# Package 'SynSigGen'

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# Description

Exposures and spectra with Poisson or negative binomial noise in exposures.

# Usage

AddNoise(input.exposure, signatures, n.binom.size = NULL)

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## **Arguments**

input.exposure The exposures to which to add noise; a numeric matrix or data frame in which

the rows are signatures and the columns are samples. Each cell indicates the

number of mutations due to a particular signature in a particular sample.

signatures The signatures in the exposure; the column names of signatures have to in-

clude all row names in input.exposure; can be an ICAMS catalog or a numeri-

cal matrix or data frame.

n.binom.size If non NULL, use negative binomial noise with this size parameter; see NegBinomial.

#### Value

A list with the elements

expsoures The numbers of mutations due to each signature after adding noise

spectra The spectra based on the noisy signature exposures.

BladderSkin1000 Generate synthetic data sets modeled on bladder TCC and skin

melanoma.

## **Description**

Creates spectra dataset consists of 500 synthetic bladder transitional cell carcinoma with high prevalence and mutation load from SBS2, and 500 synthetic skin melanoma with high prevalence and mutation load from SBS7a and SBS7b. This dataset challenges the computational approaches as SBS2 has a similar pattern to the mixture of SBS7a and SBS7b, thus the existence of these signatures may interfere computational approaches from accurately extracting these signatures.

## Usage

BladderSkin1000(seed = 191906, regress = FALSE)

## **Arguments**

seed A random seed to use.

regress Whether to compare the result with local copy of dataset using a diff.

# **Details**

This function replaces the first part of data-raw/Create.2.7a.7b.Rmd in GitHub repository steverozen/SynSig. With default arguments, this function generates the same results as the first part of data-raw/Create.2.7a.7b.Rmd.

#' The second half of data-raw/Create.2.7a.7b.Rmd is replaced by Create.2.7a.7b.Abstract.

Data set generated by this function can be found at Synapse with Synapse ID: syn18500217.

```
Create.3.5.40.Abstract
```

Create synthetic spectra based on SBS3 SBS5 SBS40

#### **Description**

This function generates synthetic spectra with mutation loads of SBS3 (signature prevalent in ovarian adenocarcinoma), SBS5 and SBS40 (signatures prevalent in renal cell carcinoma). This dataset challenges the computational approaches as these three signatures are "flat" signatures hard to be extracted accurately.

#### Usage

```
Create.3.5.40.Abstract(
   seed = 44,
   overwrite = TRUE,
   regress.dir = "data-raw/long.test.regression.data/syn.3.5.40.abst/"
)
```

## **Arguments**

seed A random seed to use.

overwrite If TRUE, overwrite existing directories / files.

regress.dir If not NULL, compare the result to the contents of this directory with a diff.

## **Details**

This function supersedes the second part of data-raw/Create.3.5.40.Rmd in GitHub repository steverozen/SynSig. With default arguments, this function generates the same results as the second half of data-raw/Create.3.5.40.Rmd.

Data set generated by this function can be found at Synapse with Synapse ID: syn18500215.

CreateAndWriteCatalog Create and write a mutational spectra catalog

# Description

Create and write a mutational spectra catalog

```
CreateAndWriteCatalog(
    sigs,
    exp,
    dir = NULL,
    write.cat.fn = ICAMS::WriteCatalog,
    extra.file.suffix = "",
    overwrite = FALSE,
    my.dir = NULL
)
```

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## **Arguments**

sigs	Signatures to use.		
exp	(Synthetic) exposures.		
dir	Deprecated, maintained only to avoid breaking old code. A subdirectory based on the deprecated global variable OutDir.		
write.cat.fn	Function to write catalogs or spectra to files.		
extra.file.suffix			
	Extra string to put before ".csv".		
overwrite	If TRUE, overwrite existing directory; useful for debugging / testing.		
my.dir	The directory in which to write the catalog and several additional files.		

## **Details**

Create a file with the catalog syn.data.csv and writes sigs to input.sigs.csv.

#### Value

Invisibly, the generated catalog.

CreateFromReal	Create a specific synthetic data set based on real exposures in one or
	more cancer types.

# Description

Create a full SignatureAnalyzer / SigProfiler test data set for a set of various tumor types.

```
CreateFromReal(
    seed,
    top.level.dir = NULL,
    enclosing.dir = NULL,
    num.syn.tumors,
    cancer.types,
    data.suite.name = NULL,
    sa.exp = SynSigGen::sa.all.real.exposures,
    sp.exp = SynSigGen::sp.all.real.exposures,
    overwrite = TRUE,
    regress.dir = NULL,
    unlink = FALSE,
    verbose = FALSE,
    bladder.regress.hack = FALSE
)
```

#### **Arguments**

seed A random seed to use. top.level.dir The directory in which to put the output; will be created if necessary. enclosing.dir Deprecated; create the output in a subdirectory of this directory. num.syn.tumors The number of tumors to create for each cancer type in cancer.types. cancer.types Search sa. exp and sp. exp for exposures from tumors matching these strings. Each string should identify one tumor type, for some definition of tumor type. Probably the tumors in each type should be non-overlapping, but the code does not enforce this and does not care. data.suite.name Deprecated; the directory created will be file.path(enclosing.dir,paste0(data.suite.name," sa.exp A matrix of exposures; this function will use the columns with column names beginning paste0(cancer.type,"::"). A matrix of exposures; this function will use the columns with column names sp.exp beginning paste0(cancer.type,"::"). overwrite If TRUE, overwrite existing directories and files. regress.dir If not NULL, compare the result to the contents of this directory with a diff. unlink If TRUE and !is.null(regress.dir), then unlink the result directory if there are no differences. verbose If TRUE print various informative messages. bladder.regress.hack Set this to TRUE to handle mixed "all" and "no hyper" signature sets for the

regression test for BladderSkin1000.

CreateMixedTumorTypeSyntheticData

Create a test data set based on  $\geq 1$  tumor types.

#### **Description**

Create a test data set based on >= 1 tumor types.

```
CreateMixedTumorTypeSyntheticData(
  top.level.dir,
  cancer.type.strings,
  num.syn.tumors,
  overwrite = FALSE,
  sa.exp = sa.all.real.exposures,
  sp.exp = sp.all.real.exposures,
  verbose = FALSE,
  bladder.regress.hack = FALSE
)
```

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## **Arguments**

top.level.dir Path to top level of directory structure to be created.

cancer.type.strings

Search the PCAWG data for tumors matching these strings. Each string should identify one tumor type, for some definition of tumor type. Probably the tumors in each type should be non-overlapping, but the code does not enforce this and

does not care.

num.syn.tumors Number of synthetic tumors to create for each cancer type.

overwrite If TRUE, overwrite existing directories / files.

sa.exp SignatureAnalyzer exposures from which to select cancer types specified by

cancer.type.strings. In the column names of sa.exp the cancer type string

should be separated from the sample identifier by two colons (::).

sp. exp SigProfiler exposures from which to select cancer types specified by cancer.type.strings.

In the column names of sp. exp the cancer type string should be separated from

the sample identifier by two colons (::).

verbose If > 0, cat various messages.

bladder.regress.hack

For use by BladderSkin1000. Forces use of non-hyper-mutated exposures for bladder-TCC even if sa.exp and sp.exp include hyper-mutated exposures.

CreateRandomSyn This is the top-level function to create a set of spectra from random

signatures.

#### **Description**

This is the top-level function to create a set of spectra from random signatures.

## Usage

```
CreateRandomSyn(
  top.level.dir,
  seed = 1443196,
  regress.dir = "data-raw/long.test.regression.data/syn.30.random.sigs/",
  num.syn.tumors = 1000,
  overwrite = FALSE,
  unlink = FALSE,
  verbose = FALSE
)
```

## Arguments

top.level.dir Directory in which to put all results. It will be created if necessary.

seed Use default for regression testing.

regress.dir If not NULL compare the known results in this directory with the created results

in top.level.dir.

num.syn.tumors Total number of synthetic tumors to create. Use the default for regression test-

ing.

overwrite If TRUE overwrite existing files and directories.

unlink If TRUE unlink the created directory after the regression test.

verbose If TRUE print a few informative messages.

 ${\tt CreateSBS1SBS5CorrelatedSyntheticData}$ 

Function to generate 20 SBS1-SBS5-correlated Synthetic datasets used in testing.

#### **Description**

This function is a wrapper around CreateSBS1SBS5CorrelatedSyntheticDataOneDataset. It will use the default parameters to repeat the results.

## Usage

```
CreateSBS1SBS5CorrelatedSyntheticData(
  top.level.dir = "./",
  regress.dir = NULL,
  overwrite = FALSE,
  add.info = TRUE,
  unlink = FALSE
)
```

## **Arguments**

top.level.dir Top-level-folder to place 20 spectra datasets generated by this function. Default:

./ (Current working directory)

regress.dir If not NULL, compare the result to the contents of this directory with a diff.

overwrite Whether to overwrite (Default: FALSE)
add.info Whether to generate additional information.

You should set it to FALSE when you want to make a diff (i.e. regressdir is not NULL). This is because Additional information may differ on different OS or R sessions, thus may prevent the dataset from passing the NewDiff4SynDatasets

check. (Default: TRUE)

unlink Whether to delete temporary dataset folder top.level.dir. (Set to TRUE for

testing)

## **Details**

This function will generate 20 datasets, each with files listed below:

ground.truth.syn.catalog.csv: Generated tumor spectra in ICAMS SBS96 CSV format.

ground.truth.syn.exposures.csv: Mutation burdens of SBS1 and SBS5 in generated tumor spectra in ICAMS CSV format.

ground.truth.syn.sigs.csv: Ground-truth SBS1 and SBS5 signatures in ICAMS SBS96 CSV format.

parameters.txt: Parameters used to generate the exposures and tumor spectra.

scatterplot.pdf: scatterplot illustrating correlation of exposures of two signatures in generated spectra

seedInUse.txt, RNGInUse.txt: seed and Random Number Generator used in generation. (For better reproducibility)

sessionInfo.txt: information related to R versions, platforms, loaded or imported packages, etc. (For better reproducibility)

 ${\tt CreateSBS1SBS5CorrelatedSyntheticDataOneDataset}$ 

Wrapper function for generating SBS1-SBS5-correlated Synthetic data

## **Description**

This function will use SigProfiler-SBS96 mutational signatures to generate imaginary tumor spectra with mutation burdens only from SBS1 and SBS5, and mutation burdens of both signatures are highly correlated.

## Usage

```
CreateSBS1SBS5CorrelatedSyntheticDataOneDataset(
    dir.name = "./S.0.5.Rsq.0.3",
    dataset.name = NULL,
    overwrite = FALSE,
    seed = 1,
    parameter.df = SynSigGen::SBS1SBS5parameter["S.0.5.Rsq.0.3", ],
    add.info = TRUE,
    verbose = FALSE
)
```

# **Arguments**

seed

dir.name Folder to place the generated tumor spectra and other output files. Default: ./S.0.5.Rsq.0.3

 ${\tt dataset.name} \qquad {\tt The \ dataset.name \ encodes \ the \ parameters \ for \ the \ synthetic \ data, \ but \ this \ is \ just}$ 

a convention. If NULL, it will be changed to the last part of the dir.name

(Default: NULL)

overwrite Whether to overwrite (Default: FALSE)

The seed number used to initialize pseudo-random number generator (RNG).

This makes the generation of the correlated datasets repeatable. (Default: 1)

parameter.df a named 1\*14 data.frame containing the following items:

- 1. main.signature The name of the main signature whose exposure can vary freely. (Default: SBS5)
- correlated.signature The name of the correlated signature whose exposure is influenced by and co-varies with the exposure of main.signature. In this study, it defaults as "SBS1".
- 3. name.prefix Default: TwoCorreSigsGen
- 4. sample.number The number of synthetic tumors you want to generate. Default: 500
- 5. main.mean.log The mean of log(count(SBS5),base = 10) Default: 2.5
- 6. main.stdev.log The standard deviation of log(count(SBS5),base = 10) Default: 0.3

- 7. correlated.stdev.log The ADDED standard deviation of log(count(SBS1),base = 10). This parameter is ADDED stdev because based on the mechanism to generate the count, log10(count(SBS1)) inherently has a stdev = slope \* main.stdev.log Default: 0.4
- 8. slope.linear The ratio for: (Correlated exposure) / (Main exposure) IN LINEAR SPACE! Default: 0.5
- 9. main.signature.lower.thres This program will force the exposure count of main.signature to be greater than this threshold. Default: 100
- 10. correlated.signature.lower.thres This program will force the exposure count of correlated.signature to be greater than this threshold. Default:
- 11. pearson.r.2.lower.thres Lower boundary of Pearson's R^2 (Default: 0.29)
- 12. pearson.r.2.higher.thres Upper boundary of Pearson's R^2 (Default: 0.31)
- 13. min.main.to.correlated.ratio.linear The lower ratio for count(SBS5) / count(SBS1) in LINEAR SPACE! (Default: 1/3)
- 14. max.main.to.correlated.ratio.linear The upper ratio for count(SBS5) / count(SBS1) in LINEAR SPACE! (Default: Inf)

add.info
verbose

Whether to generate additional information.

If TRUE cat progress messages. You should set it to FALSE when you want to make a diff using CreateSBS1SBS5CorrelatedSyntheticData (i.e. parameter regressdir is not NULL). This is because Additional information may differ on different OS or R sessions, thus may prevent the dataset from passing the NewDiff4SynDatasets check. (Default: TRUE)

#### Warning

Exposure generation function will repeat generating exposure counts using mean and stdev parameters, until the dataset has a Pearson's R^2 which falls between two boundaries of Pearson's R^2. Below are a group of parameters which have been tested successfully. If you intend to lower the Pearson's R^2, do remember to increase the main.stdev.log and correlated.stdev.log. Otherwise, the exposure generation will keep generating and discarding datasets!

#### **Details**

If you want to customize Pearson R^2 of the dataset, you need to change the standard deviations of two signatures. i.e., main.stdev.log and correlated.stdev.log.

This function will generate files listed below:

ground.truth.syn.catalog.csv: Generated tumor spectra in ICAMS SBS96 CSV format.

ground.truth.syn.exposures.csv: Mutation burdens of SBS1 and SBS5 in generated tumor spectra in ICAMS CSV format.

ground.truth.syn.sigs.csv: Ground-truth SBS1 and SBS5 signatures in ICAMS SBS96 CSV format. parameters.txt: Parameters used to generate the exposures and tumor spectra.

scatterplot.pdf: scatterplot illustrating correlation of exposures of two signatures in generated spectra

seedInUse.txt, RNGInUse.txt: seed and Random Number Generator used in generation. (For better reproducibility)

 $session Info.txt:\ information\ related\ to\ R\ versions,\ platforms,\ loaded\ or\ imported\ packages,\ etc.\ (For\ better\ reproducibility)$ 

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CreateSynCatalogs	Generate synthetic spectra catalogs given signature profiles and syn-
	thetic exposures.

#### **Description**

Generate synthetic spectra catalogs given signature profiles and synthetic exposures.

#### Usage

```
CreateSynCatalogs(signatures, exposures, sample.id.suffix = NULL)
```

## **Arguments**

signatures The signature profiles. exposures The synthetic exposures. sample.id.suffix

A string for adding a suffix to sample ID. For example, if sample.id.suffix is "abc", then SomeCancerType::s1.33 is changed to SomeCancerType::s1-abc.33. Actually, this just replaces the first "." in the sample id with "-" concatenated to sample.id.suffix. TODO(Steve): probably drop this

## Value

A list of three elements that comprise the synthetic data:

- 1. ground.truth.catalog: Spectra catalog for the software input.
- 2. ground.truth.signatures: Signatures active in ground.truth.catalog.
- 3. ground.truth.exposures: Exposures of ground.truth.signatures in ground.truth.catalog.

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.

GenerateSynFromReal

Generate synthetic exposures from real exposures.

## Description

Checkpoints the parameters and the synthetic exposures to files. It also checks that the parameters inferred from the synthetic data approximate those inferred from real.exp.

## Usage

```
GenerateSynFromReal(
  real.exp,
  num.syn.tumors,
  file.prefix,
  sample.id.prefix,
  top.level.dir = NULL
)
```

## **Arguments**

```
real.exp The actual (real) exposures upon which to base the parameters and synthetic exposures.

num.syn.tumors Generate this number of synthetic tumors.

file.prefix Prepend this to output filenames to indicate the organization of the data.

sample.id.prefix Prefix for sample identifiers for the synthetic samples.

top.level.dir Directory in which to create several files. This directory must already exist.
```

## Value

A list with elements:

- 1. parms The parameters inferred from real.exp.
- 2. syn.exp The synthetic exposures generated from parms.

Generate Synthetic Exposures

Create synthetic exposures based given parameters

## **Description**

Create synthetic exposures based given parameters

#### **Usage**

```
GenerateSyntheticExposures(
  sig.params,
  num.samples = 10,
  name = "synthetic",
  sig.matrix = NULL,
  distribution = NULL
)
```

## Arguments

sig.params Parameters from GetSynSigParamsFromExposures or another source. Should

be a matrix or data frame with one column for each signature and the following

rows:

**prob** The proportion of tumors with the signature.

**mean** The mean(log\_10(number of mutations)).

**stdev** The stdev(log\_10(number of mutations)).

The rownames need to be the column names of a signature catalog.

num. samples Number of samples to generate

name Prefix for sample identifiers in the simulated dataset

sig.matrix Signature matrix to construct synthetic tumors

distribution Probability distribution used to generate synthetic exposures due to active mu-

tational signatures. Can be neg.binom which stands for negative binomial distribution. If NULL (Default), then this function uses log normal distribution with

base 10.

#### Value

A matrix with the rows being each signature and the columns being generated samples. Each entry is the count of mutations due to one signature in one sample.

 ${\tt Generate Synthetic Tumors}$ 

Generate synthetic tumors based on real exposures in one or more cancer types

## **Description**

Generate synthetic tumors based on real exposures in one or more cancer types

```
GenerateSyntheticTumors(
   seed,
   dir,
   cancer.types,
   samples.per.cancer.type,
   input.sigs,
   real.exposures,
```

```
distribution = NULL,
  sample.prefix.name = "SP.Syn.",
  overwrite = TRUE,
  verbose = 0
)
```

## **Arguments**

seed A random seed to use.

dir The directory in which to put the output; will be created if necessary.

cancer . types A vector of character strings denoting different cancer types. This function will

search real. exposures for exposures from tumors matching these strings. See

PCAWG7::CancerTypes() for example.

samples.per.cancer.type

Number of synthetic tumors to create for each cancer type.

input.sigs A matrix of signatures. real.exposures A matrix of real exposures.

distribution Probability distribution used to generate synthetic exposures due to active mu-

tational signatures. Can be neg.binom which stands for negative binomial distribution. If NULL (Default), then this function uses log normal distribution with

base 10.

sample.prefix.name

Prefix name to add to the synthetic tumors.

overwrite If TRUE, overwrite existing directories and files.

verbose If > 0 cat various messages.

## Value

A list of three elements that comprise the synthetic data:

- 1. ground.truth.catalog: Spectra catalog with rows denoting mutation types and columns denoting sample names.
- 2. ground.truth.signatures: Signatures active in ground.truth.catalog.
- 3. ground.truth.exposures: Exposures of ground.truth.signatures in ground.truth.catalog.

## **Examples**

GenSBS1SBS5Exposure

Generate correlated exposures for multiple tumors Wrapper function around GenSBS1SBS5ExposureOneTumor: A function to generate exposure of two correlated signatures (Example: SBS1 and SBS5) for sample.number (e.g. 500) synthetic tumors. NOTE: pearson.r.2.lower.thres and pearson.r2.higher.thres are used to constraint the Pearson's R^2 of mutation burdens of two signatures in multiple tumors.

## **Description**

Generate correlated exposures for multiple tumors

Wrapper function around GenSBS1SBS5ExposureOneTumor: A function to generate exposure of two correlated signatures (Example: SBS1 and SBS5) for sample.number (e.g. 500) synthetic tumors.

NOTE: pearson.r.2.lower.thres and pearson.r2.higher.thres are used to constraint the Pearson's R^2 of mutation burdens of two signatures in multiple tumors.

## Usage

```
GenSBS1SBS5Exposure(
 main.signature = "SBS5",
  correlated.signature = "SBS1",
  sample.number = 500,
  name.prefix = "TwoCorreSigsGen",
 main.mean.log = 2.5,
 main.stdev.log = 0.25,
  correlated.stdev.log = 0.25,
  slope.linear = 1,
 main.signature.lower.thres = 50,
  correlated.signature.lower.thres = 30,
  pearson.r.2.lower.thres = 0.1,
 pearson.r.2.higher.thres = 1,
 min.main.to.correlated.ratio.linear = 1/3,
 max.main.to.correlated.ratio.linear = Inf
)
```

#### **Arguments**

main.signature Name of a signature with smaller variance in the  $\log 10$  space. (Default: "SBS5") correlated.signature

Name of a signature with larger variance in the log10 space. (Default: "SBS1") sample.number

Number of tumors whose mutation burdens will be generated. (Default: 500)

 ${\tt name.prefix} \qquad {\tt Prefix} \ \ {\tt of} \ {\tt tumor} \ {\tt name}. \ ({\tt Default:} \ "{\tt TwoCorreSigsGen"}) \ {\tt By} \ {\tt default}, \ {\tt the} \ {\tt name} \ {\tt of}$ 

 $tumors\ to\ be\ created\ will\ be:\ Two Corre Sig Gen::1,\ Two Corre Sig Gen::2,\ Two Cor$ 

reSigGen::3...

main.mean.log Mean of log10(mutation burden of main.signature)

main.stdev.log Standard deviation of log10(mutation burden of main.signature)

correlated.stdev.log

Contribute to part of the standard deviation of log10(mutation burden of correlated signature). In this script, the s.d. of log10(mutation burden of correlated signature).

lated.signature) = main.stdev.log + correlated.stdev.log

slope.linear Average ratio of mutation burden of correlated.signature over mutation bur-

den of main.signature

main.signature.lower.thres

Minimum mutation burden (number of mutations) induced by main.signature in each tumor.

correlated.signature.lower.thres

Minimum mutation burden (number of mutations) induced by correlated.signature in each tumor.

pearson.r.2.lower.thres

Minimum Pearson's  $R^2$  of mutation burdens of two signatures in sample . number tumors.

pearson.r.2.higher.thres

Maximum Pearson's  $R^2$  of mutation burdens of two signatures in sample. number tumors

min.main.to.correlated.ratio.linear

Minimum ratio of main. signature over mutation burden of correlated. signature in each tumor.

max.main.to.correlated.ratio.linear

Maximum ratio of main. signature over mutation burden of correlated. signature in each tumor.

GetSynSigParamsFromExposures

Empirical estimates of key parameters describing exposures due to signatures.

## Description

Empirical estimates of key parameters describing exposures due to signatures.

#### Usage

GetSynSigParamsFromExposures(exposures, verbose = 0, distribution = NULL)

## **Arguments**

exposures A matrix in which each column is a sample and each row is a mutation signa-

ture, with each element being the "exposure", i.e. mutation count attributed to a

(sample, signature) pair.

verbose If > 0 cat various messages.

distribution Probability distribution used to fit exposures due to one mutational signature.

Can be neg.binom which stands for negative binomial distribution. If NULL

(Default), then this function uses log normal distribution with base 10.

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#### Value

• For log normal distribution, a data frame with one column for each of a subset of the input signatures and the following rows

**prob** The proportion of tumors with the signature.

mean The mean(log\_10(number of mutations)).

**stdev** The stdev(log\_10(number of mutations)).

Signatures not present in exposures or present only in a single tumor in exposures are removed.

• For negative binomial distribution, a data frame with one column for each of a subset of the input signatures and the following rows

**prob** The proportion of tumors with the signature.

size Dispersion parameter.

mu Mean.

ManyTypes2700

Create a specific synthetic data set of 2,700 tumors.

## Description

Data set generated by this function can be found at Synapse with Synapse ID: syn18500213.

#### Usage

```
ManyTypes2700(seed = 191906, regress = FALSE)
```

## **Arguments**

seed A random seed to use.

regress Whether to compare the result with local copy of dataset using a diff.

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.

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

MergeExposures

## **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

MergeExposures

Merge all exposure matrices in a list of matrices

## Description

Merge all exposure matrices in a list of matrices

## Usage

```
MergeExposures(list.of.exposures)
```

## **Arguments**

```
list.of.exposures
```

A list of exposure matrices

## Value

The column-wise merge of all the input matrices with all rownames from all matrices preserved and corresponding entries filled with 0s.

Mutational Signatures 19

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 <a href="https://www.synapse.org/#!Synapse:syn11738312">https://www.synapse.org/#!Synapse:syn11738312</a>. 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 <a href="https://www.synapse.org/#!Synapse:syn11738313">https://www.synapse.org/#!Synapse:syn11738313</a>. 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.

#### 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
```

NewCreateAndWriteCatalog

Create and write a mutational spectra catalog

## **Description**

Create and write a mutational spectra catalog

## Usage

```
NewCreateAndWriteCatalog(
    sigs,
    exp,
    dir,
    extra.file.suffix = "",
    overwrite = FALSE
)
```

## **Arguments**

```
sigs Signatures to use.

exp (Synthetic) exposures.

dir Directory in which to put the signatures; NOTE: this will be a subdirectory based on OutDir.

extra.file.suffix
Extra string to put before ".csv".

overwrite If TRUE, overwrite existing directory; useful for debugging / testing.
```

# **Details**

Create a file with the catalog syn.data.csv and writes sigs to input.sigs.csv.

#### Value

Invisibly, the generated catalog.

NewDiff4SynDataSets

Diff two directories or files.

## **Description**

Diff two directories or files.

## Usage

```
NewDiff4SynDataSets(
  newdir,
  regressdirname,
  unlink,
  verbose = FALSE,
  long.diff = FALSE
)
```

## **Arguments**

newdir the path of dir2 for a folder to be recursively compared with dir1; it can also

be the path of a single file file 2 to diff with file 1.

regressdirname the path of dir2 for a folder to be recursively compared with dir1; it can also

be the path of a single file file2 to diff with file1.

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

verbose Whether to display additional R messages.

long.diff If TRUE, invoke diff -r (detailed text information even if the two files/folders

are the same); if FALSE, invoke diff -rq (detailed text information only if two

files/folders are different). (Default: FALSE)

#### Value

The output of the diff command.

OLD.SplitCatCOMPOSITE Split COMPOSITE (SNS1536+DBS78+ID83) catalogs in ICAMS format into 3 individual catalogs.

## **Description**

Split COMPOSITE (SNS1536+DBS78+ID83) catalogs in ICAMS format into 3 individual catalogs.

## Usage

```
OLD.SplitCatCOMPOSITE(catalog)
```

#### **Arguments**

catalog

Input catalog, can be a .csv file or matrix in ICAMS COMPOSITE format.

22 PancAdenoCA1000

#### Value

a list, containing 3 catalog matrices in MultiModalMuSig format. Each matrix contains SNS1536, DBS78 and ID83 information, respectively.

OutDir

Create file names in a given directory

## **Description**

The directory is provided by the global variable OutDir.dir, which **must** be set by the user. If OutDir.dir is NULL then just return file.name.

## Usage

```
OutDir(file.name)
```

## **Arguments**

file.name

The name of the that will be prefixed by OutDir.dir.

#### Value

file.name prefixed by OutDir.dir.

PancAdenoCA1000

Create 1000 synthetic pancreatic adenocarcinoma spectra.

# Description

This function generates synthetic tumor spectra with mutational signature prevalence and mutation load similar to pancreatic adenocarcinoma in PCAWG cohort.

## Usage

```
PancAdenoCA1000(
   seed = 191907,
   regress.dir = "data-raw/long.test.regression.data/syn.pancreas/",
   num.syn.tumors = 1000,
   top.level.dir = "../Pan-AdenoCA",
   unlink = FALSE
)
```

## **Arguments**

seed A random seed to use.

regress.dir If not NULL, compare the result to the contents of this directory with a diff.

num.syn.tumors Generate this number of synthetic tumors.

top.level.dir The directory in which to put the output; will be created if necessary.

unlink If TRUE and !is.null(regress.dir), then unlink the result directory if there

are no differences.

#### **Details**

This function replaces data-raw/Create.pancreas.Rmd in GitHub repository steverozen/SynSig. With default arguments, this function generates the same results as data-raw/Create.pancreas.Rmd.

Data set generated by this function can be found at Synapse with Synapse ID: syn18500212.

#### PlotCorrelationScatterplot

Plot scatter plot for correlation between two vectors. PlotCorrelationScatterplot is a wrapper around graphics::plot(), and a function to plot the correlation between two vectors, x and y. These vectors are expected to be exposures of two signatures. It will draw a scatterplot, and it will also print information onto the plot, including correlation between x and y, mean and stdev of x and y, etc.

## Description

Plot scatter plot for correlation between two vectors.

PlotCorrelationScatterplot is a wrapper around graphics::plot(), and a function to plot the correlation between two vectors, x and y. These vectors are expected to be exposures of two signatures.

It will draw a scatterplot, and it will also print information onto the plot, including correlation between x and y, mean and stdev of x and y, etc.

## Usage

```
PlotCorrelationScatterplot(
    x,
    y,
    xlab = NULL,
    ylab = NULL,
    main = NULL,
    optional.remarks = "",
    ...
)
```

## **Arguments**

```
x vector of exposures of main.signature (SBS5 in the paper). The exposures of
main.siganture will be aligned onto x axis.
y vector of exposures of correlated.signature (SBS1 in the paper). The exposures of correlated.signature will be aligned onto y axis.
xlab Label below x axis.
ylab Label below y axis.
```

main Title on the scatterplot. Default: NULL

optional.remarks

Remarks added below the title.

... Other parameters provided to the function graphics::plot().

PlotCorrelationScatterplotForExposures

Plot scatter plot for correlation between exposures of two signatures Plot scatter plot for correlation between exposures of two signatures, SBS1 and SBS5 in this study. PlotCorrelationScatterplotForExposures is a wrapper around PlotCorrelationScatterplot. It lets exposure.counts <- the exposure matrix, and will draw a scatterplot for exposures of two signatures.

## **Description**

Plot scatter plot for correlation between exposures of two signatures

Plot scatter plot for correlation between exposures of two signatures, SBS1 and SBS5 in this study.

PlotCorrelationScatterplotForExposures is a wrapper around PlotCorrelationScatterplot. It lets exposure.counts <- the exposure matrix, and will draw a scatterplot for exposures of two signatures.

## Usage

```
PlotCorrelationScatterplotForExposures(
  pdf.filename,
  main.signature = "SBS5",
  correlated.signature = "SBS1",
  slope.linear,
  exposure.counts,
  xlim = c(0, 4),
  ylim = c(0, 4),
  ...
)
```

#### **Arguments**

pdf.filename Name of the PDF to contain the scatterplots.

main.signature Name of a signature with smaller variance in the log10 space. (Default: "SBS5") correlated.signature

Name of a signature with larger variance in the log10 space. (Default: "SBS1")

slope.linear Average ratio of mutation burden of correlated.signature over mutation burden of main.signature

exposure.counts

Data.frame or matrix storing exposures of two signatures. The exposure.counts object is usually obtained from SynSig::ReadExposure().

xlim, ylim numeric vectors of length 2, giving the x and y coordinates ranges. Default: c(0,4)

... Other parameters provided to the function graphics::plot().

main Title on the scatterplot. Default: NULL

RCCOvary1000 25

RCCOvary1000 Create synthetic spectra based on renal cell carcinoma and ovarian adenocarcinoma	RCCOvary1000	*
--	--------------	---

## **Description**

Creates spectra dataset consists of 500 synthetic renal cell carcinoma (RCC) with high prevalence and mutation load from SBS5 and SBS40 signatures, and 500 synthetic ovarian adenocarcinoma with high prevalence and mutation load from SBS3. This dataset challenges the computational approaches as these three signatures are "flat" signatures hard to be extracted accurately.

## Usage

```
RCCOvary1000(
  seed = 191905,
  unlink = FALSE,
  regress.dir = NULL,
  top.level.dir = "tmp.3.5.40.RCC.and.ovary"
)
```

## **Arguments**

seed A random seed to use.

unlink The directory in which to put the output; will be created if necessary.

regress.dir If not NULL, compare the result to the contents of this directory with a diff.

top.level.dir The directory in which to put the output; will be created if necessary.

#### **Details**

This function Replaces the first part of data-raw/Create.3.5.40. Rmd in GitHub repository steverozen/SynSig. With default arguments, this function generates the same results as the first part of data-raw/Create.3.5.40. Rmd.

The second half of data-raw/Create.3.5.40. Rmd in steverozen/SynSig is replaced by Create.3.5.40. Abstract.

Data set generated by this function can be found at Synapse with Synapse ID: syn18500214.

ReadCatCOMPOSITE Read a COMPOSITE catalog

# Description

A COMPOSITE catalog is an rbind of a 1536 catalog, a DBS catalog, and an ID catalog. This function does not read SignatureAnalyzer signatures as found on the PCAWG7 Synapse web site, but rather as generated by this package for analysis by SignatureAnalyzer.

```
ReadCatCOMPOSITE(path, strict = FALSE)
```

#### **Arguments**

path Path of the file to read from.

strict For compatibility with other ReadCat functions; ignored.

## Value

An in memory matrix corresponding to the contents of the file at path.

## See Also

WriteCatCOMPOSITE

ReadExposure

Read an exposure matrix from a file

## Description

Read an exposure matrix from a file

## Usage

ReadExposure(file, check.names = TRUE)

# Arguments

file CSV file containing an exposure matrix

check.names Passed to utils::read.csv. IMPORTANT: If TRUE this will replace the double

colon in identifiers of the form <tumor\_type>::<sample\_id> with two periods (i.e. <tumor\_type>..<sample\_id>. If check.names is true, generate a warning

if double colons were present.

## Value

Matrix of exposures

ReadSynapseExposure

Read an exposure matrix from a Synapse file

# Description

Read an exposure matrix from a Synapse file

## Usage

ReadSynapseExposure(file)

#### **Arguments**

file

CSV file containing an exposure matrix

RealExposures 27

#### Value

Matrix of exposures

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
```

SAAndSPSynDataOneCAType

Generate parallel synthetic exposures from real SA and SP exposures and signatures

## **Description**

Generate parallel synthetic exposures from real SA and SP exposures and signatures

## Usage

```
SAAndSPSynDataOneCAType(
    sa.real.exp,
    sp.real.exp,
    ca.type,
    num.syn.tumors,
    file.prefix,
    top.level.dir = NULL
)
```

## **Arguments**

```
sa.real.exp Exposure matrix from SignatureAnalyzer.

sp.real.exp Exposure matrix from SigProfiler.

ca.type The type the cancer, which is used in sample identifiers, which SigProfiler expects.

num.syn.tumors Number of synthetic tumors to generate.

file.prefix To explain later.

top.level.dir Specifies the location to generate files.
```

#### Value

A list with the following elements:

- 1. sa.parms The parameters computed from sa.real.exp. This a matrix with a column for each signature and 3 rows:
  - (a) The proportion of tumors with given signature (in sa.real.exp).
  - (b) The mean of the log10 of the number of mutations for a given signature.
  - (c) The standard deviation of log10 of the number of mutations for a given signature.
- 2. sa.syn.exp The synthetic exposures computed from sa.parms.
- 3. sp.parms The parameters computed from sp.real.exp, with rows analogous to the rows in sa.parms.
- 4. sp.syn.exp The synthetic exposures computed from sp.parms.

@details Creates a bunch of files in location governed by top.level.dir. The main rationale for packaging this as one function is to ensure that some conventions regarding file naming are followed.

This function does **not** create the synthetic mutational spectra catalogs but **does** generate the synthetic exposures.

SBS1SBS5datasetNames 29

SBS1SBS5datasetNames	Names	of	datasets	generated	by
	CreateSBS1SBS5CorrelatedSyntheti		${\sf latedSyntheticD}$	ata.	

## Description

 $Names\ of\ datasets\ generated\ by\ {\tt CreateSBS1SBS5CorrelatedSyntheticData}.$ 

## Usage

SBS1SBS5datasetNames

#### **Format**

Character vector specifying names of datasets.

#### Note

S is the initial of "slope", which refers to **SBS1-SBS5 Exposure Ratio**. Rsq is the abbreviation for "Pearson's R squared", which refers to **SBS1-SBS5 Correlation**.

SBS1SBS5parameter	Parameters used to generate synthetic spectra with correlated SBS1 and SBS5 exposures.
-------------------	--

# Description

Parameters used to generate synthetic spectra with correlated SBS1 and SBS5 exposures.

# Usage

SBS1SBS5parameter

## **Format**

A data.frame with parameters for generating the synthetic data. The row names of the data.frame refers to the names of datasets, equals to SBS1SBS5datasetNames.

30 SynSigGen

SynSigGen SynSigGen

#### **Description**

Create catalogs of synthetic mutational spectra for assessing the performance of mutational-signature analysis programs.

#### Overview

The main focus is generating synthetic catalogs of mutational spectra (mutations in tumors) based on known mutational signature profiles and software-inferred exposures (software's estimate on number of mutations induced by mutational signatures in tumors) in the PCAWG7 data. We call this kind of synthetic data broadly "reality-based" synthetic data. The package also has a set of functions that generate random mutational signature profiles and then create synthetic mutational spectra based on these random signature profiles. We call this kind of synthetic data "random" synthetic data, while pointing out that much depends on the distributions from which the random signature profiles and attributions are generated.

## Workflow for generating "reality-based" synthetic mutational spectra

Typical workflow for generating synthetic mutational spectra is as follows.

- 1. Input (based on SignatureAnalyzer or SigProfiler analysis of PCAWG tumors) E, matrix of software-inferred exposures of mutational signatures (signatures x samples) S, mutational signature profiles (mutation types x signatures)
- 2. Obtain distribution parameters from software-inferred exposures

```
P <- GetSynSigParamsFromExposures(E, ...)</pre>
```

3. Generate exposures for synthetic mutational spectra based on P

```
synthetic.exposures <- GenerateSyntheticExposures(P, ...)</pre>
```

4. Generate synthetic mutational spectra by multiplying S and synthetic.exposures, and round the product to the nearest unit:

```
synthetic.spectra <- CreateAndWriteCatalog(S, synthetic.exposures, ...)</pre>
```

## Workflow for generating "random" synthetic mutational spectra

The top-level function for generating "random" synthetic mutational spectra is CreateRandomSyn. It adopts the following steps to generate catalogs of "random" synthetic mutational spectra.

1. Create random mutational signature profiles:

```
S <- CreateRandomMutSigProfiles(...)</pre>
```

2. Generate distribution parameters for exposures of random signatures:

```
P <- CreateMeanAndStdevForSigs(sig.names = colnames(S),...)</pre>
```

3. Create exposures for mutational signatures based on P and other parameters:

```
synthetic.exposures <- CreateRandomExposures(sigs = S, per.sig.mean.and.sd = P)</pre>
```

4. Generate synthetic mutational spectra by multiplying S and synthetic.exposures and round the product to the nearest unit:

```
synthetic.spectra <- NewCreateAndWriteCatalog(S, synthetic.exposures, ...)</pre>
```

SynSigGen 31

## Function for generating "SBS1-SBS5-correlated" synthetic mutational spectra

CreateSBS1SBS5CorrelatedSyntheticData is the top-level function for generating 20 data sets which only have 2 active signatures (SBS1 and SBS5) with positively-correlated exposures.

This function is used for generating synthetic mutational spectra used in paper "Performance of Mutational Signature Software on Correlated Signatures".

## Functions for generating synthetic tumor spectra used in paper *The repertoire of mutational sig*natures in human cancer

The repertoire of mutational signatures in human cancer (https://doi.org/10.1038/s41586-020-1943-3) involves evaluation of performances on two computational approaches (SigProfiler and SignatureAnalyzer) on 11 synthetic data sets (Synapse ID: syn18497223).

- 1. Function PancAdenoCA1000 creates 1000 pancreatic adenocarcinoma spectra data set (syn18500212).
- 2. Script

creates 2,700 synthetic spectra (syn18500213). This data set consists of 9 cancer types each with 300 synthetic tumors:

- bladder transitional cell carcinoma,
- oesophageal adenocarcinoma,
- breast adenocarcinoma,
- lung squamous cell carcinoma,
- · renal cell carcinoma,
- ovarian adenocarcinoma,
- · osteosarcoma,
- · cervical adenocarcinoma and
- · stomach adenocarcinoma.
- 3. Function RCCOvary1000 creates spectra dataset consists of 500 synthetic kidney (RCC) with high prevalence and mutation load from SBS5 and SBS40 signatures, and 500 synthetic ovarian adenocarcinoma with high prevalence and mutation load from SBS3.

#### **Notes:**

- Mutation loads from other mutational signatures (besides SBS3, SBS5, SBS30) also exist in the spectra dataset created by function RCCOvary1000;
- SBS3, SBS5, SBS40 are flat signatures. This dataset challenges the computational approaches on accurately separating these 3 mutational signatures, as mixing SBS5 and SBS40 can get a mutational signature similar to SBS3.
- 4. Function Create.3.5.40. Abstract creates 1000 synthetic spectra all constructed entirely from SBS3, SBS5, and SBS40, using mutational loads modelled on kidney-RCC (SBS5 and SBS40) and ovarian adenocarcinoma (SBS3). Most synthetic spectra have contributions from all three signatures.

32 WriteExposure

WriteCatCOMPOSITE

Write a COMPOSITE catalog or signature matrix to disk

# Description

Write a COMPOSITE catalog or signature matrix to disk

## Usage

```
WriteCatCOMPOSITE(ct, path)
```

## **Arguments**

ct A catalog or signature matrix

path Path to file to write

## See Also

ReadCatCOMPOSITE

WriteExposure

Write exposure matrix to a file

## Description

Write exposure matrix to a file

## Usage

```
WriteExposure(exposure.matrix, file)
```

# Arguments

exposure.matrix

Matrix of exposures

file File to which to write the exposure matrix (as a CSV file)

WriteSynSigParams 33

WriteSynSigParams Write key parameters describing exposures due to a signature to a file. The parameters written are prevalence, mean(log(exposure)), and sd(log(exposure)).

## **Description**

Write key parameters describing exposures due to a signature to a file.

The parameters written are prevalence, mean(log(exposure)), and sd(log(exposure)).

## Usage

```
WriteSynSigParams(
  params,
  file,
  append = FALSE,
  col.names = ifelse(append, FALSE, NA)
)
```

# Arguments

params The parameters to write.

file The path to the file to write.

append Whether to append to or overwrite file if it already exists.

col.names If NA, add column names.

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