Package: xlink (via r-universe)

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Title Genetic Association Models for X-Chromosome SNPS on Continuous, Binary and Survival Outcomes

Version 1.0.1

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URL https://github.com/qiuanzhu/xlink

BugReports https://github.com/qiuanzhu/xlink/issues

Description The expression of X-chromosome undergoes three possible biological processes: X-chromosome inactivation (XCI), escape of the X-chromosome inactivation (XCI-E),and skewed X-chromosome inactivation (XCI-S). To analyze the X-linked genetic association for phenotype such as continuous, binary, and time-to-event outcomes with the actual process unknown, we propose a unified approach of maximizing the likelihood or partial likelihood over all of the potential biological processes. The methods are described in Wei Xu, Meiling Hao (2017) <doi:10.1002/gepi.22097>. And also see Dongxiao Han, Meiling Hao, Lianqiang Qu, Wei Xu (2019) <doi:10.1177/0962280219859037>.

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Encoding UTF-8

LazyData true

Depends R (>= 3.1.0)

Imports survival (>= 2.41.3)

RoxygenNote 6.1.1

Suggests knitr, rmarkdown, testthat

VignetteBuilder knitr

Repository https://qiuanzhu.r-universe.dev

RemoteUrl https://github.com/qiuanzhu/xlink

RemoteRef HEAD

RemoteSha 068ac3c84461eea5a6b3c7ad330113f62c224989

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fit_all_models	*Model fitting results for each SNP considering as XCI, XCI-E and XCI-S type*

Description

`fit_all_models` returns model fitting results for each SNP understanding as XCI, XCI-E and XCI-S type respectively. Model comparison results is provided by using AIC as a criterion.

Usage

```
fit_all_models(resp, os, ostime, snp, gender, male, female, covars, model,
  data)
```

Arguments

resp	Response variable for continuous or binary model fitting.
os	Survival indicator, 1 for death, 0 for censoring.
ostime	Duration time of survival.
snp	Single SNP name.
gender	Gender variable.
male	Male indicator in gender variable.
female	Female indicator in gender variable.
covars	Covariates list.
model	Fitting model type. For 'linear', fitting linear model. For 'binary', fitting logistic regression model. For 'survival', fitting survival model.
data	Data set.

Value

It returns estimated parameters, confidence interval and P value for each variable. Baseline model and full model maximum likelihood estimation are provided.

See Also

lm{stats} for linear model, glm{stats} for logistic regression model, and coxph{survival} for survival model.

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fit_XCI_E_model   *Model fitting results for each SNP considering as XCI-E type*

Description

fit_XCI_E_model returns model fitting results for each SNP understanding as XCI-E type.

Usage

```
fit_XCI_E_model(resp, os, ostime, snp, gender, male, female, covars, model,
  data)
```

Arguments

resp	Response variable for continuous or binary model fitting.
os	Survival indicator, 1 for death, 0 for censoring.
ostime	Duration time of survival.
snp	Single SNP name.
gender	Gender variable.
male	Male indicator in gender variable.
female	Female indicator in gender variable.
covars	Covariates list.
model	Fitting model type. For 'linear', fitting linear model. For 'binary', fitting logistic regression model. For 'survival', fitting survival model.
data	Data set.

Value

It returns estimated parameters, confidence interval and P value for each variable. Baseline model and full model maximum likelihood estimation are provided.

See Also

lm{stats} for linear model, glm{stats} for logistic regression model, and coxph{survival} for survival model.

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fit_XCI_model   *Model fitting results for each SNP considering as XCI type*

Description

`fit_XCI_model` returns model fitting results for each SNP understanding as XCI type.

Usage

```
fit_XCI_model(resp, os, ostime, snp, gender, male, female, covars, model,
    data)
```

Arguments

resp	Response variable for continuous or binary model fitting.
os	Survival indicator, 1 for death, 0 for censoring.
ostime	Duration time of survival.
snp	Single SNP name.
gender	Gender variable.
male	Male indicator in gender variable.
female	Female indicator in gender variable.
covars	Covariates list.
model	Fitting model type. For 'linear', fitting linear model. For 'binary', fitting logistic regression model. For 'survival', fitting survival model.
data	Data set.

Value

It returns estimated parameters, confidence interval and P value for each variable. Baseline model and full model maximum likelihood estimation are provided.

See Also

`lm`{stats} for linear model, `glm`{stats} for logistic regression model, and `coxph`{survival} for survival model.

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infor_table *Information table.*

Description

`infor_table` returns information table of estimated coefficients/hazard ratio, confidence interval and P value.

Usage

```
infor_table(x, snp, covar_n, MAF_value, model)
```

Arguments

x	An output from continuous/binary/survival model.
snp	Single SNP name.
covar_n	Covariate names.
MAF_value	A minimum value of minor allele frequency.
model	Model type.

Value

Information table. If linear or binary model is chosen, it returns estimated coefficients, confidence interval and P value. If survival model is chosen, it returns hazard ratio, confidence interval and P value.

MAF *Select SNP by MAF.*

Description

MAF returns SNPs with higher MAF than default value.

Usage

```
MAF(snp, gender, male, MAF_v, data)
```

Arguments

snp	SNP name.
gender	gender variable.
male	male information.
MAF_v	minimum MAF value.
data	a dataset.

Rdata	*Simulation data for Genetic association models for X-chromosome SNPS*

Description

A simulated dataset containing 400 observations. The variables list as follows:

Usage

```
data(Rdata)
```

Format

A data frame with 400 rows and 17 variables.

Details

- ID. Identification number.
- OS. Survival indicator, 1 for death, 0 for censoring.
- OS_time. Duration time of survival.
- gender. Binary value 0,1 with P(x=1)=0.5 and hazard ratio is 1.
- Age. Uniform distribution in [20,80] and hazard ratio is 1.02.
- Smoking. Binary value 0,1 with P(x=1)=0.3 and hazard ratio is 1.2.
- Treatment. Binary value 0,1 with P(X=1)=0.3 and hazard ratio is 1.2.
- snp_1. True type in coxph model is 'XCI', minor allele frequency is 0.2, hazard ratio is 1.5.
- snp_2. True type in coxph model is 'XCI-E', minor allele frequency is 0.3, hazard ratio is 1.5.
- snp_3. True type in coxph model is 'XCI-S', minor allele frequency is 0.4, hazard ratio is 1.5.
- snp_4. True type in coxph model is 'XCI', minor allele frequency is 0.3, hazard ratio is 1.
- snp_5. True type in coxph model is 'XCI-E', minor allele frequency is 0.1, hazard ratio is 1.
- snp_6. True type in coxph model is 'XCI', minor allele frequency is 0.2, hazard ratio is 1.
- snp_7. True type in coxph model is 'XCI', minor allele frequency is 0.15, hazard ratio is 1.
- snp_8. True type in coxph model is 'XCI-E', minor allele frequency is 0.1, hazard ratio is 1.
- snp_9. True type in coxph model is 'XCI', minor allele frequency is 0.2, hazard ratio is 1.
- snp_10. True type in coxph model is 'XCI', minor allele frequency is 0.15, hazard ratio is 1.

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select_output | *Selected results table by P value*

Description

select_output returns selected SNP information by P value.

Usage

```
select_output(input, pv_thold = 1)
```

Arguments

input | Input results from xlink fit.
pv_thold | P value threshold for output.

Value

It returns estimated parameters, confidence interval, P value, MAF and Best model information.

See Also

xlink_fit{xlink} for input results.

Examples

```
Covars<-c("Age","Smoking","Treatment")
SNPs<-c("snp_1","snp_2","snp_3")
result<-xlink_fit(os="OS",ostime ="OS_time",snps=SNPs,gender ="gender",covars=Covars,
                  option =list(type="all",MAF_v=0.05), model="survival", data = Rdata)
select_output(input=result,pv_thold=10^-5)
```

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xlink | *xlink: A package for genetic association models for X-chromosome SNPS on continuous, binary and survival outcomes.*

Description

The expression of X-chromosome undergoes three possible biological processes: X-chromosome inactivation (XCI), escape of the X-chromosome inactivation (XCI-E),and skewed X-chromosome inactivation (XCI-S). To analyze the X-linked genetic association for phenotype such as continuous, binary, and time-to-event outcomes with the actual process unknown, we propose a unified approach of maximizing the likelihood or partial likelihood over all of the potential biological processes.

xlink functions

xlink_fit, select_output.

References

Xu, Wei, and Meiling Hao. 'A unified partial likelihood approach for X-chromosome association on time-to-event outcomes.' Genetic epidemiology 42.1 (2018): 80-94.

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xlink_fit	*Genetic association models for X-chromosome SNPs on continuous, binary and survival outcomes*

Description

xlink_fit returns model fitting results for each SNP with the covariates.

Usage

```
xlink_fit(resp = c(), os = c(), ostime = c(), snps = c(),
  gender = c(), covars = c(), option = c(type = c(), male = c(),
  female = c(), MAF_v = 0), model = c(), data)
```

Arguments

resp	Response variable for continuous or binary model fitting.
os	Survival indicator, 1 for death, 0 for censoring.
ostime	Duration time of survival.
snps	SNP name list for model fitting.
gender	Gender information must be included in the data. Default setting is male=1 and female=0. If not as default setting, please provide male and female information in the option.
covars	Covariates list if needed.
option	There are three options. First, type has default 'all', which provides model fitting results for each SNP understanding as 'XCI', 'XCI-E' and 'XCI-S' type respectively. If type is chosen as 'XCI' or 'XCI-E', all the SNPS consider as 'XCI' or 'XCI-E' type in corresponding model. Secondly, if gender is not as default gender setting (male=1,female=0), male and female information should be provided here.The third one, MAF_v is the low bound of the minimum allele frequency, the SNP MAF below this value will not be used in xlink_fit.
model	Fitting model. For 'linear', fitting linear model. For 'binary', fitting logistic regression model. For 'survival', fitting survival model.
data	Data set.

Value

It returns estimated parameters, confidence interval and P value for each variable in the chosen model. The baseline and full model maximum likelihood estimation are provided. If type is 'all', best model choice is provided by using AIC as an benchmark.

References

Xu, Wei, and Meiling Hao. 'A unified partial likelihood approach for X-chromosome association on time-to-event outcomes.' Genetic epidemiology 42.1 (2018): 80-94.

Han, D., Hao, M., Qu, L., & Xu, W. (2019). A novel model for the X-chromosome inactivation association on survival data. Statistical Methods in Medical Research.

See Also

lm{stats} for linear model, glm{stats} for logistic regression model, and coxph{survival} for survival model.

Examples

```
Covars<-c("Age","Smoking","Treatment")
SNPs<-c("snp_1","snp_2","snp_3")
xlink_fit(os="OS",ostime."OS_time",snps=SNPs,gender="gender",covars=Covars,
          option =list(MAF_v=0.05),model="survival",data = Rdata)
xlink_fit(resp="OS_time",snps=SNPs,gender="gender",option =list(type="XCI",MAF_v=0.05),
          model="linear",data = Rdata)
```

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