Package: ACEt (via r-universe)

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Type Package

Title Estimating Dynamic Heritability and Twin Model Comparison

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Description Twin models that are able to estimate the dynamic behaviour of the variance components in the classical twin models with respect to age using B-splines and P-splines.

License GPL (>= 3)

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Imports Rcpp (>= 0.11.1), splines, MASS, methods

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`ACEt-package` *Estimating Age Modification Effect on Genetic and Environmental Variance Components in Twin Models*

Description

The package implements two novel twin models that are able to estimate dynamic behaviour of the variance components in the classical twin models with respect to age or other covariates such as calendar year.

Details

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Type:	Package
Version:	1.8.2
Date:	2022-09-23
License:	GPL

Author(s)

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References

He, L., Sillanpää, M.J., Silventoinen, K., Kaprio, J. and Pitkäniemi, J., 2016. Estimating Modifying Effect of Age on Genetic and Environmental Variance Components in Twin Models. Genetics, 202(4), pp.1313-1328.

He, L., Pitkäniemi, J., Silventoinen, K. and Sillanpää, M.J., 2017. ACEt: An R package for estimating dynamic heritability and comparing twin models. Behavior Genetics, 47(6), pp.620-641.

Examples

```
# data(data_ace)

# AtCtEt(data_ace$mz, data_ace$dz, mod=c('d','d','c'), knot_a = 5, knot_c = 4)
# AtCtEtp(data_ace$mz, data_ace$dz, knot_a = 6, mod=c('d','l','c'))
```

`acetp_mcmc` *Compute CIs for the ACE(t)-p model*

Description

Compute the posterior mean and CIs for the ACE(t)-p model using the MCMC methods

Usage

```
acetp_mcmc(acetp, iter_num = 10000, sd = 0.1, burnin = 1000)
```

Arguments

`acetp`	An object from the 'AtCtEtp' function.
`iter_num`	The number of the iterations in the MCMC procedure.
`sd`	The standard error of the normal proposal distribution in the MCMC algorithm. The default value is 0.1.
`burnin`	The number of burn-in, which must be smaller than the number of iteration.

Value

`beta_a_mc`	The estimates of the spline coefficients for the A component based on the posterior mean from the MCMC method.
`beta_c_mc`	The estimates of the spline coefficients for the C component based on the posterior mean from the MCMC method.
`beta_e_mc`	The estimates of the spline coefficients for the E component based on the posterior mean from the MCMC method.
`cov_mc`	The posterior covariance matrix of the estimates of the spline coefficients.
`knots_a`	A vector of the knot positions for the A component.
`knots_c`	A vector of the knot positions for the C component.
`knots_e`	A vector of the knot positions for the E component.

Author(s)

Liang He

References

He, L., Sillanpää, M.J., Silventoinen, K., Kaprio, J. and Pitkäniemi, J., 2016. Estimating Modifying Effect of Age on Genetic and Environmental Variance Components in Twin Models. Genetics, 202(4), pp.1313-1328.

Examples

```
# data(data_ace)

# result <- AtCtEp(data_ace$mz, data_ace$dz, knot_a = 7, knot_c = 7)
# result_mc <- acetp_mcmc(result, iter_num=10000, burnin = 500)
```

`AtCtEt` *Fitting the ACE(t) model*

Description

The ACE(t) model with the A, C and E variance components as functions with respect to age modelled by B-splines.

Usage

```
AtCtEt(data_m, data_d, mod = c('d','d','d'), knot_a = 5, knot_c = 5, knot_e = 5,
loc = c('e','e','e'), boot=FALSE, num_b = 100, init = rep(0,3), robust = 0)
```

Arguments

`data_m`	An N_m x 3 data matrix for MZ twins. N_m is the number of MZ twin pairs. The first two columns are centered trait values (i.e. the mean should be zero) and the third column is age (or other covariates).
`data_d`	An N_d x 3 data matrix for DZ twins. N_d is the number of DZ twin pairs. The first two columns are centered trait values (i.e. the mean should be zero) and the third column is age (or other covariates).
`mod`	A character vector of length 3. Each element specifies the function for the A, C or E component respectively. The A and C components can be 'd'(dynamic), 'c'(constant) or 'n'(NA). The E component can only be 'd' or 'c'. Thus, $model = c('c','c','c')$ is corresponding to the classical ACE model.
`knot_a`	The number of interior knots of the B-spline for the A component, which must be no less than 3. The default value is 5.
`knot_c`	The number of interior knots of the B-spline for the C component, which must be no less than 3. The default value is 5.
`knot_e`	The number of interior knots of the B-spline for the E component, which must be no less than 3. The default value is 5.
`loc`	A 1x3 character vector indicating how to place knots for each component: evenly ("e") or quantile-based ("q"). The default value is "e".
`boot`	A logical indicator of whether to use the bootstrap method to calculate the confidence interval. The default is FALSE.
`num_b`	The number of replicates when the bootstrap method is used (i.e. $boot = TRUE$). The default value is 100.
`init`	A 3x1 vector of the initial values for the optimization. The default values are 1.
`robust`	An integer indicating the number of different initial values that the function will randomly generate and try in the optimization. The default value is 0.

Details

If the variance is close to the boundary (0), it is better to use the bootstrap method to get the CIs. The optimization algorithm may sometimes end up with a local minimum. It is recommended to try different random initial values by setting 'robust'.

Value

n_beta_a	The number of spline coefficients for the A component.
n_beta_c	The number of spline coefficients for the C component.
n_beta_e	The number of spline coefficients for the E component.
beta_a	The estimated spline coefficients (if the model parameter is 'd') or variance (if the model parameter is 'c') of the A component.
beta_c	The estimated spline coefficients (if the model parameter is 'd') or variance (if the model parameter is 'c') of the C component.
beta_e	The estimated spline coefficients (if the model parameter is 'd') or variance (if the model parameter is 'c') of the E component.
hessian_ap	The approximate numerical observed information matrix from the quasi-Newton algorithm.
hessian	The expected information matrix calculated analytically.
con	An indicator of convergence of the optimization algorithm. An integer code 0 indicates successful completion. See 'optim' for more details.
lik	The minus log-likelihood.
knots_a	A vector of the knot positions for the A component.
knots_c	A vector of the knot positions for the C component.
knots_e	A vector of the knot positions for the E component.
boot	A list containing pointwise CIs estimated from the bootstrap method when $boot = TRUE$

Author(s)

Liang He

References

He, L., Sillanpää, M.J., Silventoinen, K., Kaprio, J. and Pitkäniemi, J., 2016. Estimating Modifying Effect of Age on Genetic and Environmental Variance Components in Twin Models. Genetics, 202(4), pp.1313-1328.

He, L., Pitkäniemi, J., Silventoinen, K. and Sillanpää, M.J., 2017. ACEt: An R package for estimating dynamic heritability and comparing twin models. Behavior Genetics, 47(6), pp.620-641.

Examples

```
data(data_ace)

result <- AtCtEt(data_ace$mz, data_ace$dz, mod=c('d','d','c'))
```

`AtCtEtp` *Fitting the ACE(t)-p model*

Description

The ACE(t)-p model with the A, C and E variance components as functions with respect to age modelled by P-splines.

Usage

```
AtCtEtp(data_m, data_d, knot_a = 8, knot_c = 8, knot_e = 8, eps = 0.1,
mod=c('d','d','d'), robust = 0)
```

Arguments

`data_m`	An N_m x 3 data matrix for MZ twins. N_m is the number of MZ twin pairs. The first two columns are centered trait values (i.e. the mean should be zero) and the third column is age (or other covariates).
`data_d`	An N_d x 3 data matrix for DZ twins. N_d is the number of DZ twin pairs. The first two columns are centered trait values (i.e. the mean should be zero) and the third column is age (or other covariates).
`knot_a`	The number of interior knots of the B-spline for the A component. The default value is 8.
`knot_c`	The number of interior knots of the B-spline for the C component. The default value is 8.
`knot_e`	The number of interior knots of the B-spline for the E component. The default value is 8.
`eps`	Tolerance for convergence of the EM algorithm iterations. The default value is 0.1.
`mod`	A character vector of length 3. Each element specifies the function for the A, C or E component respectively. The components can be 'd'(dynamic), 'c'(constant) or 'l'(linear). The default is c('d','d','d').
`robust`	An integer indicating the number of different initial values that the function will randomly generate and try in the optimization. The default value is 0.

Details

When the 'mod' argument for a component is 'd'(dynamic), the corresponding 'beta' is the spline coefficients. When the 'mod' argument for a component is 'l'(linear), the corresponding 'beta' is a vector of two values, the exponential of which (exp(beta)) are the variances at the minimum and maximum age (or other covariates) provided in the data. When the 'mod' argument for a component is 'c'(constant), the corresponding 'beta' has only one value and exp(beta) is the variance.

Value

var_b_a	The estimated variance for the penalized coefficient for the A components.
var_b_c	The estimated variance for the penalized coefficient for the C components.
var_b_e	The estimated variance for the penalized coefficient for the E components.
beta_a	The estimated spline coefficients of the A component. See 'details' for more information.
beta_c	The estimated spline coefficients of the C component. See 'details' for more information.
beta_e	The estimated spline coefficients of the E component. See 'details' for more information.
con	An indicator of convergence of the optimization algorithm. An integer code 0 indicates successful completion. See 'optim' for more details.
lik	The minus log marginal likelihood.
knot_a	A vector of the knot positions for the A component.
knot_c	A vector of the knot positions for the C component.
knot_e	A vector of the knot positions for the E component.

Author(s)

Liang He

References

He, L., Sillanpää, M.J., Silventoinen, K., Kaprio, J. and Pitkäniemi, J., 2016. Estimating Modifying Effect of Age on Genetic and Environmental Variance Components in Twin Models. Genetics, 202(4), pp.1313-1328.

He, L., Pitkäniemi, J., Silventoinen, K. and Sillanpää, M.J., 2017. ACEt: An R package for estimating dynamic heritability and comparing twin models. Behavior Genetics, 47(6), pp.620-641.

Examples

```
# data(data_ace)

# result <- AtCtEtp(data_ace$mz, data_ace$dz, knot_e = 7, knot_c = 5, mod=c('d','d','d'))
```

`AtDtEt` *Fitting the ADE(t) model*

Description

The ADE(t) model with the A, D and E variance components as functions with respect to age modelled by B-splines.

Usage

```
AtDtEt(data_m, data_d, mod = c('d','d','d'), knot_a = 5, knot_d = 5, knot_e = 5,
loc = c('e','e','e'), boot=FALSE, num_b = 100, init = rep(0,3), robust = 0)
```

Arguments

data_m	An N_m x 3 data matrix for MZ twins. N_m is the number of MZ twin pairs. The first two columns are centered trait values (i.e. the mean should be zero) and the third column is age (or other covariates).
data_d	An N_d x 3 data matrix for DZ twins. N_d is the number of DZ twin pairs. The first two columns are centered trait values (i.e. the mean should be zero) and the third column is age (or other covariates).
mod	A character vector of length 3. Each element specifies the function for the A, D or E component respectively. The A and D components can be 'd'(dynamic), 'c'(constant) or 'n'(NA). The E component can only be 'd' or 'c'. Thus, $model = c('c','c','c')$ is corresponding to the classical ADE model.
knot_a	The number of interior knots of the B-spline for the A component, which must be no less than 3. The default value is 5.
knot_d	The number of interior knots of the B-spline for the D component, which must be no less than 3. The default value is 5.
knot_e	The number of interior knots of the B-spline for the E component, which must be no less than 3. The default value is 5.
loc	A 1x3 character vector indicating how to place knots for each component: evenly ("e") or quantile-based ("q"). The default value is "e".
boot	A logical indicator of whether to use the bootstrap method to calculate the confidence interval. The default is FALSE.
num_b	The number of replicates when the bootstrap method is used (i.e. $boot = TRUE$). The default value is 100.
init	A 3x1 vector of the initial values for the optimization. The default values are 1.
robust	An integer indicating the number of different initial values that the function will randomly generate and try in the optimization. The default value is 0.

Details

If the variance is close to the boundary (0), it is better to use the bootstrap method to get the CIs. The optimization algorithm may sometimes end up with a local minimum. It is recommended to try different random initial values by setting 'robust'.

Value

n_beta_a	The number of spline coefficients for the A component.
n_beta_d	The number of spline coefficients for the D component.
n_beta_e	The number of spline coefficients for the E component.
beta_a	The estimated spline coefficients (if the model parameter is 'd') or variance (if the model parameter is 'c') of the A component.

beta_d	The estimated spline coefficients (if the model parameter is 'd') or variance (if the model parameter is 'c') of the D component.
beta_e	The estimated spline coefficients (if the model parameter is 'd') or variance (if the model parameter is 'c') of the E component.
hessian_ap	The approximate numerical observed information matrix from the quasi-Newton algorithm.
hessian	The expected information matrix calculated analytically.
con	An indicator of convergence of the optimization algorithm. An integer code 0 indicates successful completion. See 'optim' for more details.
lik	The minus log-likelihood.
knots_a	A vector of the knot positions for the A component.
knots_d	A vector of the knot positions for the D component.
knots_e	A vector of the knot positions for the E component.
boot	A list containing pointwise CIs estimated from the bootstrap method when $boot = TRUE$

Author(s)

Liang He

References

He, L., Sillanpää, M.J., Silventoinen, K., Kaprio, J. and Pitkäniemi, J., 2016. Estimating Modifying Effect of Age on Genetic and Environmental Variance Components in Twin Models. Genetics, 202(4), pp.1313-1328.

He, L., Pitkäniemi, J., Silventoinen, K. and Sillanpää, M.J., 2017. ACEt: An R package for estimating dynamic heritability and comparing twin models. Behavior Genetics, 47(6), pp.620-641.

Examples

```
data(data_ace)

result <- AtDtEt(data_ace$mz, data_ace$dz, mod=c('d','d','c'))
```

---

data_ace *Example data for the ACEt models*

Description

This is an example dataset consisting of traits and ages for MZ and DZ twins.

Usage

```
data(data_ace)
```

Format

The format is: mz: a matrix of simulated data for MZ twins. dz: a matrix of simulated data for DZ twins.

Examples

```
data(data_ace)
```

`plot_acet` *Plot variance curves for various ACE(t) or ACE(t)-p models with 95% CIs*

Description

Plot variance curves or a heritability curve (with 95% CIs) of the A, C and E components with respect to age modelled by B-splines or P-splines.

Usage

```
plot_acet(acet, boot = FALSE, heri = FALSE, xlab, ylab, main, col, legend = TRUE)
```

Arguments

`acet`	An object obtained from the B-splines or P-splines functions. For the P-splines functions, an object from the MCMC method must be used.
`boot`	An logical indicator of whether the confidence bands estimated from the bootstrap method are plotted. The default is FALSE. Only available for the AtCtEt model.
`heri`	A logical indicator of whether to plot the dynamic heritability curve. The default is FALSE.
`xlab`	The 'xlab' argument in the plot funciton. The default is 'Age'.
`ylab`	The 'ylab' argument in the plot funciton. The default is 'Variance'.
`main`	The 'main' argument in the plot funciton. The default is 'Variance curves of the A, C, and E components' for variances and 'Dynamic heritability' for heritability.
`col`	The 'col' argument in the plot funciton.
`legend`	An logical indicator of whether the default legend is plotted.

Author(s)

Liang He

References

He, L., Sillanpää, M.J., Silventoinen, K., Kaprio, J. and Pitkäniemi, J., 2016. Estimating Modifying Effect of Age on Genetic and Environmental Variance Components in Twin Models. Genetics, 202(4), pp.1313-1328.

Examples

```
# data(data_ace)
# result <- AtCtEtp(data_ace$mz, data_ace$dz, knot_a = 5, knot_c = 4)
# result_mc <- acetp_mcmc(result, iter_num=10000, burnin = 500)
# plot_acet(result_mc)

# result <- AtCtEt(data_ace$mz, data_ace$dz, mod=c('d','c','c'), knot_a = 9)
# plot_acet(result)
```

`test_acetp` *Hypothesis testing of the ACE(t)-p models*

Description

Comparison of different ACE(t)-p models to test a linear or a constant variance component.

Usage

```
test_acetp(acetp, comp, sim = 100, robust = 0, pe = TRUE, verbose = TRUE)
```

Arguments

`acetp`	An object from the AtCtEtp function.
`comp`	The component for which linearity or constancy is tested. This component must be specified as splines or linear in the AtCtEtp function.
`sim`	The number of the bootstrap resampling for approximating the null distribution when testing linearity.
`robust`	An integer indicating the number of different initial values that the function will randomly generate and try in the optimization. The default value is 0.
`pe`	A logical argument indicating whether to use penalized spline model to test linearity. The default value is TRUE.
`verbose`	A logical argument indicating whether to print testing information and results. The default value is TRUE.

Details

When pe=TRUE, the linearity is tested under a p-spline framework in which an LRT is performed. Otherwise, a χ^2 test is performed for linearity under a spline framework without penalty on smoothness.

Value

`p`	The p-value for the test.
`llr`	The LRT statistic for testing linearity.
`llr_sim`	The simulated null distribution of the LRT statistic for testing linearity.
`chisq`	The chisq statistic for testing a constant or linearity.

Author(s)

Liang He

References

He, L., Sillanpää, M.J., Silventoinen, K., Kaprio, J. and Pitkäniemi, J., 2016. Estimating Modifying Effect of Age on Genetic and Environmental Variance Components in Twin Models. Genetics, 202(4), pp.1313-1328.

He, L., Pitkäniemi, J., Silventoinen, K. and Sillanpää, M.J., 2017. ACEt: An R package for estimating dynamic heritability and comparing twin models. Behavior Genetics, 47(6), pp.620-641.

Examples

```
# data(data_ace)

# result <- AtCtEtp(data_ace$mz, data_ace$dz, knot_e = 7, knot_c = 5, mod=c('d','d','l'))
# re <- test_acetp(result, comp='e')
```

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