Package 'POINT'

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Type Package

Title Protein Structure Guided Local Test

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Description Provides an implementation of a rare variant association test that utilizes protein tertiary structure to increase signal and to identify likely causal variants. Performs structure-guided collapsing, which leads to local tests that borrow information from neighboring variants on a protein and that provide association information on a variant-specific level. For details of the implemented method see West, R. M., Lu, W., Rotroff, D. M., Kuenemann, M., Chang, S-M., Wagner M. J., Buse, J. B., Motsinger-Reif, A., Fourches, D., and Tzeng, J-Y. (2019) <doi:10.1371/journal.pcbi.1006722>.

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Depends methods, stats, rARPACK, Matrix, CompQuadForm

NeedsCompilation no

Encoding UTF-8

RoxygenNote 7.2.1

Collate 'A_Kernel.R' 'A_BurdenKernel.R' 'A_LinearKernel.R' 'A_PolyKernel.R' 'B_PvMethod.R' 'B_PvMethod_Davies.R' 'B_PvMethod_Liu.R' 'C_BinomialTrait.R' 'C_GaussianTrait.R' 'D_NullResult.R' 'calcLocalKernel.R' 'distanceMatrix.R' 'mainCode.R' 'point.R' 'pvResamp.R'

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Description

A rare variant association test that utilizes protein tertiary structure to increase signal and to identify likely causal variants. Performs structure-guided collapsing, which leads to local tests that borrow information from neighboring variants on a protein and that provide association information on a variant-specific level.

Usage

```
point(
  yy,
  X,
  snp,
  proteinCoord,
  ...,
  trait = "binomial",
  cValues = c(0, 0.1, 0.2, 0.3, 0.4, 0.5),
  weighted = TRUE,
  weight = NULL,
  kernel = "linear",
  d = NULL,
  pvMethod = "davies",
  nperturb = 1000,
  verbose = TRUE
)
```

Arguments

yy	numeric vector; phenotype values.
X	numeric matrix; non-genetic covariates.
snp	numeric matrix; genotype snp matrix (count of minor alleles). Matrix cannot contain missing values.
proteinCoord	numeric matrix; columns correspond to 3 dimensional coordinates (x,y,z) of each variant in the protein tertiary structure.
...	optional additional arguments for p-value methods CompQuadForm::davies and CompQuadForm::liu.
trait	character; type of phenotype data. Must be one of {'gaussian','binomial'} quantitative or case control data, respectively.
cValues	numeric vector; c values from which to choose the optimal neighborhood size for borrowing significant information.
weighted	logical; whether or not to weight the local kernel test using (non-distance based) weights.

weight	numeric vector (optional) If NULL and weighted is TRUE (1.0-MAF)^24. Ignored if weighted is FALSE.
kernel	character; type of local kernel to use; Must be one of {'burden', 'linear', 'polynomial'}.
d	numeric; If kernel = 'poly', d is the order of the polynomial kernel.
pvMethod	character; method of calculating the p-value of each single marker test for fixed c values. Must be one of {'davies', 'liu'}.
nperturb	numeric, number of perturbations/resamples (perturbed test statistics) to calculate p-value of minP statistic.
verbose	logical; generate progress screen prints.

Value

Returns a matrix the rows of which correspond to individual markers. Columns correspond to:
(1) minP statistic;
(2) local kernel test p-value;
(3) optimal scale value from input cValues;
(4) minor allele frequency; and
(5) single variant score test p-value.

Examples

```
# number of subjects
nsubj <- 1000

# number of markers
nm <- 5

# generate coordinates for proteins
protein <- cbind( stats::rnorm(n = nm, mean = 17.6, sd =  6.6),
                  stats::rnorm(n = nm, mean =  1.6, sd = 13.6),
                  stats::rnorm(n = nm, mean = 22.9, sd = 10.4) )

# generate snp matrix
snp <- matrix(data = rbinom(n = nsubj*nm, size = 1, p = 0.02),
              nrow = nsubj, ncol = nm)
colnames(snp) = paste0("m",1:nm)

# generate binmoial response
MAF <- colMeans(x = snp)/2
causal <- numeric(nm)
causal[c(2,4)] <- 1.0
betaG <- 0.4*abs(log10(x = MAF))*causal

#no non-genetic covariates
X <- NULL
mu <- -0.05 + snp %*% betaG

pryy <- exp(mu)/(1+exp(mu))
yy <- sapply(X = pryy, FUN = stats::rbinom, n = 1, size = 1)
```

```
res <- point(yy = yy, X = X, snp = snp, proteinCoord = protein,
             trait = 'binomial', cValues = c(0.1,0.2),
             weighted = TRUE, weight = NULL, kernel = 'linear',
             pvMethod = 'liu', nperturb = 100,
             verbose = FALSE)
```

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