Package 'SynSigRun'

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```
Type Package
Title Run Mutational Signature Analysis Software Packages Using Mutational Spectra gener-
     ated by SynSigGen
Version 0.1.1
Author Steven G. Rozen, Yang Wu
Maintainer Steven G. Rozen <steverozen@gmail.com>
Description Create catalogs of synthetic mutational spectra and assess the
     performance of mutational signature analysis programs on these.
License GPL-3
Language en-US
Encoding UTF-8
LazyData true
biocViews
Imports data.table,
     devtools,
     dplyr,
     ICAMS,
     lsa,
     magrittr,
     rlang,
     stats,
     SynSigGen,
     tibble,
Remotes github::steverozen/SynSigGen
Depends R (>= 3.5)
RoxygenNote 7.1.1
Suggests BiocManager,
     decompTumor2Sig,
     deconstructSigs,
     DelayedArray,
     hdp,
     knitr,
     maftools,
```

mSigAct,

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```
{\tt CopyBestSignatureAnalyzerResult}
```

Find the SignatureAnalyzer results directory with the best results and make a copy of it as sa.results.dir/best.run/

Description

Find the SignatureAnalyzer results directory with the best results and make a copy of it as sa.results.dir/best.run/

Usage

```
CopyBestSignatureAnalyzerResult(
  sa.results.dir,
  verbose = FALSE,
  overwrite = FALSE
)
```

Arguments

```
sa.results.dir See BestSignatureAnalyzerResult verbose See BestSignatureAnalyzerResult overwrite If TRUE overwrite existing "best.run"
```

Value

The path of the best directory that was copied as a string, with the list directories examined as the attribute run.directories.

Diff4SynDataSets

diff new directory / files against regression data for testing.

Description

diff new directory / files against regression data for testing.

Usage

```
Diff4SynDataSets(dirname, unlink)
```

Arguments

dirname the root name of the directories to diff.

unlink if TRUE unlink tmpdirname, but do not unlink if there are diffs.

Value

The output of the diff command.

4 InstalldeconstructSigs

FixSASigNames

Standardize SignatureAnalyzer signature names

Description

For example, change BI_COMPOSITE_SNV_SBS83_P to BI_COMPOSITE_SBS83_P

Usage

FixSASigNames(sig.names)

Arguments

sig.names

Vector of signature names

Details

This is necessary because for COMPOSITE signatures we rbind coordinated "SNV", "DNP", and "INDEL" signatures.

Value

Vector of signatures names with "_SNV" removed.

InstalldecompTumor2Sig

Install decompTumor2Sig from Bioconductor

Description

Install decompTumor2Sig from Bioconductor

Usage

InstalldecompTumor2Sig()

InstalldeconstructSigs

Install deconstructSigs from CRAN

Description

Install deconstructSigs from CRAN

Usage

InstalldeconstructSigs()

InstallmutSignatures 5

Description

Install mutSignatures from github

Usage

```
InstallmutSignatures()
```

MapSPToSASignatureNamesInExposure

With the signatures represented in a matrix of exposures, find the nearest SignatureAnalyzer exposure.

Description

With the signatures represented in a matrix of exposures, find the nearest SignatureAnalyzer exposure.

Usage

```
MapSPToSASignatureNamesInExposure(
   sp.exposures,
   sa.sig.names.to.consider = colnames(sa.96.sigs)
)
```

Arguments

```
sp.exposures The exposures
sa.sig.names.to.consider
A subset of the colnames of sa.96.sigs
```

Details

IMPORTANT: uses the package global variables sa.96.sigs and sp.sigs.

Value

A list with

- 1. exp2 Copy of sp.exposures with the rownames(signature names) updated according to the match.
- 2. sp.to.sa.sig.match
- 3. sa.to.sp.sig.match Best matches in the opposite direction

6 MutationalSignatures

Mutational Signatures Reference mutational signature profiles from PCAWG7.

Description

Reference mutational signature profiles from PCAWG7.

Usage

```
sa.96.sigs
sa.COMPOSITE.sigs
sa.DBS.sigs
sa.ID.sigs
sp.sigs
```

Format

Numerical matrix with rows indicating mutation types and columns indicating signatures.

An object of class matrix (inherits from array) with 96 rows and 60 columns.

An object of class matrix (inherits from array) with 1697 rows and 60 columns.

An object of class matrix (inherits from array) with 78 rows and 15 columns.

An object of class matrix (inherits from array) with 83 rows and 29 columns.

An object of class matrix (inherits from array) with 96 rows and 65 columns.

Details

sa.96.sigs provides SignatureAnalyzer mutational signature profiles collapsed from COMPOS-ITE to 96-channel SNS signatures.

```
sa.COMPOSITE.sigs provides COMPOSITE mutational signature profiles extracted by Signature-Analyzer. sa.COMPOSITE.sigs are an rbind of the contents of https://www.synapse.org/#! Synapse:syn11738311 (SBS 1536), https://www.synapse.org/#!Synapse:syn11738308 (DBS), and https://www.synapse.org/#!Synapse:syn11738309 (ID).
```

sa.DBS.sigs provides the DBS signatures extracted by SignatureAnalyzer, from https://www.synapse.org/#!Synapse:syn11738312. These are not the DBS signatures that are part of sa.COMPOSITE.sigs; these were extracted from the ID catalogs alone.

sa. ID. sigs provides the ID signatures extracted by SignatureAnalyzer, from https://www.synapse.org/#!Synapse:syn11738313.These are not the ID signatures that are part of sa.COMPOSITE.sigs; these were extracted from the ID catalogs alone.

sp. sigs provides signatures extracted by SigProfiler.

RealExposures 7

Source

```
https://www.synapse.org/#!Synapse:syn11738310
https://www.synapse.org/#!Synapse:syn11738311
https://www.synapse.org/#!Synapse:syn11738308
https://www.synapse.org/#!Synapse:syn11738309
https://www.synapse.org/#!Synapse:syn11738312
https://www.synapse.org/#!Synapse:syn11738313
https://www.synapse.org/#!Synapse:syn11738319
```

RealExposures

Real exposure (signature attributions) from SignatureAnalyzer and SigProfiler

Description

Real exposure (signature attributions) from SignatureAnalyzer and SigProfiler

Usage

```
sa.all.real.exposures
sp.all.real.exposures
sa.no.hyper.real.exposures
sp.no.hyper.real.exposures
```

Format

Numerical matrix with rows indicating signatures and columns indicating (tumor) samples.

An object of class matrix (inherits from array) with 60 rows and 2780 columns.

An object of class matrix (inherits from array) with 65 rows and 2780 columns.

An object of class matrix (inherits from array) with 35 rows and 2624 columns.

An object of class matrix (inherits from array) with 65 rows and 2624 columns.

Note

Prefix sa indicates SignatureAnalyzers, sp indicates SigProfiler; all indicates all samples, no. hyper means that hypermutated tumors as defined for SignatureAnalyzer have been removed.

Source

```
https://dx.doi.org/10.7303/syn11761237.4
https://dx.doi.org/10.7303/syn11738669.5
https://dx.doi.org/10.7303/syn11761198.4
https://dx.doi.org/10.7303/syn11761237.4
```

 ${\bf RundecompTumor2SigAttributeOnly}$

Run decompTumor2Sig attribution on a spectra catalog file and known signatures.

Description

Run decompTumor2Sig attribution on a spectra catalog file and known signatures.

Usage

```
RundecompTumor2SigAttributeOnly(
  input.catalog,
  gt.sigs.file,
  out.dir,
  seedNumber = 1,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog	File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.
gt.sigs.file	File containing input mutational signatures. Columns are signatures, rows are mutation types.
out.dir	Directory that will be created for the output; abort if it already exits. Log files will be in paste0(out.dir,"/tmp").
seedNumber	Specify the pseudo-random seed number used to run deconstructSigs. Setting seed can make the attribution of deconstructSigs repeatable. Default: 1.
test.only	If TRUE, only analyze the first 10 columns read in from input.catalog. Default: \ensuremath{FALSE}
overwrite	If TRUE, overwrite existing output. Default: FALSE

Details

Creates several files in paste@(out.dir, "/sa.output.rdata"). These are TODO(Steve): list the files

Value

The inferred exposure of deconstructSigs, invisibly.

 ${\tt RundeconstructSigsAttributeOnly}$

Run deconstructSigs attribution on a spectra catalog file and known signatures.

Description

Run deconstructSigs attribution on a spectra catalog file and known signatures.

Usage

```
RundeconstructSigsAttributeOnly(
  input.catalog,
  gt.sigs.file,
  out.dir,
  seedNumber = 1,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog	File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.
gt.sigs.file	File containing input mutational signatures. Columns are signatures, rows are mutation types.
out.dir	Directory that will be created for the output; abort if it already exits. Log files will be in paste0(out.dir,"/tmp").
seedNumber	Specify the pseudo-random seed number used to run deconstructSigs. Setting seed can make the attribution of deconstructSigs repeatable. Default: 1.
test.only	If TRUE, only analyze the first 10 columns read in from input.catalog. Default: FALSE $$
overwrite	If TRUE, overwrite existing output. Default: FALSE

Details

Creates several files in paste@(out.dir, "/sa.output.rdata"). These are TODO(Steve): list the files

Value

The inferred exposure of deconstructSigs, invisibly.

10 RunhdpLessHier

RunhdpLessHier

Run hdp extraction and attribution on a spectra catalog file

Description

Run hdp extraction and attribution on a spectra catalog file

Usage

```
RunhdpLessHier(
  input.catalog,
  out.dir,
  CPU.cores = 1,
  seedNumber = 1,
  K.guess,
  multi.types = FALSE,
  remove.noise = FALSE,
  num.posterior = 4,
  post.burnin = 4000,
  post.n = 50,
  post.space = 50,
  post.cpiter = 3,
  test.only = FALSE,
  overwrite = FALSE,
  verbose = TRUE
```

Arguments

input.catalog	File containing a spectra catalog in ICAMS format.
out.dir	Directory that will be created for the output; abort if it already exits. Log files will be in paste0(out.dir,"/tmp").
CPU.cores	Number of CPUs to use in running hdp_posterior.
seedNumber	Specify the pseudo-random seed number used to run hdp. Setting seed can make the attribution of hdp repeatable. Default: 1.
K.guess	Suggested initial value of the number of signatures, passed to dp_activate as initcc.
multi.types	A logical scalar or a character vector. If FALSE, hdp will regard all input spectra as one tumor type, and will allocate them to one single dirichlet process node. If TRUE, hdp will infer tumor types based on the string before "::" in their names. e.g. Tumor type for "SA.Syn.Ovary-AdenoCA::S.500" would be "SA.Syn.Ovary-AdenoCA"
	If it is a character vector, it should be a vector of case-sensitive tumor types. e.g. c("SA.Syn.Ovary-AdenoCA", "SA.Syn.Ovary-AdenoCA", "SA.Syn.Kidney-RCC").
remove.noise	Whether to remove noise signature "hdp.0"? In normal cases scenarios, only few mutations will be assigned to noise signature. For result visualization and assessment of hdp package, select TRUE; for diag-
	To result visualization and assessment of http package, select true, for diag-

nostic purposes, select FALSE.

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num.posterior Number of posterior sampling chains; can set to 1 for testing. Pass to hdp_posterior burnin. post.burnin post.n Pass to hdp_posterior n. post.space Pass to hdp_posterior space. post.cpiter Pass to hdp_posterior cpiter. If TRUE, only analyze the first 10 columns in input.catalog. test.only overwrite If TRUE, overwrite existing output. verbose If TRUE then message progress information.

Details

Creates several files in out.dir. These are: TODO(Steve): list the files TODO(Wuyang)

Value

The inferred exposure of hdp, invisibly.

Runmaftools Run m

Run maftools extraction ONLY on a spectra catalog file

Description

WARNING: maftools can only do signature extraction!

Usage

```
Runmaftools(
  input.catalog,
  out.dir,
  CPU.cores = NULL,
  K.exact = NULL,
  K.range = NULL,
  nrun.est.K = 10,
  pConstant = NULL,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog File containing input spectra catalog. Columns are samples (tumors), rows are
mutation types.

out.dir Directory that will be created for the output; abort if it already exits. Log files
will be in paste@(out.dir,"/tmp").

CPU.cores Number of CPUs to use in running maftools. For a server, 30 cores would
be a good choice; while for a PC, you may only choose 2-4 cores. By default
(CPU.cores = NULL), the CPU.cores would be equal to (parallel::detectCores())/2,
total number of CPUs divided by 2.

K.exact, K.range

K.exact is the exact value for the number of signatures active in spectra (K). Specify K.exact if you know exactly how many signatures are active in the input.catalog, which is the ICAMS-formatted spectra file.

K.range is A numeric vector (K.min, K.max) of length 2 which tell maftools to search the best signature number active in spectra, K, in this range of Ks. Specify K.range if you don't know how many signatures are active in the input.catalog.

WARNING: You must specify only one of K. exact or K. range!

Default: NULL

nrun.est.K Number of NMF runs for each possible number of signature. This is used in the

step to estimate the most plausible number of signatures in input spectra catalog.

NOTE: Unlike other NMF-based packages, parameter nrun.extract is hard-

coded as 1.

pConstant A small positive value (a.k.a. pseudocount) to add to every entry in the input.catalog.

Specify a value ONLY if an "non-conformable arrays error" is raised.

test.only If TRUE, only analyze the first 10 columns read in from input.catalog.

overwrite If TRUE, overwrite existing output.

Details

```
Creates several files in out.dir. These are: TODO(Steve): list the files TODO(Wuyang)
```

Value

The extracted signatures of maftools, invisibly.

RunmSigActAttributeOnly

Run mSigAct attribution on a spectra catalog file and known signatures.

Description

Run mSigAct attribution on a spectra catalog file and known signatures.

```
RunmSigActAttributeOnly(
  input.catalog,
  gt.sigs.file,
  out.dir,
  CPU.cores = NULL,
  seedNumber = 1,
  test.only = FALSE,
  overwrite = FALSE
)
```

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Arguments

input.catalog	File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.
gt.sigs.file	File containing input mutational signatures. Columns are signatures, rows are mutation types.
out.dir	Directory that will be created for the output; abort if it already exits. Log files will be in paste0(out.dir,"/tmp").
CPU.cores	Number of CPUs to use in running sigfit. For a server, 30 cores would be a good choice; while for a PC, you may only choose 2-4 cores. By default (CPU.cores = NULL), the CPU.cores would be equal to (parallel::detectCores())/2, total number of CPUs divided by 2.
seedNumber	Specify the pseudo-random seed number used to run mSigAct. Setting seed can make the attribution of mSigAct repeatable. Default: 1.
test.only	If TRUE, only analyze the first 10 columns read in from input.catalog. Default: FALSE $$
overwrite	If TRUE, overwrite existing output. Default: FALSE

Details

Creates several files in paste@(out.dir, "/sa.output.rdata"). These are TODO(Steve): list the files

Value

The inferred exposure of mSigAct, invisibly.

RunMutationalPatterns $\ Run\ MutationalPatterns\ extraction\ and\ attribution\ on\ a\ spectra\ catalog\ file$

Description

WARNING: MutationalPatterns can only do exposure attribution using SBS96 spectra catalog and signature catalog!

```
RunMutationalPatterns(
  input.catalog,
  out.dir,
  CPU.cores = NULL,
  K.exact = NULL,
  K.range = NULL,
  nrun.est.K = 10,
  nrun.extract = 200,
  test.only = FALSE,
  overwrite = FALSE
)
```

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Arguments

input.catalog File containing input spectra catalog. Columns are samples (tumors), rows are

mutation types.

out.dir Directory that will be created for the output; abort if it already exits. Log files

will be in paste0(out.dir,"/tmp").

CPU. cores Number of CPUs to use in running MutationalPatterns. For a server, 30 cores

would be a good choice; while for a PC, you may only choose 2-4 cores. By de-

 $fault \, (CPU.cores = NULL), the \, CPU.cores \, would \, be \, equal \, to \, (parallel::detectCores())/2, \\$

total number of CPUs divided by 2.

K.exact, K.range

K.exact is the exact value for the number of signatures active in spectra (K). Specify K.exact if you know exactly how many signatures are active in the

input.catalog, which is the ICAMS-formatted spectra file.

K.range is A numeric vector (K.min, K.max) of length 2 which tell MutationalPatterns to search the best signature number active in spectra, K, in this range of Ks. Specify K.range if you don't know how many signatures are active in

the input.catalog.

WARNING: You must specify only one of K. exact or K. range!

Default: NULL

nrun.est.K Number of NMF runs for each possible number of signature. This is used in the

step to estimate the most plausible number of signatures in input spectra catalog.

nrun.extract number of NMF runs for extracting signatures and inferring exposures.

test.only If TRUE, only analyze the first 10 columns read in from input.catalog. De-

fault: FALSE

overwrite If TRUE, overwrite existing output. Default: FALSE

Details

Creates several files in out.dir. These are: TODO(Steve): list the files

TODO(Wuyang)

NOTE: The seed is hard-coded in Mutational Patterns as 123456.

pConstant is harded-coded as 1e-04.

Value

A list contains:

- \$signature extracted signatures,
- \$exposure inferred exposures,

of MutationalPatterns, invisibly.

 ${\tt RunMutationalPatternsAttributeOnly}$

Run MutationalPatterns attribution on a spectra catalog file and known signatures.

Description

Run MutationalPatterns attribution on a spectra catalog file and known signatures.

Usage

```
RunMutationalPatternsAttributeOnly(
  input.catalog,
  gt.sigs.file,
  out.dir,
  seedNumber = 1,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog	File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.
gt.sigs.file	File containing input mutational signatures. Columns are signatures, rows are mutation types.
out.dir	Directory that will be created for the output; abort if it already exits. Log files will be in paste0(out.dir,"/tmp").
seedNumber	Specify the pseudo-random seed number used to run MutationalPatterns. Setting seed can make the attribution of MutationalPatterns repeatable. Default: 1.
test.only	If TRUE, only analyze the first 10 columns read in from input.catalog. Default: \ensuremath{FALSE}
overwrite	If TRUE, overwrite existing output. Default: FALSE

Details

Creates several files in paste@(out.dir, "/sa.output.rdata"). These are TODO(Steve): list the files

Value

The inferred exposure of MutationalPatterns, invisibly.

16 RunmutSignatures

RunmutSignatures

Run mutSignatures extraction and attribution on a spectra catalog file

Description

Run mutSignatures extraction and attribution on a spectra catalog file

Usage

```
RunmutSignatures(
  input.catalog,
  out.dir,
  algorithm = "brunet",
  CPU.cores = NULL,
  iterations = 1000,
  seedNumber = 1,
  K.exact = NULL,
  K.range = NULL,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog File containing input spectra catalog. Columns are samples (tumors), rows are

mutation types.

out.dir Directory that will be created for the output; abort if it already exits. Log files

will be in paste0(out.dir,"/tmp").

algorithm NMF implementation used to to extract signatures and attribute exposures. Only

"alexa", "brunet" or "lin" is valid.

"alexa" or "brunet": Jean-Philippe Brunet's implementation. This is the most

widely used NMF implementation for signature extraction. DOI: 10.1073/pnas.0308531101

"lin": Chih-Jen Lin's implementation. DOI:10.1109/TNN.2007.895831

Default: "alexa".

CPU. cores Number of CPUs to use in running sigfit. For a server, 30 cores would be a good

choice; while for a PC, you may only choose 2-4 cores. By default (CPU.cores = NULL), the CPU.cores would be equal to (parallel::detectCores())/2,

total number of CPUs divided by 2.

iterations Number of iterations in signature extraction. Default: 1000.

seedNumber Specify the pseudo-random seed number used to run sigfit. Setting seed can

make the attribution of sigfit repeatable. Default: 1.

K.exact, K.range

K. exact is the exact value for the number of signatures active in spectra (K). Specify K. exact if you know exactly how many signatures are active in the

input.catalog, which is the ICAMS-formatted spectra file.

K.range is A numeric vector (K.min, K.max) of length 2 which tell sigfit to search the best signature number active in spectra, K, in this range of Ks. Specify K.range if you don't know how many signatures are active in the input.catalog.

K.max - K.min >= 3, otherwise an error will be thrown.

WARNING: You must specify only one of K. exact or K. range!

Default: NULL

test.only If TRUE, only analyze the first 10 columns read in from input.catalog. De-

fault: FALSE

overwrite If TRUE, overwrite existing output. Default: FALSE

Details

```
Creates several files in out.dir. These are: TODO(Steve): list the files TODO(Wuyang)
```

Value

The inferred exposure of mutSignatures, invisibly.

RunmutSignaturesAttributeOnly

Run mutSignatures attribution on a spectra catalog file and known signatures.

Description

Run mutSignatures attribution on a spectra catalog file and known signatures.

Usage

```
RunmutSignaturesAttributeOnly(
  input.catalog,
  gt.sigs.file,
  out.dir,
  seedNumber = 1,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog	File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.
gt.sigs.file	File containing input mutational signatures. Columns are signatures, rows are mutation types.
out.dir	Directory that will be created for the output; abort if it already exits. Log files will be in paste0(out.dir,"/tmp").
seedNumber	Specify the pseudo-random seed number used to run mutSignatures. Setting seed can make the attribution of mutSignatures repeatable. Default: 1.
test.only	If TRUE, only analyze the first 10 columns read in from input.catalog. Default: \ensuremath{FALSE}
overwrite	If TRUE, overwrite existing output. Default: FALSE

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Details

Creates several files in paste@(out.dir, "/sa.output.rdata"). These are TODO(Steve): list the files

Value

The inferred exposure of mutSignatures, invisibly.

RunmutSpec

Run mutSpec extraction and attribution on a spectra catalog file

Description

NOTE: mutSpec can only do exposure attribution using SBS96 spectra catalog and signature catalog!

Usage

```
RunmutSpec(
  input.catalog,
  out.dir,
  CPU.cores = NULL,
  seedNumber = 1,
  K.exact = NULL,
  K.range = NULL,
  nrun.est.K = 50,
  nrun.extract = 200,
  pConstant = NULL,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.

out.dir Directory that will be created for the output; abort if it already exits. Log files

will be in paste0(out.dir,"/tmp").

CPU. cores Number of CPUs to use in running mutSpec. For a server, 30 cores would

be a good choice; while for a PC, you may only choose 2-4 cores. By default (CPU.cores = NULL), the CPU.cores would be equal to (parallel::detectCores())/2,

total number of CPUs divided by 2.

seedNumber Specify the pseudo-random seed number used to run mutSpec. Setting seed can

make the attribution of mutSpec repeatable. Default: 1.

K.exact, K.range

K.exact is the exact value for the number of signatures active in spectra (K). Specify K.exact if you know exactly how many signatures are active in the input.catalog, which is the ICAMS-formatted spectra file.

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K.range is A numeric vector (K.min, K.max) of length 2 which tell mutSpec to search the best signature number active in spectra, K, in this range of Ks. Specify K.range if you don't know how many signatures are active in the input.catalog. WARNING: You must specify only one of K.exact or K.range!

Default: NULL

Number of NMF runs for each possible number of signature. This is used in the step to estimate the most plausible number of signatures in input spectra catalog. number of NMF runs for extracting signatures and inferring exposures.

A small positive value (a.k.a. pseudocount) to add to every entry in the input.catalog. Specify a value ONLY if an "non-conformable arrays error" is raised.

If TRUE, only analyze the first 10 columns read in from input.catalog. De-

fault: FALSE

overwrite If TRUE, overwrite existing output. Default: FALSE

Details

nrun.est.K

nrun.extract

pConstant

test.only

Creates several files in out.dir. These are:

- extracted.signatures.csv
- inferred.exposures.csv
- sessionInfo

Value

The inferred exposure of mutSpec, invisibly.

Runsigfit

Run sigfit extraction and attribution on a spectra catalog file

Description

WARNING: sigfit can only do exposure attribution using SBS96 spectra catalog and signature catalog!

```
Runsigfit(
  input.catalog,
  out.dir,
  model = "nmf",
  CPU.cores = NULL,
  seedNumber = 1,
  K.exact = NULL,
  K.range = NULL,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog File containing input spectra catalog. Columns are samples (tumors), rows are

mutation types.

out.dir Directory that will be created for the output; abort if it already exits. Log files

will be in paste0(out.dir,"/tmp").

model Algorithm to be used to extract signatures and attribute exposures. Only "nmf"

or "emu" is valid. Default: "nmf".

CPU. cores Number of CPUs to use in running sigfit. For a server, 30 cores would be a good

choice; while for a PC, you may only choose 2-4 cores. By default (CPU.cores = NULL), the CPU.cores would be equal to (parallel::detectCores())/2,

total number of CPUs divided by 2.

seedNumber Specify the pseudo-random seed number used to run sigfit. Setting seed can

make the attribution of sigfit repeatable. Default: 1.

K.exact, K.range

K. exact is the exact value for the number of signatures active in spectra (K). Specify K. exact if you know exactly how many signatures are active in the

 $input.\, catalog,\, which\, is\, the\, ICAMS-formatted\, spectra\, file.$

K.range is A numeric vector (K.min, K.max) of length 2 which tell sigfit to search the best signature number active in spectra, K, in this range of Ks. Specify K.range if you don't know how many signatures are active in the input.catalog.

K.max - K.min ≥ 3 , otherwise an error will be thrown.

WARNING: You must specify only one of K. exact or K. range!

Default: NULL

test.only If TRUE, only analyze the first 10 columns read in from input.catalog. De-

fault: FALSE

overwrite If TRUE, overwrite existing output. Default: FALSE

Details

Creates several files in out.dir. These are: TODO(Steve): list the files

TODO(Wuyang)

Value

The inferred exposure of sigfit, invisibly.

RunsigfitAttributeOnly

Run sigfit attribution on a spectra catalog file and known signatures.

Description

Run sigfit attribution on a spectra catalog file and known signatures.

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Usage

```
RunsigfitAttributeOnly(
  input.catalog,
  gt.sigs.file,
  out.dir,
  model = "nmf",
  seedNumber = 1,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog	File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.
gt.sigs.file	File containing input mutational signatures. Columns are signatures, rows are mutation types.
out.dir	Directory that will be created for the output; abort if it already exits. Log files will be in paste0(out.dir,"/tmp").
model	Algorithm to be used to extract signatures and attribute exposures. Only "nmf" or "emu" is valid. Default: "nmf".
seedNumber	Specify the pseudo-random seed number used to run sigfit. Setting seed can make the attribution of sigfit repeatable. Default: 1.
test.only	If TRUE, only analyze the first 10 columns read in from input.catalog. Default: FALSE $$
overwrite	If TRUE, overwrite existing output. Default: FALSE

Details

Creates several files in paste@(out.dir,"/sa.output.rdata"). These are TODO(Steve): list the files

Value

The inferred exposure of sigfit, invisibly.

Runsigminer	Run sigminer extraction and attribution on a spectra catalog file

Description

Run sigminer extraction and attribution on a spectra catalog file

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Usage

```
Runsigminer(
  input.catalog,
  out.dir,
  CPU.cores = NULL,
  seedNumber = 1,
  K.max = NULL,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog File containing input spectra catalog. Columns are samples (tumors), rows are mutation types. out.dir Directory that will be created for the output; abort if it already exits. Log files will be in paste0(out.dir,"/tmp"). CPU.cores Number of CPUs to use in running sigminer. For a server, 30 cores would be a good choice; while for a PC, you may only choose 2-4 cores. By default (CPU.cores = NULL), the CPU.cores would be equal to (parallel::detectCores())/2, total number of CPUs divided by 2. seedNumber Specify the pseudo-random seed number used to run SomaticSignatures. Setting seed can make the attribution of SomaticSignatures repeatable. Default: 1. K.max K.max is the maximum number of signatures users expect to active in input.catalog. As this approach cannot specify K. exact, you can specify K. max = K. exact If you know exactly how many signatures are active in the input.catalog. On the other hand, you may specify max(K.range) if you don't know how many signatures are active in the input.catalog. test.only If TRUE, only analyze the first 10 columns read in from input.catalog. Default: FALSE If TRUE, overwrite existing output. Default: FALSE overwrite

Details

```
Creates several files in out.dir. These are: TODO(Steve): list the files TODO(Wuyang)
```

Value

A list contains:

- \$signature extracted signatures,
- \$exposure inferred exposures,

of sigminer, invisibly.

RunSignatureAnalyzerAttribution

Run SignatureAnalyzer attribution on a catalog file and output by RunSignatureAnalyzerOnFile().

Description

Normally, please call SignatureAnalyzerOneRun instead of this function.

Usage

```
RunSignatureAnalyzerAttribution(
  input.catalog,
  read.catalog.function,
  extracted.signature.file,
  raw.exposures.file,
  write.signature.function,
  out.dir,
  test.only = FALSE,
  input.exposures = NULL,
  delete.tmp.files = TRUE,
  overwrite = FALSE,
  verbose = FALSE
)
```

Arguments

input.catalog File containing input catalog. Columns are samples (tumors), rows are signatures. SignatureAnalyzer does not care about the row names (I think) TODO(Steve): check this.

 ${\tt read.catalog.function}$

Function taking a file path as its only argument and returning a catalog as a numeric matrix.

extracted.signature.file

A .csv file containing extracted signatures. Normally, this file is named "sa.output.sigs.csv" and is generated by function RunSignatureAnalyzerOnFile(). It expects to have the same format as the input.catalog, thus it will be read by read.catalog.function too.

raw.exposures.file

A .csv file containing raw attributions of exposures. Normally, this file is named "sa.output.raw.exp.csv" and is generated by function RunSignatureAnalyzerOnFile().

write.signature.function

Function with first argument the signatures generated by SignatureAnalyzer and second argument the file to write to.

out.dir Directory that will be created for the output; abort if it already exits. Log files will be in paste0(out.dir,"/tmp").

test.only If TRUE, only analyze the first 10 columns read in from input.catalog.

input.exposures

A file with the synthetic exposures used to generate input.catalog; if provided here, this is copied over to the output directory for downstream analysis.

```
delete.tmp.files
```

If TRUE delete the many temporary files generated by SignatureAnalyzer.

overwrite If TRUE, overwrite existing output.

verbose If TRUE cat a message regarding progress.

Details

Save the final attribution of a catalog matrix into a file named "sa.output.fine.exp.csv" under the folder out.dir.

Value

The final attribution matrix. (i.e. exp. fine. tuned)

RunSignatureAnalyzerOnFile

Run SignatureAnalyzer on a file containing a catalog AFTER the SignatureAnalyzer code has been source'ed.

Description

Normally, please call SignatureAnalyzerOneRun instead of this function.

Usage

```
RunSignatureAnalyzerOnFile(
  input.catalog,
  out.dir,
  input.exposures = NULL,
  maxK = 30,
  tol = 1e-07,
  test.only = FALSE,
  delete.tmp.files = TRUE,
  overwrite = FALSE
)
```

Arguments

input.catalog File containing input catalog. Columns are samples (tumors), rows are signa-

tures. SignatureAnalyzer does not care about the row names (I think) TODO(Steve):

check this.

out.dir Directory that will be created for the output; abort if it already exits. Log files

will be in paste0(out.dir,"/tmp").

input.exposures

A file with the synthetic exposures used to generate input.catalog; if provided

here, this is copied over to the output directory for downstream analysis.

maxK The maximum number of signatures to consider extracting.

tol Controls when SignatureAnalyzer will terminate its search; tol was 1.e-05 for

the PCAWG7 analysis.

test.only If TRUE, only analyze the first 10 columns read in from input.catalog.

```
delete.tmp.files

If TRUE delete the many temporary files generated by SignatureAnalyzer.

overwrite If TRUE, overwrite existing output
```

Details

Creates several files in out.dir:

- 1. sa.output.sigs.csv Normalized signatures (no all-0 signatures, column sums all 0)
- 2. sa.output.raw.exp.csv Raw exposures (attributions)
- 3. sa.output.exp.csv Same as sa.output.raw.exp.csv
- 4. sa.output.other.data.csv, contains a summary of important information, including the number of signatures extracted.
- 5. input.syn.exp.csv Optional, a copy of input.exposures, if it was provided.

Value

A list with the following elements:

- 1. signatures. W The raw signature matrix, *including* columns of all zeros.
- 2. exposures.H The raw exposure matrix, *excluding* rows of all zeros. The matrix product of the non-zero columns of signatures.w and exposures.H approximates the input spectrum matrix.
- 3. likelihood The likelihood as returned by SignatureAnalyzer.
- 4. evidence -1 * the posterior probability as returned by SignatureAnalyzer.
- 5. relevance One for each column of the signatures. W, as returned by SignatureAnalyzer.
- 6. error A measure of reconstruction error (?) as returned by SignatureAnalyzer
- 7. normalized.sigs The non-O columns of signatures.W normalized so that each column sum is 1.

RunSignatureEstimationQPAttributeOnly

Run SignatureEstimation Quadratic Programming (QP) attribution on a spectra catalog file and known signatures.

Description

Run SignatureEstimation Quadratic Programming (QP) attribution on a spectra catalog file and known signatures.

```
RunSignatureEstimationQPAttributeOnly(
  input.catalog,
  gt.sigs.file,
  out.dir,
  seedNumber = 1,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog	File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.
gt.sigs.file	$\label{eq:containing} \mbox{File containing input mutational signatures. Columns are signatures, rows are mutation types.}$
out.dir	Directory that will be created for the output; abort if it already exits. Log files will be in $paste0(out.dir,"/tmp")$.
seedNumber	Specify the pseudo-random seed number used to run SignatureEstimation. Setting seed can make the attribution of SignatureEstimation repeatable. Default: 1.
test.only	If TRUE, only analyze the first 10 columns read in from input.catalog. Default: \ensuremath{FALSE}
overwrite	If TRUE, overwrite existing output. Default: FALSE

Value

Invisibly returns a list which contains:

- \$exposuresCounts: the exposure counts inferred in ICAMSxtra format,
- \$exposureErrors: the MSE in ICAMSxtra format,
- \$SEoutput: A list which contains:
 - \$exposures: exposure proportion in SignatureEstimation format, and errors invisibly.
 - \$errors: mean squared error (MSE) between normalized reconstructed spectra and normalized ground-truth mutational spectra.

RunSignatureEstimationSAAttributeOnly

Run SignatureEstimation Simulated Annealing (SA) attribution on a spectra catalog file and known signatures.

Description

Run SignatureEstimation Simulated Annealing (SA) attribution on a spectra catalog file and known signatures.

```
RunSignatureEstimationSAAttributeOnly(
  input.catalog,
  gt.sigs.file,
  out.dir,
  seedNumber = 1,
  test.only = FALSE,
  overwrite = FALSE
)
```

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Arguments

input.catalog	File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.
gt.sigs.file	$\label{eq:containing} \mbox{File containing input mutational signatures. Columns are signatures, rows are mutation types.}$
out.dir	Directory that will be created for the output; abort if it already exits. Log files will be in $paste0(out.dir,"/tmp")$.
seedNumber	Specify the pseudo-random seed number used to run SignatureEstimation. Setting seed can make the attribution of SignatureEstimation repeatable. Default: 1.
test.only	If TRUE, only analyze the first 10 columns read in from input.catalog. Default: \ensuremath{FALSE}
overwrite	If TRUE, overwrite existing output. Default: FALSE

Value

Invisibly returns a list which contains:

- \$exposuresCounts: the exposure counts inferred in ICAMSxtra format,
- \$exposureErrors: the MSE in ICAMSxtra format,
- \$SEoutput: A list which contains:
 - \$exposures: exposure proportion in SignatureEstimation format, and errors invisibly.
 - \$errors: mean squared error (MSE) between normalized reconstructed spectra and normalized ground-truth mutational spectra.

RunsigneR RunsigneR extraction and attribution on a spectra catalog file

Description

Run signeR extraction and attribution on a spectra catalog file

```
RunsigneR(
  input.catalog,
  out.dir,
  seedNumber = 1,
  K.exact = NULL,
  K.range = NULL,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog File containing input spectra catalog. Columns are samples (tumors), rows are

mutation types.

out.dir Directory that will be created for the output; abort if it already exits. Log files

will be in paste0(out.dir,"/tmp").

seedNumber Specify the pseudo-random seed number used to run signeR. Setting seed can

make the attribution of signeR repeatable. Default: 1.

K.exact, K.range

K. exact is the exact value for the number of signatures active in spectra (K). Specify K. exact if you know exactly how many signatures are active in the

input.catalog, which is the ICAMS-formatted spectra file.

K.range is A numeric vector (K.min, K.max) of length 2 which tell signeR to search the best signature number active in spectra, K, in this range of Ks. Specify K.range if you don't know how many signatures are active in the input.catalog.

WARNING: You must specify only one of K. exact or K. range!

Default: NULL

test.only If TRUE, only analyze the first 10 columns read in from input.catalog. De-

fault: FALSE

overwrite If TRUE, overwrite existing output. Default: FALSE

Details

```
Creates several files in out.dir. These are: TODO(Steve): list the files TODO(Wuyang)
```

Value

The inferred exposure of signeR, invisibly.

RunSomaticSignatures Run SomaticSignatures.NMF extraction and attribution on a spectra catalog file

Description

Run SomaticSignatures.NMF extraction and attribution on a spectra catalog file

```
RunSomaticSignatures(
  input.catalog,
  out.dir,
  CPU.cores = NULL,
  seedNumber = 1,
  K.exact = NULL,
  K.range = NULL,
  nrun.est.K = 30,
  nrun.extract = 1,
  pConstant = NULL,
```

```
test.only = FALSE,
overwrite = FALSE
)
```

Arguments

input.catalog File containing input spectra catalog. Columns are samples (tumors), rows are

mutation types.

out.dir Directory that will be created for the output; abort if it already exits. Log files

will be in paste0(out.dir,"/tmp").

CPU. cores Number of CPUs to use in running SomaticSignatures.NMF. For a server, 30

cores would be a good choice; while for a PC, you may only choose 2-4 cores.

By default (CPU.cores = NULL), the CPU.cores would be equal to (parallel::detectCores())/2,

total number of CPUs divided by 2.

seedNumber Specify the pseudo-random seed number used to run SomaticSignatures. Setting

seed can make the attribution of SomaticSignatures repeatable. Default: 1.

K.exact, K.range

K.exact is the exact value for the number of signatures active in spectra (K). Specify K.exact if you know exactly how many signatures are active in the

input.catalog, which is the ICAMS-formatted spectra file.

K.range is A numeric vector (K.min,K.max) of length 2 which tell SomaticSignatures.NMF to search the best signature number active in spectra, K, in this range of Ks. Specify K.range if you don't know how many signatures are active in the input.catalog.

WARNING: You must specify only one of K. exact or K. range!

Default: NULL

nrun.est.K Number of NMF runs for each possible number of signature. This is used in the

step to estimate the most plausible number of signatures in input spectra catalog.

nrun.extract number of NMF runs for extracting signatures and inferring exposures.

pConstant A small positive value (a.k.a. pseudocount) to add to every entry in the input.catalog.

Specify a value ONLY if an "non-conformable arrays error" is raised.

test.only If TRUE, only analyze the first 10 columns read in from input.catalog. De-

fault: FALSE

overwrite If TRUE, overwrite existing output. Default: FALSE

Details

SomaticSignatures.NMF used approach in Hutchins et al. (2008) to estimate K: it selects the first inflection point of residual sum of squares (RSS) function by finding the smallest K where the second derivate of RSS at its neighbouring Ks have opposite signs.

This requires calculation of second derivative of residual sum of squares (RSS) at >2 integers, and thus requires at least 3 Ks to be assessed.

Value

A list contains:

- \$signature extracted signatures,
- \$exposure inferred exposures,

of SomaticSignatures.NMF, invisibly.

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References

http://dx.doi.org/10.1093/bioinformatics/btn526

RunSparseSignatures Run

Run SparseSignatures extraction and attribution on a spectra catalog file

Description

Run SparseSignatures extraction and attribution on a spectra catalog file

Usage

```
RunSparseSignatures(
  input.catalog,
  out.dir,
  seedNumber = 1,
  K.exact = NULL,
  K.range = NULL,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog File containing input spectra catalog. Columns are samples (tumors), rows are

mutation types.

out.dir Directory that will be created for the output; abort if it already exits. Log files

will be in paste0(out.dir,"/tmp").

seedNumber Specify the pseudo-random seed number used to run SparseSignatures. Setting

seed can make the attribution of SparseSignatures repeatable. Default: 1.

K.exact, K.range

K. exact is the exact value for the number of signatures active in spectra (K). Specify K. exact if you know exactly how many signatures are active in the

input.catalog, which is the ICAMS-formatted spectra file.

K.range is A numeric vector (K.min, K.max) of length 2 which tell SparseSignatures to search the best signature number active in spectra, K, in this range of Ks. Specify K.range if you don't know how many signatures are active in the

input.catalog.

WARNING: You must specify only one of K. exact or K. range!

Default: NULL

test.only If TRUE, only analyze the first 10 columns read in from input.catalog. De-

fault: FALSE

overwrite If TRUE, overwrite existing output. Default: FALSE

Details

```
Creates several files in out.dir. These are: TODO(Steve): list the files TODO(Wuyang)
```

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Value

The inferred exposure of SparseSignatures, invisibly.

Runtcsm

Run tesm extraction and attribution on a spectra catalog file

Description

Run tcsm extraction and attribution on a spectra catalog file

Usage

```
Runtcsm(
  input.catalog,
  out.dir,
  seedNumber = 1,
  CPU.cores = 1,
  K.exact = NULL,
  K.range = NULL,
  covariates = NULL,
  test.only = FALSE,
  overwrite = FALSE,
  feature.file = NULL,
  sigma.output.file = NULL,
  gamma.output.file = NULL)
)
```

Arguments

input.catalog File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.

out.dir Directory that will be created for the output; abort if it already exits. Log files

will be in paste0(out.dir,"/tmp").

seedNumber Specify the pseudo-random seed number used to run tcsm. Setting seed can

make the attribution of tcsm repeatable.

CPU.cores Number of CPUs to use in running MutationalPatterns. For a server, 30 cores

would be a good choice; while for a PC, you may only choose 2-4 cores. By default (CPU.cores = NULL), the CPU.cores would be equal to (parallel::detectCores())/2,

total number of CPUs divided by 2.

K.exact, K.range

K.exact is the exact value for the number of signatures active in spectra (K). Specify K.exact if you know exact how many signatures are active in the input.catalog,

which is the ICAMS-formatted spectra file.

K.range is A numeric vector (K.min, K.max) of length 2 which tell tesm to search the best signature number active in spectra, K, in this range of Ks. Specify K.range if you don't know how many signatures are active in the input.catalog.

K.max - K.min >= 3, otherwise an error will be thrown. WARNING: You must specify only one of K or K.range!

test.only If TRUE, only analyze the first 10 columns read in from input.catalog.

overwrite If TRUE, overwrite existing output.

Details

```
Creates several files in out.dir. These are: TODO(Steve): list the files TODO(Wuyang)
```

Value

The inferred exposure of tcsm, invisibly.

RunYAPSAAttributeOnly Run YAPSA attribution on a spectra catalog file and known signatures.

Description

Run YAPSA attribution on a spectra catalog file and known signatures.

Usage

```
RunYAPSAAttributeOnly(
  input.catalog,
  gt.sigs.file,
  out.dir,
  seedNumber = 1,
  signature.cutoff = NULL,
  test.only = FALSE,
  overwrite = FALSE
)
```

Arguments

input.catalog	File containing input spectra catalog. Columns are samples (tumors), rows are mutation types.	
gt.sigs.file	File containing input mutational signatures. Columns are signatures, rows are mutation types.	
out.dir	Directory that will be created for the output; abort if it already exits. Log files will be in paste0(out.dir,"/tmp").	
seedNumber	Specify the pseudo-random seed number used to run YAPSA. Setting seed can make the attribution of YAPSA repeatable. Default: 1.	
signature.cutoff		
	A numeric vector of values less than 1. Signatures from within W with an overall exposure less than the respective value in in_cutoff_vector will be discarded. Default: vector length of number of sigs with all zeros	
test.only	If TRUE, only analyze the first $10\ {\rm columns}\ {\rm read}\ {\rm in}\ {\rm from}\ {\rm input.catalog}.$ Default: FALSE	
overwrite	If TRUE, overwrite existing output. Default: FALSE	

Details

Creates several files in paste@(out.dir, "/sa.output.rdata"). These are TODO(Steve): list the files

Value

The inferred exposure of YAPSA, invisibly.

SAMultiRunOneCatalog Run SignatureAnalyzer many times on one catalog and put results in specified location.

Description

Run SignatureAnalyzer many times on one catalog and put results in specified location.

Usage

```
SAMultiRunOneCatalog(
  num.runs,
  signatureanalyzer.code.dir,
  input.catalog,
  out.dir,
  maxK = 30,
  tol = 1e-07,
  test.only = FALSE,
  delete.tmp.files = TRUE,
  overwrite = FALSE,
  mc.cores = 1,
  verbose = FALSE,
  seed = NULL
)
```

Arguments

num.runs The number of times run SignatureAnalyzer on each catalog (matrix of mutational spectra).

signatureanalyzer.code.dir

The directory holding the SignatureAnalyzer code.

input.catalog The catalog to analyze.

out.dir Root of directory tree that will contain the results.

maxK The maximum number of signatures to consider extracting.

tol Controls when SignatureAnalyzer will terminate its search; tol was 1.e-05 for

the PCAWG7 analysis.

test.only If TRUE, only analyze the first 10 columns read in from input.catalog.

delete.tmp.files

If TRUE delete the many temporary files generated by SignatureAnalyzer.

overwrite If TRUE overwrite previous results in same directory tree.

mc.cores Number of cores to use for mclapply; ignored on Windows.

verbose If TRUE cat a message regarding progress.

seed If not NULL call RNGkind(kind = "L'Ecuyer-CMRG"); set.seed(seed).

SignatureAnalyzer4MatchedCatalogs

Run SignatureAnalyzer on 4 coordinated data sets and put results in specified location.

Description

Run SignatureAnalyzer on 4 coordinated data sets and put results in specified location.

Usage

```
SignatureAnalyzer4MatchedCatalogs(
  num.runs = 20,
  signatureanalyzer.code.dir,
  dir.root,
  maxK = 30,
  tol = 1e-07,
  test.only = FALSE,
  delete.tmp.files = TRUE,
  slice = 1:4,
  overwrite = FALSE,
  mc.cores = 1
)
```

Arguments

num.runs Number of SignatureAnalyzer runs per data set. signatureanalyzer.code.dir The directory holding the SignatureAnalyzer code. dir.root Root of directory tree that contains the input data and to which the results will be written. maxK The maximum number of signatures to consider extracting. Controls when SignatureAnalyzer will terminate its search; tol was 1.e-05 for tol the PCAWG7 analysis. If TRUE, only analyze the first 10 columns read in from input.catalog. test.only delete.tmp.files If TRUE delete the many temporary files generated by SignatureAnalyzer. slice Vector of integers from 1:4. Only run on the corresponding data set (see Details). overwrite if TRUE overwrite preexisting results. The number of cores to use with mclapply; automatically overridden to 1 on mc.cores

Details

The 4 coordinated data sets are

Windows.

```
    sa.sa.96
    sp.sp
```

```
    sa.sa.COMPOSITE
    sp.sa.COMPOSITE
```

which are described elsewhere.

SignatureAnalyzerOneRun

Source SignatureAnalyzer and run it once on a single data set and put results in specified location.

Description

Source SignatureAnalyzer and run it once on a single data set and put results in specified location.

Usage

```
SignatureAnalyzerOneRun(
    signatureanalyzer.code.dir,
    input.catalog,
    out.dir,
    seedNumber = NULL,
    input.exposures = NULL,
    maxK = 30,
    tol = 1e-07,
    test.only = FALSE,
    delete.tmp.files = TRUE,
    verbose = 0,
    overwrite = FALSE
)
```

Arguments

signatureanalyzer.code.dir

The directory holding the SignatureAnalyzer code.

input.catalog File containing input catalog. Columns are samples (tumors), rows are signa-

tures. SignatureAnalyzer does not care about the row names (I think) TODO(Steve):

check this.

out.dir Directory that will be created for the output; abort if it already exits. Log files

will be in paste0(out.dir,"/tmp").

seedNumber Specify the pseudo-random seed number used to run SignatureAnalyzer. Setting

seed can make the attribution of SignatureAnalyzer repeatable. If NULL, this

function will not specify seed number. Default: NULL.

input.exposures

A file with the synthetic exposures used to generate input.catalog; if provided

here, this is copied over to the output directory for downstream analysis.

maxK The maximum number of signatures to consider extracting.

tol Controls when SignatureAnalyzer will terminate its search; tol was 1.e-05 for

the PCAWG7 analysis.

test.only If TRUE, only analyze the first 10 columns read in from input.catalog.

```
delete.tmp.files
```

If TRUE delete the many temporary files generated by SignatureAnalyzer.

verbose If TRUE, then print various messages.
overwrite If TRUE, overwrite existing output

Details

Creates several files in out.dir:

- 1. sa.output.sigs.csv Normalized signatures (no all-0 signatures, column sums all 0)
- 2. sa.output.raw.exp.csv Raw exposures (attributions)
- 3. sa.output.exp.csv Same as sa.output.raw.exp.csv
- 4. sa.output.other.data.csv, contains a summary of important information, including the number of signatures extracted.
- 5. input.syn.exp.csv Optional, a copy of input.exposures, if it was provided.

Value

A list with the following elements:

- 1. signatures.W The raw signature matrix, *including* columns of all zeros.
- 2. exposures.H The raw exposure matrix, *excluding* rows of all zeros. The matrix product of the non-zero columns of signatures.w and exposures.H approximates the input spectrum matrix.
- 3. likelihood The likelihood as returned by SignatureAnalyzer.
- 4. evidence -1 * the posterior probability as returned by SignatureAnalyzer.
- 5. relevance One for each column of the signatures. W, as returned by Signature Analyzer.
- 6. error A measure of reconstruction error (?) as returned by SignatureAnalyzer
- 7. normalized.sigs The non-0 columns of signatures. W normalized so that each column sum is 1.

SignatureAnalyzerPrepHyper1Secondary

Prepare the "hypermutated" segment (a.k.a "Secondary" segment of a split non-hyper and hyper data set.)

Description

Prepare the "hypermutated" segment (a.k.a "Secondary" segment of a split non-hyper and hyper data set.)

```
SignatureAnalyzerPrepHyper1Secondary(
  non.hyper.results,
  primary.catalog,
  hyper.catalog,
  secondary.catalog,
  overwrite = TRUE
)
```

Arguments

non.hyper.results

The directory containing the the results of the analysis of the non-hyper-mutated (a.k.a "PRIMARY") mutational spectra.

primary.catalog

The catalog of non-hyper-mutated mutational spectra from which the results in non.hyper.results were derived.

hyper.catalog The catalog of hyper-mutated mutational spectra which will be part of the input for the secondary analysis.

secondary.catalog

The final output catalog on which the secondary analysis will be performed; this is a cbind of pseudo-spectra generated from the PRIMARY signatures with the hyper.catalog.

overwrite If TRUE overwrite possible previously computed files and/or directories.

SignatureAnalyzerPrepHyper4

Prepare the "hypermutated" segment (a.k.a "Secondary" segment of a split non-hyper and hyper data set.)

Description

Prepare the "hypermutated" segment (a.k.a "Secondary" segment of a split non-hyper and hyper data set.)

Usage

SignatureAnalyzerPrepHyper4(parent.dir, overwrite = FALSE)

Arguments

parent.dir A directory that must contain subdirectories syn.SA.hyper.low and syn.SA.hyper.mixed.

syn.SA.hyper.low must contain the synthetic non-hypermutated data and the results of running SignatureAnalyzer on the non-hyper segment, with subdirec-

tories sa.sa.96, sa.sa.COMPOSITE, sp.sa.COMPOSITE, and sp.sp. syn.SA.hyper.mixed

must contain the synthetic hypermutated data. The results of the initial SignatureAnalyzer run will be placed here to prepare this directory for the second

SignatureAnalyzer run.

overwrite If TRUE overwrite existing directories and files.

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 ${\tt Source Signature Analyzer Code}$

Source SignatureAnalyzer Codes.

Description

Source Signature Analyzer Codes.

Usage

SourceSignatureAnalyzerCode(signatureanalyzer.code.dir)

Arguments

signatureanalyzer.code.dir

The directory which stores SignatureAnalyzer program files. It must include a folder named INPUT_SignatureAnalyzer and a R script named SignatureAnalyzer.PCAWG.function

SynSigRun

SynSigRun: An easy-to-use package for non-experts which runs software packages reproducibly with synthetic tumors generated by SynSigGen.

Description

SynSigRun gives necessary information to mutational-signature analysis programs. These programs used catalogs of synthetic mutational spectra created by package SynSigGen, and results were assessed by SynSigEval.

Workflow

Typical workflow for conducting a mutational signature analysis with mutational spectra is as follows.

Input mutational spectra:

Mutational spectra can be obtained from vcf files of real samples (see "Importing mutational spectra from ICAMS"). Mutational spectra can also be generated in-silico by R package SynSigGen, and then imported by ICAMS (see "(In SynSigGen) Creating Synthetic Mutational Spectra").

Importing mutational spectra from ICAMS:

Relevant functions are:

- 1. ReadCatalog
- 2. StrelkaSBSVCFFilesToCatalog
- 3. StrelkaIDVCFFilesToCatalog
- 4. MutectVCFFilesToCatalog

See ICAMS package documentation for more details.

(In SynSigGen) Creating Synthetic Mutational Spectra:

These functions create synthetic mutational spectra based on parameters derived from mutational signature profiles and exposures.

Relevant functions for generate exposures are:

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- 1. GenerateSynFromReal
- 2. GenerateSyntheticExposures
- 3. GenSBS1SBS5Exposure

After generating exposures for spectra dataset, SynSigGen used these functions to generate mutational spectra:

- 1. CreateFromReal
- 2. CreateMixedTumorTypeSyntheticData
- 3. CreateRandomSyn

See SynSigGen package documentation for more details.

(In SynSigRun) Run mutational analysis computational approaches:

Relevant functions are:

- RunhdpLessHier
- 2. Runmaftools
- 3. RunMutationalPatterns
- 4. RunsigneR
- 5. Runtcsm

(In SynSigEval) Summarize results:

Summarize results of of signature extraction and exposure inference (a.k.a. signature attribution):

Relevant functions are:

- 1. SummarizeSigOnehelmsmanSubdir
- 2. SignatureAnalyzerSummarizeTopLevel
- 3. SignatureAnalyzerSummarizeSBS1SBS5
- $4. \ {\tt SummarizeSigOneSigProExtractorSubdir}$
- 5. SummarizeSigProExtractor
- $6. \ {\tt SummarizeSigOneExtrAttrSubdir}$

Package SynSigEval uses functions in ICAMSxtra to compare two sets of mutational signatures. Often we will be interested in comparing signature profiles extracted from synthetic data to the ground-truth signature profiles:

- Match1Sig
- $2. \ {\tt MatchSigs1Direction}$
- 3. MatchSigs2Directions
- 4. MatchSigsAndRelabel

Folder structure for rHYJHQw9YVdJnAj2cTbwWgpO52F33bqI-38- and rHYJHQw9YVdJnAj2cTbwWgpO52F33b 39-:

Summary function will fit to the new 5-level folder structure:

First Level - top.level.dir: dataset folder (e.g. "S.0.1.Rsq.0.1", "syn.pancreas"). All spectra datasets under any top.level.dir have the same exposure.

Second Level - ground. truth. exposure.dir: spectra folder: (e.g. "sp.sp", "sa.sa.96"). All spectra datasets under any second.level.dir have the same signature and the same exposure counts.

Third Level - third.level.dir:

1. It can be ("Attr") for storing results of packages which can only do signature attribution of known signatures ("Attr");

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2. It can be ("ExtrAttr"), folder to store results of computational approaches which can do denovo extraction and following attribution, without knowing the number of ground-truth mutational signatures active in the spectra data set.

3. It can also be ("ExtrAttrExact"), folder to store results of computational approaches which can do de-novo extraction and following attribution, given the number of ground-truth mutational signatures active in the spectra data set.

Fourth Level - tool.dir: The results of a computational approach (e.g. "sigproextractor.results", "SignatureEstimation.Q Under this level, tool.dir may contain multiple run.dir, each is a run of the computational approach using a specific number of seed.

Fifth level - run.dir: contains results from a run of the computational approach using a specific number of seed. (e.g. "seed.1")

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