>, where mcmc is an object initialized by initializeMCMCObject). Returns the logPosterior trace

Value

vector representing logPosterior trace

getMixtureAssignmentEstimate
Returns mixture assignment estimates for each gene

Description

Posterior estimates for the mixture assignment of specified genes

Usage

```
getMixtureAssignmentEstimate(parameter, gene.index, samples)
```

Arguments

parameter	on object created by initializeParameterObject
gene.index	a integer or vector of integers representing the gene(s) of interesst.
samples	number of samples for the posterior estimate

Details

The returned vector is unnamed as gene ids are only stored in the genome object, but the gene.index vector can be used to match the assignment to the genome.

Value

returns a vector with the mixture assignment of each gene corresbonding to gene.index in the same order as the genome.

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)
sphi_init <- c(1,1)
numMixtures <- 2
geneAssignment <- c(rep(1,floor(length(genome)/2)),rep(2,ceiling(length(genome)/2)))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
                                       gene.assignment = geneAssignment,
                                       mixture.definition = "allUnique")
model <- initializeModelObject(parameter = parameter, model = "ROC")
samples <- 2500
thinning <- 50
adaptiveWidth <- 25
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning, adaptive.width=adaptiveWidth,
                         est.expression=TRUE, est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)
divergence.iteration <- 10
## Not run:
```

```
runMCMC(mcmc = mcmc, genome = genome, model = model,
        ncores = 4, divergence.iteration = divergence.iteration)

# get the mixture assignment for all genes
mixAssign <- getMixtureAssignmentEstimate(parameter = parameter,
                                          gene.index = 1:length(genome), samples = 1000)

# get the mixture assignment for a subsample
mixAssign <- getMixtureAssignmentEstimate(parameter = parameter,
                                          gene.index = 5:100, samples = 1000)
# or
mixAssign <- getMixtureAssignmentEstimate(parameter = parameter,
                                        gene.index = c(10, 30:50, 3, 90), samples = 1000)

## End(Not run)
```

`getNames` *Gene Names of Genome*

Description

returns the identifiers of the genes within the genome specified.

Usage

```
getNames(genome, simulated = FALSE)
```

Arguments

`genome`	A genome object initialized with `initializeGenomeObject`.
`simulated`	A logical value denoting if the gene names to be listed are simulated or not. The default value is FALSE.

Value

gene.names Returns the names of the genes as a vector of strings.

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

## reading genome
genome <- initializeGenomeObject(file = genome_file)

## return all gene ids for the genome
geneIDs <- getNames(genome, FALSE)
```

getNc *Calculate the Effective Number of Codons*

Description

getNc returns the Effective Number of Codons for a genome.

Usage

```
getNc(genome)
```

Arguments

genome	A genome object initialized with initializeGenomeObject.

Value

Returns a named vector with the Effective Number of Codons for each gene

Examples

```
genome_file <- system.file("extdata", "more_genes.fasta", package = "AnaCoDa")
## reading genome
genome <- initializeGenomeObject(file = genome_file)

nc <- getNc(genome)
```

getNcAA *Calculate the Effective Number of Codons for each Amino Acid*

Description

getNcAA returns the Effective Number of Codons for each Amino Acid.

Usage

```
getNcAA(genome)
```

Arguments

genome	A genome object initialized with initializeGenomeObject.

Value

Returns an object of type data.frame with the Effective Number of Codons for each amino acid in each gene.

Examples

```
genome_file <- system.file("extdata", "more_genes.fasta", package = "AnaCoDa")
## reading genome
genome <- initializeGenomeObject(file = genome_file)

nc <- getNcAA(genome)
```

`getNoiseOffsetPosteriorMean` *getNoiseOffsetPosteriorMean*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Calculate posterior mean of standard deviation parameter of lognormal describing distribution of synthesis rates

Arguments

`index`	mixture index to use. Should be number between 0 and n-1, where n is number of mixtures
`samples`	number of samples over which to calculate posterior mean

Value

returns posterior mean for standard deviation of lognormal distribution of synthesis rates

---

`getNoiseOffsetVariance` *getNoiseOffsetVariance*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Calculate variance of noise offset parameter used when fitting model with empirical estimates of synthesis rates (ie. withPhi fits)

Arguments

`index`	mixture index to use. Should be number between 0 and n-1, where n is number of mixtures
`samples`	number of samples over which to calculate variance
`unbiased`	If TRUE, should calculate variance using unbiased (N-1). Otherwise, used biased (N) correction

Value

returns variance for noise offset

`getObservedSynthesisRateSet` *Get gene observed synthesis rates*

Description

`getObservedSynthesisRateSet` returns the observed synthesis rates of the genes within the genome specified.

Usage

```
getObservedSynthesisRateSet(genome, simulated = FALSE)
```

Arguments

`genome`	A genome object initialized with `initializeGenomeObject`.
`simulated`	A logical value denoting if the synthesis rates to be listed are simulated or not. The default value is FALSE.

Value

Returns a data.frame with the observed expression values in genome

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")
expression_file <- system.file("extdata", "expression.csv", package = "AnaCoDa")
## reading genome
genome <- initializeGenomeObject(file = genome_file)


## return expression values as a data.frame with gene ids in the first column.
expressionValues <- getObservedSynthesisRateSet(genome = genome)
```

getSamples *getSamples*

Description

Method of MCMC class (access via mcmc$<function name>, where mcmc is an object initialized by initializeMCMCObject). Return number of samples set for MCMCAlgorithm object

Value

number of samples used during MCMC

getSelectionCoefficients *Calculate Selection coefficients*

Description

`getSelectionCoefficients` calculates the selection coefficient of each codon in each gene.

Usage

```
getSelectionCoefficients(genome, parameter, samples = 100)
```

Arguments

`genome`	A genome object initialized with `initializeGenomeObject` to add observed expression data.
`parameter`	an object created by `initializeParameterObject`.
`samples`	The number of samples used for the posterior estimates.

Value

A matrix with selection coefficients.

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)
sphi_init <- 1
numMixtures <- 1
geneAssignment <- rep(1, length(genome))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
                                       gene.assignment = geneAssignment,
```

```
                                        mixture.definition = "allUnique")
model <- initializeModelObject(parameter = parameter, model = "ROC")
samples <- 2500
thinning <- 50
adaptiveWidth <- 25
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning,
                             adaptive.width=adaptiveWidth, est.expression=TRUE,
                             est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)
divergence.iteration <- 10
## Not run:
runMCMC(mcmc = mcmc, genome = genome, model = model,
        ncores = 4, divergence.iteration = divergence.iteration)

## return estimates for selection coefficients s for each codon in each gene
selection.coefficients <- getSelectionCoefficients(genome = genome,
                                                   parameter = parameter, samples = 1000)

## End(Not run)
```

`getStdDevSynthesisRatePosteriorMean`
getStdDevSynthesisRatePosteriorMean

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Calculate posterior mean of standard deviation parameter of lognormal describing distribution of synthesis rates

Arguments

`samples`	number of samples over which to calculate posterior mean
`mixture`	mixture index to use. Should be number between 0 and n-1, where n is number of mixtures

Value

returns posterior mean for standard deviation of lognormal distribution of synthesis rates

`getStdDevSynthesisRateVariance` *getStdDevSynthesisRateVariance*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Calculate variance of standard deviation parameter of lognormal describing distribution of synthesis rates

Arguments

`samples`	number of samples over which to calculate variance
`mixture`	mixture index to use. Should be number between 0 and n-1, where n is number of mixtures
`unbiased`	If TRUE, should calculate variance using unbiased (N-1). Otherwise, used biased (N) correction

Value

returns variance for standard deviation of lognormal distribution of synthesis rates

`getStepsToAdapt` *getStepsToAdapt*

Description

Method of MCMC class (access via mcmc$<function name>, where mcmc is an object initialized by initializeMCMCObject). Return number of iterations (total iterations = samples * thinning) to allow proposal widths to adapt

Value

number of sample steps to adapt

`getSynthesisRate` *getSynthesisRate*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Get current synthesis rates for all genes and all mixtures

Value

2 by 2 vector of numeric values

getSynthesisRatePosteriorMeanForGene
getSynthesisRatePosteriorMeanForGene

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Get posterior mean synthesis rate value for a gene

Arguments

samples	number of samples over which to calculate mean
geneIndex	corresponding index of gene in genome for which posterior mean synthesis rate will be calculated. Should be a number between 1 and length(genome)
log_scale	Calculate posterior mean on log scale

Value

posterior mean synthesis rate for gene

getSynthesisRatePosteriorVarianceForGene
getSynthesisRatePosteriorVarianceForGene

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Get synthesis rate variance for a gene

Arguments

samples	number of samples over which to calculate variance
geneIndex	corresponding index of gene in genome for which synthesis rate variance will be calculated. Should be a number between 1 and length(genome)
unbiased	Should calculate variance using unbiased (N-1) or biased (N) correction
log_scale	Calculate variance on log scale

Value

posterior mean synthesis rate for gene

getThinning *getThinning*

Description

Method of MCMC class (access via mcmc$<function name>, where mcmc is an object initialized by initializeMCMCObject). Return thinning value, which is the number of iterations (total iterations = samples * thinning) not being kept

Value

thinning value used during MCMC

getTrace *extracts an object of traces from a parameter object.*

Description

extracts an object of traces from a parameter object.

Usage

```
getTrace(parameter)
```

Arguments

parameter	A Parameter object that corresponds to one of the model types.

Value

trace Returns an object of type Trace extracted from the given parameter object

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)
sphi_init <- c(1,1)
numMixtures <- 2
geneAssignment <- c(rep(1,floor(length(genome)/2)),rep(2,ceiling(length(genome)/2)))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
                                       gene.assignment = geneAssignment,
                                       mixture.definition = "allUnique")

trace <- getTrace(parameter) # empty trace object since no MCMC was perfomed
```

getTraceObject *getTraceObject*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Get Trace object stored by a Parameter object. Useful for plotting certain parameter traces.

Value

Trace object

initializeCovarianceMatrices
Initialize Covariance Matrices

Description

Initialize Covariance Matrices

Usage

```
initializeCovarianceMatrices(
  parameter,
  genome,
  numMixtures,
  geneAssignment,
  init.csp.variance = 0.0025
)
```

Arguments

parameter	A Parameter object that corresponds to one of the model types. Valid values are "ROC", "PA", and "FONSE".
genome	An object of type Genome necessary for the initialization of the Parameter object.
numMixtures	The number of mixture elements for the underlying mixture distribution (numMixtures > 0).
geneAssignment	A vector holding the initial mixture assignment for each gene. The vector length has to equal the number of genes in the genome. Valid values for the vector range from 1 to numMixtures. It is possible but not advised to leave a mixture element empty.
init.csp.variance	initial proposal variance for codon specific parameter, default is 0.0025.

Value

parameter Returns the Parameter argument, now modified with initialized mutation, selection, and covariance matrices.

`initializeGenomeObject` *Genome Initialization*

Description

`initializeGenomeObject` initializes the Rcpp Genome object

Usage

```
initializeGenomeObject(
  file,
  genome = NULL,
  observed.expression.file = NULL,
  fasta = TRUE,
  positional = FALSE,
  match.expression.by.id = TRUE,
  append = FALSE
)
```

Arguments

`file`	A file of coding sequences in fasta or RFPData format
`genome`	A genome object can be passed in to concatenate the input file to it (optional).
`observed.expression.file`	String containing the location of a file containing empirical expression rates (optional). Default value is NULL.
`fasta`	Boolean value indicating whether `file` argument is a fasta file (TRUE) or an RFPData file (FALSE). Default value is TRUE.
`positional`	Boolean indicating if the positional information in the RFPData file is necessary. Default value is FALSE
`match.expression.by.id`	If TRUE, observed expression values will be assigned by matching sequence identifier. If FALSE, observed expression values will be assigned by order. Default value is TRUE.
`append`	If TRUE, function will read in additional genome data to append to an existing genome. If FALSE, genome data is cleared before reading in data (no preexisting data). Default value is FALSE.

Value

This function returns the initialized Genome object.

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")
genes_file <- system.file("extdata", "more_genes.fasta", package = "AnaCoDa")
expression_file <- system.file("extdata", "expression.csv", package = "AnaCoDa")

## reading genome
genome <- initializeGenomeObject(file = genome_file)

## reading genome and observed expression data
genome <- initializeGenomeObject(file = genome_file, observed.expression.file = expression_file)

## add aditional genes to existing genome
genome <- initializeGenomeObject(file = genome_file)
genome <- initializeGenomeObject(file = genes_file, genome = genome, append = TRUE)
```

---

initializeMCMCObject *Initialize MCMC*

Description

`initializeMCMCObject` initializes a MCMC object to perform a model fitting for a parameter and model object.

Usage

```
initializeMCMCObject(
  samples,
  thinning = 1,
  adaptive.width = 100,
  est.expression = TRUE,
  est.csp = TRUE,
  est.hyper = TRUE,
  est.mix = TRUE
)
```

Arguments

`samples`	Number of samples to be produced when running the MCMC algorithm. No default value.
`thinning`	The thinning interval between consecutive observations. If set to 1, every step will be saved as a sample. Default value is 1.
`adaptive.width`	Number that determines how often the acceptance/rejection window should be altered. Default value is 100 samples. Proportion of MCMC steps where the proposal distribution is adaptive can be set using `mcmc$setStepsToAdapt`. The default parameter passed in as -1 uses the full iterations.

est.expression	Boolean that tells whether or not synthesis rate values should be estimated in the MCMC algorithm run. Default value is TRUE.
est.csp	Boolean that tells whether or not codon specific values should be estimated in the MCMC algorithm run. Default value is TRUE.
est.hyper	Boolean that tells whether or not hyper parameters should be estimated in the MCMC algorithm run. Default value is TRUE. Setting for expression noise parameter sepsilon can be overridden by setting fix.observation.noise in initializeModelObject()
est.mix	Boolean that tells whether or not the genes' mixture element should be estimated in the MCMC algorithm run. Default value is TRUE.

Details

initializeMCMCObject sets up the MCMC object (monte carlo markov chain) and returns the object so a model fitting can be done. It is important to note that est.expression and est.hyper will affect one another negatively if their values differ.

Value

mcmc Returns an intialized MCMC object.

Examples

```
## initializing an object of type mcmc

samples <- 2500
thinning <- 50
adaptiveWidth <- 25

## estimate all parameter types
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning, adaptive.width=adaptiveWidth,
                      est.expression=TRUE, est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)

## do not estimate expression values, initial conditions will remain constant
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning, adaptive.width=adaptiveWidth,
                     est.expression=FALSE, est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)

## do not estimate hyper parameters, initial conditions will remain constant
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning, adaptive.width=adaptiveWidth,
                     est.expression=TRUE, est.csp=TRUE, est.hyper=FALSE, est.mix = TRUE)
```

---

initializeModelObject *Model Initialization*

Description

initializes the model object.

Usage

```
initializeModelObject(
  parameter,
  model = "ROC",
  with.phi = FALSE,
  fix.observation.noise = FALSE,
  rfp.count.column = 1
)
```

Arguments

parameter	An object created with initializeParameterObject.
model	A string containing the model to run (ROC, FONSE, or PA), has to match parameter object.
with.phi	(ROC only) A boolean that determines whether or not to include empirical phi values (expression rates) for the calculations. Default value is FALSE
fix.observation.noise	(ROC only) Allows fixing the noise term sepsilon in the observed expression dataset to its initial condition. This value should override the est.hyper=TRUE setting in initializeMCMCObject() The initial condition for the observed expression noise is set in the parameter object. Default value is FALSE.
rfp.count.column	(PA and PANSE only) A number representing the RFP count column to use. Default value is 1.

Details

initializeModelObject initializes a model. The type of model is determined based on the string passed to the model argument. The Parameter object has to match the model that is initialized. E.g. to initialize a ROC model, it is required that a ROC parameter object is passed to the function.

Value

This function returns the model object created.

Examples

```
#initializing a model object

genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")
expression_file <- system.file("extdata", "expression.csv", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file,
                                 observed.expression.file = expression_file)
sphi_init <- c(1,1)
numMixtures <- 2
geneAssignment <- c(rep(1,floor(length(genome)/2)),rep(2,ceiling(length(genome)/2)))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
```

```
                                        gene.assignment = geneAssignment,
                                        mixture.definition = "allUnique")

# initializing a model object assuming we have observed expression (phi)
# values stored in the genome object.
initializeModelObject(parameter = parameter, model = "ROC", with.phi = TRUE)

# initializing a model object ignoring observed expression (phi)
# values stored in the genome object.
initializeModelObject(parameter = parameter, model = "ROC", with.phi = FALSE)
```

`initializeParameterObject` *Initialize Parameter*

Description

`initializeParameterObject` initializes a new parameter object or reconstructs one from a restart file

Usage

```
initializeParameterObject(
  genome = NULL,
  sphi = NULL,
  num.mixtures = 1,
  gene.assignment = NULL,
  initial.expression.values = NULL,
  model = "ROC",
  split.serine = TRUE,
  mixture.definition = "allUnique",
  mixture.definition.matrix = NULL,
  init.with.restart.file = NULL,
  mutation.prior.mean = 0,
  mutation.prior.sd = 0.35,
  propose.by.prior = FALSE,
  init.csp.variance = 0.0025,
  init.sepsilon = 0.1,
  init.w.obs.phi = FALSE,
  init.initiation.cost = 4,
  init.partition.function = 1
)
```

Arguments

genome	An object of type Genome necessary for the initialization of the Parameter object. The default value is NULL.

sphi — Initial values for sphi. Expected is a vector of length numMixtures. The default value is NULL.

num.mixtures — The number of mixtures elements for the underlying mixture distribution (numMixtures > 0). The default value is 1.

gene.assignment — A vector holding the initial mixture assignment for each gene. The vector length has to equal the number of genes in the genome. Valid values for the vector range from 1 to numMixtures. It is possible but not advised to leave a mixture element empty. The default Value is NULL.

initial.expression.values — (Optional) A vector with intial phi values. The length of the vector has to equal the number of genes in the Genome object and the order of the genes should match the order of the genes in the Genome. The default value is NULL.

model — Specifies the model used. Valid options are "ROC", "PA", "PANSE", or "FONSE". The default model is "ROC". ROC is described in Gilchrist et al. 2015. PA, PANSE and FONSE are currently unpublished.

split.serine — Whether serine should be considered as one or two amino acids when running the model. TRUE and FALSE are the only valid values. The default value for split.serine is TRUE.

mixture.definition — A string describing how each mixture should be treated with respect to mutation and selection. Valid values consist of "allUnique", "mutationShared", and "selectionShared". The default value for mixture.definition is "allUnique". See details for more information.

mixture.definition.matrix — A matrix representation of how the mutation and selection categories correspond to the mixtures. The default value for mixture.definition.matrix is NULL. If provided, the model will use the matrix to initialize the mutation and selection categories instead of the definition listed directly above. See details for more information.

init.with.restart.file — File name containing information to reinitialize a previous Parameter object. If given, all other arguments will be ignored. The default value for init.with.restart.file is NULL.

mutation.prior.mean — Controlling the mean of the normal prior on mutation paramters. If passed in as single number (default is 0), this will be the mean value for all categories, for all codons. User may also supply a vector with n * 40 values, where n is the number of mutation categories. Future versions will check the number of rows matches the number of mutation categories definded by user.

mutation.prior.sd — Controlling the standard deviation of the normal prior on the mutation parameters. If passed in as single number (default is 0.35), this will be the standard deviation value for all categories, for all codons. User may also supply a vector with n * 40 values, where n is the number of mutation categories. Future versions will check the number of rows matches the number of mutation categories definded by user.

`propose.by.prior`
: Mutation bias parameters will be proposed based on the means and standard deviations set in mutation.prior.mean and mutation.prior.sd

`init.csp.variance`
: specifies the initial proposal width for codon specific parameter (default is 0.0025). The proposal width adapts during the runtime to reach a taget acceptance rate of ~0.25

`init.sepsilon`
: specifies the initial value for sepsilon. default is 0.1

`init.w.obs.phi`
: If TRUE, initialize phi values with observed phi values (data from RNAseq, mass spectrometry, ribosome footprinting) Default is FALSE. If multiple observed phi values exist for a gene, the geometric mean of these values is used as initial phi. When using this function, one should remove any genes with missing phi values, as these genes will not have an initial phi value.

`init.initiation.cost`
: FOR FONSE ONLY. Initializes the initiation cost a_1 at this value.

`init.partition.function`
: FOR PANSE ONLY. initializes the partition function Z.

Details

`initializeParameterObject` checks the values of the arguments given to insure the values are valid.

The mixture definition and mixture definition matrix describes how the mutation and selection categories are set up with respect to the number of mixtures. For example, if mixture.definition = "allUnique" and numMixtures = 3, a matrix representation would be `matrix(c(1,2,3,1,2,3), ncol=2)` where each row represents a mixture, the first column represents the mutation category, and the second column represents the selection category. Another example would be mixture.definition = "selectionShared" and numMixtures = 4 (`matrix(c(1,2,3,4,1,1,1,1), ncol=2)`). In this case, the selection category is the same for every mixture. If a matrix is given, and it is valid, then the mutation/selection relationship will be defined by the given matrix and the keyword will be ignored. A matrix should only be given in cases where the keywords would not create the desired matrix.

Value

parameter Returns an initialized Parameter object.

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")
restart_file <- system.file("extdata", "restart_file.rst", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)

## initialize a new parameter object
sphi_init <- 1
numMixtures <- 1
geneAssignment <- rep(1, length(genome))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
```

```
                                        num.mixtures = numMixtures,
                                        gene.assignment = geneAssignment,
                                        mixture.definition = "allUnique")

## re-initialize a parameter object from a restart file. Useful for checkpointing
parameter <- initializeParameterObject(init.with.restart.file = restart_file)

## initialize a parameter object with a custon mixture definition matrix
def.matrix <- matrix(c(1,1,1,2), ncol=2)
geneAssignment <- c(rep(1,floor(length(genome)/2)),rep(2,ceiling(length(genome)/2)))
parameter <- initializeParameterObject(genome = genome, sphi = c(0.5, 2), num.mixtures = 2,
                                        gene.assignment = geneAssignment,
                                        mixture.definition.matrix = def.matrix)
```

`initializeSynthesisRateByGenome`
initializeSynthesisRateByGenome

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Initialize synthesis rates using SCUO values calcuated from the genome

Arguments

`genome`	a Genome object

`initializeSynthesisRateByList`
initializeSynthesisRateByList

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Initialize synthesis rates with values passed in as a list

Arguments

`expression`	a list of values to use as initial synthesis rate values. Should be same size as number of genes in genome.

`initializeSynthesisRateByRandom`
initializeSynthesisRateByRandom

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Initialize synthesis rates by drawing a from a lognormal distribution with mean = -(sd_phi)^2/2 and sd = sd_phi

Arguments

`sd_phi`	a positive value which will be the standard deviation of the lognormal distribution

---

`initMutationCategories`
initMutationCategories

Description

Initialize values for mutation CSP. File should be of comma-separated with header. Three columns should be of order Amino_acid,Codon,Value

Arguments

`files`	list of files containing starting values. Number of files should equal the number of categories.
`numCategories`	number of mutation categories (should be less than or equal to number of mixtures)
`fix`	Can use this parameter to fix mutation at current values (won't change over course of MCMC run)

`initSelectionCategories` *initSelectionCategories*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Initialize values for selection CSP. File should be of comma-separated with header. Three columns should be of order Amino_acid,Codon,Value

Arguments

`files`	list of files containing starting values. Number of files should equal the number of categories.
`numCategories`	number of mutation categories (should be less than or equal to number of mixtures)
`fix`	Can use this parameter to fix selection at current values (won't change over course of MCMC run)

`length.Rcpp_Genome` *Length of Genome*

Description

`length` gives the length of a genome

Usage

```
## S3 method for class 'Rcpp_Genome'
length(x)
```

Arguments

`x`	A genome object initialized with `initializeGenomeObject`.

Value

returns the number of genes in a genome

Examples

```
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

## reading genome
genome <- initializeGenomeObject(file = genome_file)
length(genome) # 10
```

loadMCMCObject *Load MCMC Object*

Description

loadMCMCObject creates a new MCMC object and fills it with the information in the file given.

Usage

```
loadMCMCObject(files)
```

Arguments

files	The filenames where the data will be stored.

Details

This MCMC object is not intended to be used to do another model fitting, only to graph the stored results.

Value

This function has no return value.

Examples

```
## loading mcmc objects from the filesystem
## Not run:
# load one mcmc object
mcmc <- loadMCMCObject(files = "mcmc.Rda")

# load and combine multiple mcmc objects. Useful when using checkpointing
mcmc <- loadMCMCObject(files = c("mcmc1.Rda", "mcmc2.Rda"))

## End(Not run)
```

loadParameterObject *Load Parameter Object*

Description

loadParameterObject will load a parameter object from the filesystem

Usage

```
loadParameterObject(files)
```

Arguments

files	A list of parameter filenames to be loaded. If multiple files are given, the parameter objects will be concatenated in the order provided

Details

The function loads one or multiple files. In the case of multiple file, e.g. due to the use of check pointing, the files will be concatenated to one parameter object. See writeParameterObject for the writing of parameter objects

Value

Returns an initialized Parameter object.

Examples

```
## Not run:
# load a single parameter object
parameter <- loadParameterObject("parameter.Rda")

# load and concatenate multiple parameter object
parameter <- loadParameterObject(c("parameter1.Rda", "parameter2.Rda"))

## End(Not run)
```

---

plot.Rcpp_FONSEModel *Plot Model Object*

Description

Plots traces from the model object such as synthesis rates for each gene. Will work regardless of whether or not expression/synthesis rate levels are being estimated. If you wish to plot observed/empirical values, these values MUST be set using the initial.expression.values parameter found in initializeParameterObject. Otherwise, the expression values plotted will just be SCUO values estimated upon initialization of the Parameter object.

Usage

```
## S3 method for class 'Rcpp_FONSEModel'
plot(
  x,
  genome,
  samples = 100,
  mixture = 1,
  simulated = FALSE,
  codon.window = NULL,
  ...
)
```

Arguments

x	An Rcpp model object initialized with `initializeModelObject`.
genome	An Rcpp genome object initialized with `initializeGenomeObject`.
samples	The number of samples in the trace
mixture	The mixture for which to graph values.
simulated	A boolean value that determines whether to use the simulated genome.
codon.window	A boolean value that determines the codon window to use for calculating codon frequencies. If NULL (the default), use complete sequences.
...	Optional, additional arguments. For this function, a possible title for the plot in the form of a list if set with "main".

Value

This function has no return value.

---

plot.Rcpp_FONSEParameter *Plot Parameter*

Description

`plot` graphs the mutation or selection parameter for a ROC or FONSE parameter object for each mixture element.

Usage

```
## S3 method for class 'Rcpp_FONSEParameter'
plot(
  x,
  what = "Mutation",
  samples = 100,
  mixture.name = NULL,
  with.ci = TRUE,
  ...
)
```

Arguments

x	A parameter object
what	Which aspect of the parameter to plot. Default value is "Mutation".
samples	Number of samples to plot using the posterior mean. Default value is 100.
mixture.name	a vector with names/descriptions of the mixture distributions in the parameter object
with.ci	Plot with or without confidence intervals. Default value is TRUE
...	Arguments to be passed to methods, such as graphical parameters.

Details

Graphs are based off the last # samples for the posterior mean.

Value

This function has no return value.

---

plot.Rcpp_MCMCAlgorithm *Plot MCMC algorithm*

Description

This function will plot the logLikelihood trace, and if the Hmisc package is installed, it will plot a subplot of the logLikelihood trace with the first few samples removed.

Usage

```
## S3 method for class 'Rcpp_MCMCAlgorithm'
plot(x, what = "LogPosterior", zoom.window = NULL, ...)
```

Arguments

x	An Rcpp_MCMC object initialized with `initializeMCMCObject`.
what	character defining if log(Posterior) (Default) or log(Likelihood) options are: LogPosterior or logLikelihood
zoom.window	A vector describing the start and end of the zoom window.
...	Arguments to be passed to methods, such as graphical parameters.

Value

This function has no return value.

---

plot.Rcpp_ROCModel *Plot Model Object*

Description

Plots traces from the model object such as synthesis rates for each gene. Will work regardless of whether or not expression/synthesis rate levels are being estimated. If you wish to plot observed/empirical values, these values MUST be set using the initial.expression.values parameter found in initializeParameterObject. Otherwise, the expression values plotted will just be SCUO values estimated upon initialization of the Parameter object.

Usage

```
## S3 method for class 'Rcpp_ROCModel'
plot(x, genome = NULL, samples = 100, mixture = 1, simulated = FALSE, ...)
```

Arguments

x	An Rcpp model object initialized with `initializeModelObject`.
genome	An Rcpp genome object initialized with `initializeGenomeObject`.
samples	The number of samples in the trace
mixture	The mixture for which to graph values.
simulated	A boolean value that determines whether to use the simulated genome.
...	Optional, additional arguments. For this function, a possible title for the plot in the form of a list if set with "main".

Value

This function has no return value.

---

plot.Rcpp_ROCParameter

Plot Parameter

Description

`plot` graphs the mutation or selection parameter for a ROC or FONSE parameter object for each mixture element.

Usage

```
## S3 method for class 'Rcpp_ROCParameter'
plot(
  x,
  what = "Mutation",
  samples = 100,
  mixture.name = NULL,
  with.ci = TRUE,
  ...
)
```

Arguments

x	A parameter object
what	Which aspect of the parameter to plot. Default value is "Mutation".
samples	Number of samples to plot using the posterior mean. Default value is 100.

mixture.name	a vector with names/descriptions of the mixture distributions in the parameter object
with.ci	Plot with or without confidence intervals. Default value is TRUE
...	Arguments to be passed to methods, such as graphical parameters.

Details

Graphs are based off the last # samples for the posterior mean.

Value

This function has no return value.

---

plot.Rcpp_Trace *Plot Trace Object*

Description

Plots different traces, specified with the what parameter.

Usage

```
## S3 method for class 'Rcpp_Trace'
plot(
  x,
  what = c("Mutation", "Selection", "MixtureProbability", "Sphi", "Mphi", "Aphi",
   "Sepsilon", "ExpectedPhi", "Expression", "NSEProb", "NSERate", "InitiationCost",
    "PartitionFunction"),
  geneIndex = 1,
  mixture = 1,
  log.10.scale = F,
  ...
)
```

Arguments

x	An Rcpp trace object initialized with initializeTraceObject.
what	A string containing one of the following to graph: Mutation, Selection, Alpha, LambdaPrime, MeanWaitingTime, VarWaitingTime MixtureProbability, Sphi, Mphi, Aphi, Spesilon, ExpectedPhi, Expression.
geneIndex	When plotting expression, the index of the gene to be plotted.
mixture	The mixture for which to plot values.
log.10.scale	A logical value determining if figures should be plotted on the log.10.scale (default=F). Should not be applied to mutation and selection parameters estimated by ROC/FONSE.
...	Optional, additional arguments. For this function, may be a logical value determining if the trace is ROC-based or not.

Value

This function has no return value.

`plotAcceptanceRatios` *Plot Acceptance ratios*

Description

Plots acceptance ratios for codon-specific parameters. Will be by amino acid for ROC and FONSE models, but will be by codon for PA and PANSE models. Note assumes estimating parameters for all codons.

Usage

```
plotAcceptanceRatios(trace, main = "CSP Acceptance Ratio Traces")
```

Arguments

`trace`	An Rcpp trace object initialized with `initializeTraceObject`.
`main`	The title of the plot.

Value

This function has no return value.

`plotCodonSpecificParameters`
Plot Codon Specific Parameter

Description

Plots a codon-specific set of traces, specified with the `type` parameter.

Usage

```
plotCodonSpecificParameters(
  trace,
  mixture,
  type = "Mutation",
  main = "Mutation Parameter Traces",
  ROC.or.FONSE = TRUE,
  log.10.scale = F
)
```

Arguments

trace	An Rcpp trace object initialized with initializeTraceObject.
mixture	The mixture for which to plot values.
type	A string containing one of the following to graph: Mutation, Selection, Alpha, LambdaPrime, MeanWaitingTime, VarWaitingTime.
main	The title of the plot.
ROC.or.FONSE	A logical value determining if the Parameter was ROC/FONSE or not.
log.10.scale	A logical value determining if figures should be plotted on the log.10.scale (default=F). Should not be applied to mutation and selection parameters estimated by ROC/FONSE.

Value

This function has no return value.

---

readPhiValue *readPhiValue*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Read synthesis rate values from file. File should be two column file <gene_id,phi> and is expected to have a header row

Arguments

filename	name of file to be read

---

runMCMC *Run MCMC*

Description

runMCMC will run a monte carlo markov chain algorithm for the given mcmc, genome, and model objects to perform a model fitting.

Usage

```
runMCMC(mcmc, genome, model, ncores = 1, divergence.iteration = 0)
```

Arguments

mcmc	MCMC object that will run the model fitting algorithm.
genome	Genome that the model fitting will run on. Should be the same genome associated with the parameter and model objects.
model	Model to run the fitting on. Should be associated with the given genome.
ncores	Number of cores to perform the model fitting with. Default value is 1.
divergence.iteration	Number of steps that the initial conditions can diverge from the original conditions given. Default value is 0.

Details

runMCMC will run for the number of samples times the number thinning given when the mcmc object is initialized. Updates are provided every 100 steps, and the state of the chain is saved every thinning steps.

Value

This function has no return value.

Examples

```
#fitting a model to a genome using the runMCMC function

genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)
sphi_init <- c(1,1)
numMixtures <- 2
geneAssignment <- c(rep(1,floor(length(genome)/2)),rep(2,ceiling(length(genome)/2)))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
                                       gene.assignment = geneAssignment,
                                       mixture.definition = "allUnique")
model <- initializeModelObject(parameter = parameter, model = "ROC")
samples <- 2500
thinning <- 50
adaptiveWidth <- 25
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning,
                             adaptive.width=adaptiveWidth, est.expression=TRUE,
                             est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)
divergence.iteration <- 10
## Not run:
runMCMC(mcmc = mcmc, genome = genome, model = model,
        ncores = 4, divergence.iteration = divergence.iteration)

## End(Not run)
```

setAdaptiveWidth *setAdaptiveWidth*

Description

Method of MCMC class (access via mcmc$<function name>, where mcmc is an object initialized by initializeMCMCObject). Set sample adaptiveWidth value, which is the number of samples (not iterations) between adapting parameter proposal widths

Arguments

_adaptiveWidth	postive value

setGroupList *setGroupList*

Description

Method of Parameter class (access via parameter$<function name>, where parameter is an object initialized by initializeParameterObject). Set amino acids (ROC, FONSE) or codons (PA, PANSE) for which parameters will be estimated. Note that non-default groupLists are still in beta testing and should be used with caution.

Arguments

List	of strings epresenting groups for parameters to be estimated. Should be one letter amino acid (ROC, FONSE) or list of sense codons (PA, PANSE).

setRestartFileSettings *setRestartFileSettings*

Description

Method of MCMC class (access via mcmc$<function name>, where mcmc is an object initialized by initializeMCMCObject). Set restart file output name and frequency prior to running MCMC

Arguments

filename	name of restart file
interval	number of samples (ie. iterations * thinning) between writing new restart file
multiple	if true, will output a new restart file at each interval (file name will include sample it was written at)

setRestartSettings *Set Restart Settings*

Description

setRestartSettings sets the needed information (what the file is called, how often the file should be written) to write information to restart the MCMC algorithm from a given point.

Usage

```
setRestartSettings(mcmc, filename, samples, write.multiple = TRUE)
```

Arguments

mcmc	MCMC object that will run the model fitting algorithm.
filename	Filename for the restart files to be written.
samples	Number of samples that should occur before a file is written.
write.multiple	Boolean that determines if multiple restart files are written. Default value is TRUE.

Details

setRestartSettings writes a restart file every set amount of samples that occur. Also, if write.multiple is true, instead of overwriting the previous restart file, the sample number is prepended onto the file name and multiple rerstart files are generated for a run.

Value

This function has no return value.

Examples

```
## set restart settings for checkpointing

samples <- 2500
thinning <- 50
adaptiveWidth <- 25

## estimate all parameter types
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning,
                             adaptive.width=adaptiveWidth, est.expression=TRUE,
                             est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)

# prompts the mcmc to write a restart file every 100 samples during the run.
setRestartSettings(mcmc = mcmc, filename = "test_restart", samples = 100)

# prompts the mcmc to write a restart file every 100 samples during the run,
# but will overwrite it each time.
```

```
setRestartSettings(mcmc = mcmc, filename = "test_restart", samples = 100,
                   write.multiple = FALSE)
```

`setSamples` *setSamples*

Description

Method of MCMC class (access via mcmc$<function name>, where mcmc is an object initialized by initializeMCMCObject). Set number of samples set for MCMCAlgorithm object

Arguments

`_samples`	postive value

`setStepsToAdapt` *setStepsToAdapt*

Description

Method of MCMC class (access via mcmc$<function name>, where mcmc is an object initialized by initializeMCMCObject). Set number of iterations (total iterations = samples * thinning) to allow proposal widths to adapt

Arguments

`steps`	a postive value

`setThinning` *setThinning*

Description

Set thinning value, which is the number of iterations (total iterations = samples * thinning) not being kept

Arguments

`_thinning`	postive value

`simulateGenome` *simulateGenome*

Description

Method of Model class (access via model$<function name>, where model is an object initialized by initializeModelObject). Will simulate a version of the given genome using the current set of parameters stored in the Parameter object. This can be written to a FASTA file using genome$writeFasta(<filename>,simulated = TRUE).

Arguments

`genome`	a Genome object initialized by initializeGenomeObject

`summary.Rcpp_Genome` *Summary of Genome*

Description

`summary` summarizes the description of a genome, such as number of genes and average gene length.

Usage

```
## S3 method for class 'Rcpp_Genome'
summary(object, ...)
```

Arguments

`object`	A genome object initialized with `initializeGenomeObject`.
`...`	Optional, additional arguments to be passed to the main summary function that affect the summary produced.

Value

This function returns by default an object of class c("summaryDefault", table").

writeMCMCObject *Write MCMC Object*

Description

writeMCMCObject stores the MCMC information from the model fitting run in a file.

Usage

```
writeMCMCObject(mcmc, file)
```

Arguments

mcmc	MCMC object that has run the model fitting algorithm.
file	A filename where the data will be stored.

Value

This function has no return value.

Examples

```
## saving the MCMC object after model fitting
genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)
sphi_init <- c(1,1)
numMixtures <- 2
geneAssignment <- c(rep(1,floor(length(genome)/2)),rep(2,ceiling(length(genome)/2)))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
                                       gene.assignment = geneAssignment,
                                       mixture.definition = "allUnique")
samples <- 2500
thinning <- 50
adaptiveWidth <- 25
mcmc <- initializeMCMCObject(samples = samples, thinning = thinning,
                             adaptive.width=adaptiveWidth, est.expression=TRUE,
                             est.csp=TRUE, est.hyper=TRUE, est.mix = TRUE)
divergence.iteration <- 10
## Not run:
runMCMC(mcmc = mcmc, genome = genome, model = model,
        ncores = 4, divergence.iteration = divergence.iteration)
writeMCMCObject(mcmc = mcmc, file = file.path(tempdir(), "file.Rda"))


## End(Not run)
```

writeParameterObject *Write Parameter Object to a File*

Description

writeParameterObject will write the parameter object as binary to the filesystem

Usage

```
writeParameterObject(parameter, file)
```

Arguments

parameter	parameter on object created by initializeParameterObject.
file	A filename that where the data will be stored.

Details

As Rcpp object are not serializable with the default R save function, therefore this custom save function is provided (see loadParameterObject).

Value

This function has no return value.

Examples

```
## Not run:

genome_file <- system.file("extdata", "genome.fasta", package = "AnaCoDa")

genome <- initializeGenomeObject(file = genome_file)
sphi_init <- c(1,1)
numMixtures <- 2
geneAssignment <- c(rep(1,floor(length(genome)/2)),rep(2,ceiling(length(genome)/2)))
parameter <- initializeParameterObject(genome = genome, sphi = sphi_init,
                                       num.mixtures = numMixtures,
                                       gene.assignment = geneAssignment,
                                       mixture.definition = "allUnique")

## writing an empty parameter object as the runMCMC routine was not called yet
writeParameterObject(parameter = parameter, file = file.path(tempdir(), "file.Rda"))


## End(Not run)
```

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