Package 'biodosetools'

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Title An R Shiny Application for Biological Dosimetry

Version 3.6.1

Description A tool to perform all different statistical tests and calculations
needed by Biological Dosimetry Laboratories.

License GPL-3

URL <https://biodosetools-team.github.io/biodosetools/>,

<https://github.com/biodosetools-team/biodosetools/>

BugReports <https://github.com/biodosetools-team/biodosetools/issues/>

Depends R (>= 3.5.0)

Imports bsplus, dplyr (>= 1.0.0), ggplot2, magrittr, MASS, maxLik,
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R topics documented:

AIC_from_data   *Calculate AIC (Akaike's 'An Information Criterion')*

Description

Calculate AIC (Akaike's 'An Information Criterion')

Usage

```
AIC_from_data(
  general_fit_coeffs,
  data,
  dose_var = "dose",
  yield_var = "yield",
  fit_link = "identity"
)
```

Arguments

general_fit_coeffs
                Generalised fit coefficients matrix.

data	Data (dose, yield) to calculate AIC from.
dose_var	Name of the dose variable (enquoted).
yield_var	Name of the yield variable (enquoted).
fit_link	A specification for the model link function.

Value

Numeric value of AIC.

---

biodosetools	biodosetools *package*

Description

Shiny App To Be Used By Biological Dosimetry Laboratories

Details

See the README on [GitHub](#)

---

calculate_aberr	*Aberration calculation functions*

Description

Aberration calculation functions

Usage

```
calculate_aberr_power(data, aberr_prefix = "C", power = 1)

calculate_aberr_mean(X, N)

calculate_aberr_var(X, X2, N)

calculate_aberr_disp_index(mean, var)

calculate_aberr_u_value(X, N, mean, var, assessment_u = 1)

init_aberr_table(
  data,
  type = c("count", "case"),
  aberr_module = c("dicentrics", "translocations", "micronuclei")
)
```

Arguments

data	Count or case data.
aberr_prefix	Prefix of the aberrations in the data.
power	Power of aberration.
X	Sum of detected aberrations.
N	Number of cells analysed.
X2	Quadratic sum of detected aberrations.
mean	Mean.
var	Variance.
assessment_u	Expected u-value of the assessment. For a Poisson distribution this should be unity.
type	Type of input data. Either "count" and "case".
aberr_module	Aberration module.

---

calculate_aberr_table   *Calculate aberrations table*

Description

Calculate aberrations table

Usage

```
calculate_aberr_table(
  data,
  type = c("count", "case"),
  aberr_module = c("dicentrics", "translocations", "micronuclei"),
  assessment_u = 1
)
```

Arguments

data	Count or case data.
type	Type of input data. Either "count" and "case".
aberr_module	Aberration module, required for type = "case".
assessment_u	Expected u-value of the assessment. For a Poisson distribution this should be unity.

Value

Data frame containing cell count (N), aberrations (X), and other coefficients (dispersion index, u-value, ...), as well as raw count or case data.

```
calculate_genome_factor
```
Calculate genomic conversion factor

Description

Method based on the paper by Lucas, J. N. et al. (1992). Rapid Translocation Frequency Analysis in Humans Decades after Exposure to Ionizing Radiation. International Journal of Radiation Biology, 62(1), 53-63. <doi:10.1080/09553009214551821>.

Usage

```
calculate_genome_factor(dna_table, chromosomes, colors, sex)
```

Arguments

dna_table	DNA content fractions table. Can be dna_content_fractions_morton or dna_content_table_ihgsc.
chromosomes	Vector of stained chromosomes.
colors	Vector of colors of the stains.
sex	Sex of the individual.

Value

Numeric value of genomic conversion factor.

calculate_model_stats   *Calculate model statistics*

Description

Calculate model statistics

Usage

```
calculate_model_stats(
  model_data,
  fit_coeffs_vec,
  glm_results = NULL,
  fit_algorithm = NULL,
  response = "yield",
  link = c("identity", "log"),
  type = c("theory", "raw"),
  Y = NULL,
  mu = NULL,
  n = NULL,
  npar = NULL,
  genome_factor = NULL,
  calc_type = c("fitting", "estimation")
)
```

Arguments

model_data	Data of the model.
fit_coeffs_vec	Vector of fitting coefficients.
glm_results	Results of glm.
fit_algorithm	String of the algorithm used.
response	Type of response.
link	Fit link.
type	Theoretical or raw glm model statistics.
Y	Y response (required in constraint-maxlik-optimization).
mu	mu response required in constraint-maxlik-optimization).
n	number of parameters (required in constraint-maxlik-optimization).
npar	number of parameters (required in constraint-maxlik-optimization).
genome_factor	Genomic conversion factor used in translocations.
calc_type	Calculation type, either "fitting" or "estimation".

Value

Data frame of model statistics.

```
calculate_trans_rate_manual
```
Calculate manual translocation rate

Description

Calculate manual translocation rate

Usage

```
calculate_trans_rate_manual(cells, genome_factor, expected_aberr_value)
```

Arguments

cells   Number of cells N.

genome_factor   Genomic conversion factor.

expected_aberr_value
                     Expected aberrations.

Value

Numeric value of translocation rate.

```
calculate_trans_rate_sigurdson
```
Calculate Sigurdson's translocation rate

Description

Method based on the paper by Sigurdson, A. J. et al. (2008). International study of factors affecting human chromosome translocations. Mutation Research/Genetic Toxicology and Environmental Mutagenesis, 652(2), 112-121. <doi:10.1016/j.mrgentox.2008.01.005>.

Usage

```
calculate_trans_rate_sigurdson(
  cells,
  genome_factor,
  age_value,
  sex_bool = FALSE,
  sex_value = "none",
  smoker_bool = FALSE,
  ethnicity_value = "none",
  region_value = "none"
)
```

Arguments

`cells`	Number of cells N.
`genome_factor`	Genomic conversion factor.
`age_value`	Age of the individual.
`sex_bool`	If TRUE, `sex_value` will be used.
`sex_value`	Sex of the individual, either "male" of "female".
`smoker_bool`	Whether the individual smokes or not.
`ethnicity_value`	
	Ethnicity of the individual.
`region_value`	Region of the individual.

Value

Numeric value of translocation rate.

`calculate_yield`	*Calculate yield from dose*

Description

Calculate yield from dose

Usage

```
calculate_yield(
  dose,
  type = c("estimate", "lower", "upper"),
  general_fit_coeffs,
  general_fit_var_cov_mat = NULL,
  protracted_g_value = 1,
  conf_int = 0.95
)
```

Arguments

`dose`	Numeric value of dose.
`type`	Type of yield calculation. Can be "estimate", "lower", or "upper".
`general_fit_coeffs`	
	Generalised fit coefficients matrix.
`general_fit_var_cov_mat`	
	Generalised variance-covariance matrix.
`protracted_g_value`	
	Protracted $G(x)$ value.
`conf_int`	Curve confidence interval, 95% by default.

Value

Numeric value of yield.

```
calculate_yield_infimum
```
Calculate theoretical yield infimum

Description

Calculate theoretical yield infimum

Usage

```
calculate_yield_infimum(
  type = c("estimate", "lower", "upper"),
  general_fit_coeffs,
  general_fit_var_cov_mat = NULL,
  conf_int = 0.95
)
```

Arguments

`type`	Type of yield calculation. Can be "estimate", "lower", or "upper".
`general_fit_coeffs`	
	Generalised fit coefficients matrix.
`general_fit_var_cov_mat`	
	Generalised variance-covariance matrix.
`conf_int`	Curve confidence interval, 95% by default.

Value

Numeric value of yield infimum.

`correct_boundary`   *Correct boundary of irradiated fractions to be bounded by 0 and 1*

Description

Correct boundary of irradiated fractions to be bounded by 0 and 1

Usage

```
correct_boundary(x)
```

Arguments

x   Numeric value.

Value

Numeric value in [0, 1] range.

---

correct_conf_int   *Correct yield confidence interval*

Description

Correct yield confidence interval if simple method is required.

Usage

```
correct_conf_int(
  conf_int,
  general_fit_var_cov_mat,
  protracted_g_value = 1,
  type,
  dose = seq(0, 10, 0.2)
)
```

Arguments

conf_int   Confidence interval.

general_fit_var_cov_mat
                        Generalised variance-covariance matrix.

protracted_g_value
                        Protracted $G(x)$ value.

type   Type of yield calculation. Can be "estimate", "lower", or "upper".

dose   Numeric value of dose.

Value

Numeric value of corrected confidence interval.

correct_negative_vals	*Correct negative values*

Description

Correct negative values

Usage

```
correct_negative_vals(x)
```

Arguments

x	Numeric value.

Value

Numeric value corrected to zero if negative.

correct_yield	*Correct yields if they are below the curve*

Description

Correct yields if they are below the curve

Usage

```
correct_yield(
  yield,
  type = "estimate",
  general_fit_coeffs,
  general_fit_var_cov_mat,
  conf_int
)
```

Arguments

yield	Numeric value of yield.
type	Type of yield calculation. Can be "estimate", "lower", or "upper".
general_fit_coeffs	Generalised fit coefficients matrix.
general_fit_var_cov_mat	Generalised variance-covariance matrix.
conf_int	Curve confidence interval.

Value

Numeric value of corrected yield.

---

dna_content_fractions_ihgsc

DNA Content Fractions of Human Chromosomes (IHGSC)

Description

Normalised DNA Content of Human Chromosomes from the International Human Genome Sequencing Consortium.

Usage

```
dna_content_fractions_ihgsc
```

Format

A data frame with 24 rows and 3 variables:

chromosome Chromosome.

fraction_male Normalised content of megabases on male human DNA.

fraction_female Normalised content of megabases on female human DNA.

Details

Last accessed in July 2020.

Source

<https://www.ncbi.nlm.nih.gov/grc/human/data>

---

dna_content_fractions_morton

DNA Content Fractions of Human Chromosomes (Morton 1991)

Description

Normalised DNA Content of Human Chromosomes from Morton, N. E. (1991). Parameters of the human genome. Proceedings of the National Academy of Sciences, 88(17), 7474-7476.

Usage

```
dna_content_fractions_morton
```

Format

A data frame with 24 rows and 3 variables:

chromosome Chromosome.

fraction_male Normalised content of megabases on male human DNA.

fraction_female Normalised content of megabases on female human DNA.

Source

doi:10.1073/pnas.88.17.7474

---

estimate_hetero_mixed_poisson

Heterogeneous dose estimation (Mixed Poisson model)

Description

Method based on the paper by Pujol, M. et al. (2016). A New Model for Biological Dose Assessment in Cases of Heterogeneous Exposures to Ionizing Radiation. Radiation Research, 185(2), 151-162. <doi:10.1667/RR14145.1>.

Usage

```
estimate_hetero_mixed_poisson(
  case_data,
  fit_coeffs,
  fit_var_cov_mat,
  conf_int = 0.95,
  protracted_g_value = 1,
  gamma,
  gamma_error
)
```

Arguments

case_data	Case data in data frame form.
fit_coeffs	Fitting coefficients matrix.
fit_var_cov_mat	
	Fitting variance-covariance matrix.
conf_int	Confidence interval, 95% by default.
protracted_g_value	
	Protracted $G(x)$ value.
gamma	Survival coefficient of irradiated cells.
gamma_error	Error of the survival coefficient of irradiated cells.

Value

List containing estimated mixing proportions data frame, estimated yields data frame, estimated
doses data frame, estimated fraction of irradiated blood data frame, AIC, and `conf_int_*` used.

---

estimate_partial_body_dolphin

Partial-body dose estimation (Dolphin's method)

Description

Method based on the paper by Dolphin, G. W. (1969). Biological Dosimetry with Particular Ref-
erence to Chromosome Aberration Analysis: A Review of Methods. International Atomic En-
ergy Agency (IAEA) Retrieved from `https://inis.iaea.org/search/search.aspx?orig_q=`
`RN:45029080`.

Usage

```
estimate_partial_body_dolphin(
  case_data,
  fit_coeffs,
  fit_var_cov_mat,
  conf_int = 0.95,
  protracted_g_value = 1,
  genome_factor = 1,
  gamma,
  aberr_module = c("dicentrics", "translocations", "micronuclei")
)
```

Arguments

`case_data`	Case data in data frame form.
`fit_coeffs`	Fitting coefficients matrix.
`fit_var_cov_mat`	
	Fitting variance-covariance matrix.
`conf_int`	Confidence interval, 95% by default.
`protracted_g_value`	
	Protracted $G(x)$ value.
`genome_factor`	Genomic conversion factor used in translocations, else 1.
`gamma`	Survival coefficient of irradiated cells.
`aberr_module`	Aberration module.

Value

List containing estimated doses data frame, observed fraction of cells scored which were irradiated,
estimated fraction of irradiated blood data frame, AIC, and `conf_int_*` used.

```
estimate_whole_body_delta
```
Whole-body dose estimation (delta method)

Description

Method based on 2001 manual by the International Atomic Energy Agency (IAEA). Cytogenetic Analysis for Radiation Dose Assessment, Technical Reports Series (2001). Retrieved from `https://www.iaea.org/publications/6303/cytogenetic-analysis-for-radiation-dose-assessment`.

Usage

```
estimate_whole_body_delta(
  case_data,
  fit_coeffs,
  fit_var_cov_mat,
  conf_int = 0.95,
  protracted_g_value = 1,
  aberr_module = c("dicentrics", "translocations", "micronuclei")
)
```

Arguments

`case_data`	Case data in data frame form.
`fit_coeffs`	Fitting coefficients matrix.
`fit_var_cov_mat`	
	Fitting variance-covariance matrix.
`conf_int`	Confidence interval, 95% by default.
`protracted_g_value`	
	Protracted $G(x)$ value.
`aberr_module`	Aberration module.

Value

List containing estimated doses data frame, AIC, and `conf_int` used.

```
estimate_whole_body_merkle
```
Whole-body dose estimation (Merkle's method)

Description

Method based on the paper by Merkle, W. (1983). Statistical methods in regression and calibration analysis of chromosome aberration data. Radiation and Environmental Biophysics, 21(3), 217-233. <doi:10.1007/BF01323412>.

Usage

```
estimate_whole_body_merkle(
  case_data,
  fit_coeffs,
  fit_var_cov_mat,
  conf_int_yield = 0.83,
  conf_int_curve = 0.83,
  protracted_g_value = 1,
  genome_factor = 1,
  aberr_module = c("dicentrics", "translocations", "micronuclei")
)
```

Arguments

case_data	Case data in data frame form.
fit_coeffs	Fitting coefficients matrix.
fit_var_cov_mat	
	Fitting variance-covariance matrix.
conf_int_yield	Confidence interval of the yield, 83% by default.
conf_int_curve	Confidence interval of the curve, 83% by default.
protracted_g_value	
	Protracted $G(x)$ value.
genome_factor	Genomic conversion factor used in translocations, else 1.
aberr_module	Aberration module.

Value

List containing estimated doses data frame, AIC, and conf_int_* used.

---

fit   *Perform dose-effect fitting algorithm*

Description

Perform dose-effect fitting. A generalized linear model (GLM) is used by default, with a maximum likelihood estimation (MLE) as a fallback method.

Usage

```
fit(
  count_data,
  model_formula,
  model_family,
  fit_link = "identity",
  aberr_module = c("dicentrics", "translocations", "micronuclei"),
  algorithm = c("glm", "maxlik")
)
```

Arguments

`count_data`	Count data in data frame form.
`model_formula`	Model formula.
`model_family`	Model family.
`fit_link`	Family link.
`aberr_module`	Aberration module.
`algorithm`	Optional selection of algorithm to be used, either "glm" (for GLM) or "maxlik" (for MLE). By default, "glm" is used, with "maxlik" as a fallback method.

Details

The GLM method is based on the paper by Edwards, A. A. et al. (1979). Radiation induced chromosome aberrations and the Poisson distribution. Radiation and Environmental Biophysics, 16(2), 89-100. <doi:10.1007/BF01323216>.

The MLE method is based on the paperby Oliveira, M. et al. (2016). Zero-inflated regression models for radiation-induced chromosome aberration data: A comparative study. Biometrical Journal, 58(2), 259-279. <doi:10.1002/bimj.201400233>.

Value

List object containing fit results either using GLM or maxLik optimization.

`fit_glm_method`	*Perform GLM (Generalised Linear Model) fitting*

Description

Method based on the paper by Edwards, A. A. et al. (1979). Radiation induced chromosome aberrations and the Poisson distribution. Radiation and Environmental Biophysics, 16(2), 89-100. <doi:10.1007/BF01323216>.

Usage

```
fit_glm_method(
  count_data,
  model_formula,
  model_family = c("automatic", "poisson", "quasipoisson", "nb2"),
  fit_link = "identity",
  aberr_module = c("dicentrics", "translocations", "micronuclei")
)
```

Arguments

`count_data`	Count data in data frame form.
`model_formula`	Model formula.
`model_family`	Model family.
`fit_link`	Family link.
`aberr_module`	Aberration module.

Value

List object containing GLM fit results.

`fit_maxlik_method`	*Perform max-likelihood optimization fitting*

Description

Method based on the paper by Oliveira, M. et al. (2016). Zero-inflated regression models for radiation-induced chromosome aberration data: A comparative study. Biometrical Journal, 58(2), 259-279. <doi:10.1002/bimj.201400233>.

Usage

```
fit_maxlik_method(
  data,
  model_formula,
  model_family = c("automatic", "poisson", "quasipoisson", "nb2"),
  fit_link,
  aberr_module = c("dicentrics", "translocations", "micronuclei")
)
```

Arguments

`data`	Count data.
`model_formula`	Model formula.
`model_family`	Model family.
`fit_link`	Family link.
`aberr_module`	Aberration module.

Value

List object containing maxLik fit results.

---

get_deltamethod_std_err

Get standard errors using delta method

Description

Delta method for approximating the standard error of a transformation $g(X)$ of a random variable $X = (x1, x2, ...)$, given estimates of the mean and covariance matrix of X.

Usage

```
get_deltamethod_std_err(
  fit_is_lq,
  variable = c("dose", "fraction_partial", "fraction_hetero"),
  mean_estimate,
  cov_estimate,
  protracted_g_value = NA,
  d0 = NA
)
```

Arguments

`fit_is_lq`	Whether the fit is linear quadratic (`TRUE`) or linear (`FALSE`).
`variable`	Variable resulting of the transformation $g(X)$.
`mean_estimate`	The estimated mean of X.
`cov_estimate`	The estimated covariance matrix of X.
`protracted_g_value`	
	Protracted $G(x)$ value.
`d0`	Survival coefficient of irradiated cells.

Value

Numeric value containing the standard error of the dose estimate.

---

include_help   *Include Markdown help*

Description

Include Markdown help

Usage

```
include_help(...)
```

Arguments

...	Character vector specifying directory and or file to point to inside the current package.

---

load_rmd_report   *Load RMarkdown report*

Description

Load RMarkdown report

Usage

```
load_rmd_report(...)
```

Arguments

...	Character vector specifying directory and or file to point to inside the current package.

---

plot_estimated_dose_curve
                    Plot dose estimation curve

Description

Plot dose estimation curve

Usage

```
plot_estimated_dose_curve(
  est_doses,
  fit_coeffs,
  fit_var_cov_mat,
  protracted_g_value = 1,
  conf_int_curve,
  aberr_name
)
```

Arguments

`est_doses`	List of dose estimations results from `estimate_*()` family of functions.
`fit_coeffs`	Fitting coefficients matrix.
`fit_var_cov_mat`	
	Fitting variance-covariance matrix.
`protracted_g_value`	
	Protracted $G(x)$ value.
`conf_int_curve`	Confidence interval of the curve.
`aberr_name`	Name of the aberration to use in the y-axis.

Value

ggplot2 object.

`plot_fit_dose_curve`   *Plot fit dose curve*

Description

Plot fit dose curve

Usage

```
plot_fit_dose_curve(fit_results_list, aberr_name)
```

Arguments

`fit_results_list`	
	List of fit results.
`aberr_name`	Name of the aberration to use in the y-axis.

Value

ggplot2 object.

---

prepare_maxlik_count_data
Prepare count data for max-likelihood optimization fitting

Description

Prepare count data for max-likelihood optimization fitting

Usage

```
prepare_maxlik_count_data(
  count_data,
  model_formula,
  aberr_module = c("dicentrics", "translocations", "micronuclei")
)
```

Arguments

count_data	Count data in data frame form.
model_formula	Model formula.
aberr_module	Aberration module.

Value

Data frame of parsed count data.

---

project_yield   *Project yield into dose-effect fitting curve*

Description

Project yield into dose-effect fitting curve

Usage

```
project_yield(
  yield,
  type = "estimate",
  general_fit_coeffs,
  general_fit_var_cov_mat = NULL,
  protracted_g_value = 1,
  conf_int = 0.95
)
```

Arguments

`yield`	Yield to be projected.
`type`	Type of yield calculation. Can be "estimate", "lower", or "upper".
`general_fit_coeffs`	
	Generalised fit coefficients matrix.
`general_fit_var_cov_mat`	
	Generalised variance-covariance matrix.
`protracted_g_value`	
	Protracted $G(x)$ value.
`conf_int`	Curve confidence interval, 95% by default.

Value

Numeric value of projected dose.

`protracted_g_function`   *Calculate protracted function* $G(x)$

Description

Calculation based on the paper by Lea, D. E. & Catcheside, D. G. (1942). The mechanism of the induction by radiation of chromosome aberrations in*Tradescantia*. Journal of Genetics, 44(2-3), 216-245. <doi:10.1007/BF02982830>.

Usage

```
protracted_g_function(time, time_0 = 2)
```

Arguments

`time`	Time over which the irradiation occurred.
`time_0`	The mean lifetime of the breaks, which has been shown to be on the order of ~ 2 hours (default value).

Value

Numeric value of $G(x)$.

---

run_app   *Run the Shiny Application*

Description

Run the Shiny Application

Usage

```
run_app(...)
```

Arguments

...   A series of options to be used inside the app.

Value

Used for side-effect.

R_factor   *Calculate R regression confidence factor*

Description

Calculate R regression confidence factor depending on selected confidence interval and type of fit.

Usage

```
R_factor(general_fit_coeffs, conf_int = 0.95)
```

Arguments

general_fit_coeffs
                Generalised fit coefficients matrix.

conf_int   Confidence interval, 95% by default.

Value

Numeric value of R regression confidence factor.

yield_error_fun   *Calculate yield error*

Description

Calculate yield error using Merkle's method

Usage

```
yield_error_fun(dose, general_fit_var_cov_mat = NULL, protracted_g_value = 1)
```

Arguments

dose   Numeric value of dose.

general_fit_var_cov_mat

Generalised variance-covariance matrix.

protracted_g_value

Protracted $G(x)$ value.

Value

Numeric value of yield error.

yield_fun   *Calculate yield*

Description

Calculate yield

Usage

```
yield_fun(dose, general_fit_coeffs, protracted_g_value = 1)
```

Arguments

dose   Numeric value of dose.

general_fit_coeffs

Generalised fit coefficients matrix.

protracted_g_value

Protracted $G(x)$ value.

Value

Numeric value of yield.

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