Package 'Hapi'

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Type Package

Title Inference of Chromosome-Length Haplotypes Using Genomic Data of Single Gamete Cells

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Description Inference of chromosome-length haplotypes using a few haploid gametes of an individual. The gamete genotype data may be generated from various platforms including genotyping arrays and sequencing even with low-coverage. Hapi simply takes genotype data of known hetSNPs in single gamete cells as input and report the high-resolution haplotypes as well as confidence of each phased hetSNPs. The package also includes a module allowing downstream analyses and visualization of identified crossovers in the gametes.

Depends R (>= 3.4.0)

License GPL-3

Encoding UTF-8

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Imports HMM, ggplot2

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VignetteBuilder knitr

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`Hapi-package` *Hapi is a novel easy-to-use package that only requires 3 to 5 gametes to reconstruct accurate and high-resolution haplotypes of an individual. The gamete genotype data may be generated from various platforms including genotyping arrays and next generation sequencing even with low-coverage. Hapi simply takes genotype data of known hetSNPs in single gamete cells as input and report the high-resolution haplotypes as well as confidence level of each phased hetSNPs. The package also includes a module allowing downstream analyses and visualization of crossovers in the gametes.*

Description

Hapi is a novel easy-to-use package that only requires 3 to 5 gametes to reconstruct accurate and high-resolution haplotypes of an individual. The gamete genotype data may be generated from various platforms including genotyping arrays and next generation sequencing even with low-coverage. Hapi simply takes genotype data of known hetSNPs in single gamete cells as input and report the

high-resolution haplotypes as well as confidence level of each phased hetSNPs. The package also includes a module allowing downstream analyses and visualization of crossovers in the gametes.

`base2num` *Convert genotype coded in A/T/C/G to 0/1*

Description

Convert base (A/T/C/G) coded genotype to numeric (0/1) coded

Usage

```
base2num(gmt, ref, alt)
```

Arguments

`gmt`	a dataframe of genotype data of gamete cells
`ref`	a character represents reference allele
`alt`	a character represents alternative allele

Value

a dataframe containing converted genotype

Author(s)

Ruidong Li

Examples

```
ref <- sample(c('A','T'),500, replace=TRUE)
alt <- sample(c('C','G'),500, replace=TRUE)

gmt <- data.frame(chr=rep(1,500), pos=seq_len(500),
    ref=ref, alt=alt, gmt1=ref, gmt2=alt, gmt3=ref,
    gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
    stringsAsFactors = FALSE)

gmtDa <- base2num(gmt=gmt[5:9], ref=ref, alt=alt)
```

`crossover` *Crossover information across all gamete cells*

Description

Crossover information across all gamete cells

gamete11 *Haplotypes of a single gamete cell for visualization*

Description

Haplotypes of a single gamete cell for visualization

gmt *Raw genotyping data*

Description

Raw genotyping data

hapiAssemble *Consensus haplotype assembly*

Description

Assemble the consensus high-resolution haplotypes

Usage

```
hapiAssemble(gmt, draftHap, keepLowConsistency = TRUE,
  consistencyThresh = 0.85)
```

Arguments

gmt	a dataframe of genotype data of gamete cells
draftHap	a dataframe with draft haplotype information
keepLowConsistency	logical, if low-consistent gamete cells should be kept
consistencyThresh	a numeric value of the threshold determining low-consistent gamete cells compared with the draft haplotype. Default is 0.85

Value

a dataframe containing phased haplotypes

Author(s)

Ruidong Li

Examples

```
finalDraft <- rep(0,500)
names(finalDraft) <- seq_len(500)

ref <- rep(0,500)
alt <- rep(1,500)

gmtDa <- data.frame(gmt1=ref, gmt2=alt, gmt3=ref,
gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
stringsAsFactors = FALSE)

idx1 <- sort(sample(seq_len(500), 30, replace = FALSE))
idx2 <- sort(sample(seq_len(500), 30, replace = FALSE))
idx3 <- sort(sample(seq_len(500), 30, replace = FALSE))

gmtDa[idx1,1] <- NA
gmtDa[idx2,2] <- NA
gmtDa[idx3,3] <- NA

consensusHap <- hapiAssemble(draftHap = finalDraft, gmt = gmtDa)
```

---

hapiAssembleEnd *Assembly of haplotypes in regions at the end of a chromosome*

Description

Assembly of haplotypes in regions at the end of a chromosome

Usage

```
hapiAssembleEnd(gmt, draftHap, consensusHap, k = 300)
```

Arguments

gmt	a dataframe of genotype data of gamete cells
draftHap	a dataframe with draft haplotype information
consensusHap	a dataframe of the consensus haplotype information
k	a numeric value for the number of hetSNPs that will be combined with markers beyond the framework for assembly. Default is 300

Value

a dataframe containing phased haplotypes

Author(s)

Ruidong Li

Examples

```
finalDraft <- rep(0,500)
names(finalDraft) <- seq_len(500)

ref <- rep(0,500)
alt <- rep(1,500)

gmtDa <- data.frame(gmt1=ref, gmt2=alt, gmt3=ref,
gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
stringsAsFactors = FALSE)

idx1 <- sort(sample(seq_len(500), 30, replace = FALSE))
idx2 <- sort(sample(seq_len(500), 30, replace = FALSE))
idx3 <- sort(sample(seq_len(500), 30, replace = FALSE))

gmtDa[idx1,1] <- NA
gmtDa[idx2,2] <- NA
gmtDa[idx3,3] <- NA

consensusHap <- data.frame(hap1=rep(0,500),hap2=rep(1,500),
total=rep(5,500),rate=rep(1,500),
confidence=rep('F',500),
stringsAsFactors = FALSE)
rownames(consensusHap) <- seq_len(500)

consensusHap <- hapiAssembleEnd(gmt = gmtDa, draftHap = finalDraft,
consensusHap = consensusHap, k = 300)
```

---

hapiAutoPhase *Automatic inference of haplotypes*

Description

Automatic inference of haplotypes

Usage

```
hapiAutoPhase(gmt, code = "atcg")
```

Arguments

gmt	a dataframe of genotype data of gamete cells
code	a character indicating the code style of genotype data. One of `'atcg'` and `'01'`. Default is `'atcg'`

Value

a dataframe of inferred consensus haplotypes

Author(s)

Ruidong Li

Examples

```
ref <- sample(c('A','T'),500, replace=TRUE)
alt <- sample(c('C','G'),500, replace=TRUE)

gmt <- data.frame(chr=rep(1,500), pos=seq_len(500),
    ref=ref, alt=alt, gmt1=ref, gmt2=alt, gmt3=ref,
    gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
    stringsAsFactors = FALSE)

hapOutput <- hapiAutoPhase(gmt=gmt, code='atcg')
```

---

hapiBlockMPR *Maximum Parsimony of Recombination (MPR) for proofreading of draft haplotypes*

Description

Maximum Parsimony of Recombination (MPR) for proofreading of draft haplotypes

Usage

```
hapiBlockMPR(draftHap, gmtFrame, cvlink = 2, smallBlock = 100)
```

Arguments

draftHap	a dataframe with draft haplotype information
gmtFrame	a dataframe of raw genotype data in the framework
cvlink	a numeric value of number of cvlinks. Default is 2
smallBlock	a numeric value determining the size of small blocks that should be excluded from the draft haplotypes

Value

a dataframe of draft haplotypes after proofreading

Author(s)

Ruidong Li

Examples

```
ref <- rep(0,500)
alt <- rep(1,500)

gmtFrame <- data.frame(gmt1=ref, gmt2=alt, gmt3=ref,
gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
stringsAsFactors = FALSE)

idx1 <- sort(sample(seq_len(500), 30, replace = FALSE))
idx2 <- sort(sample(seq_len(500), 30, replace = FALSE))
idx3 <- sort(sample(seq_len(500), 30, replace = FALSE))

gmtFrame[idx1,1] <- NA
gmtFrame[idx2,2] <- NA
gmtFrame[idx3,3] <- NA

imputedFrame <- data.frame(gmt1=ref, gmt2=alt, gmt3=ref,
gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
stringsAsFactors = FALSE)

draftHap <- hapiPhase(imputedFrame)

finalDraft <- hapiBlockMPR(draftHap, gmtFrame, cvlink=2, smallBlock=100)
```

`hapiCVCluster` *Filter out hetSNPs in potential complex regions*

Description

Filter out hetSNPs in potential complex regions

Usage

```
hapiCVCluster(draftHap, minDistance = 1e+06, cvlink = 2)
```

Arguments

`draftHap`	a dataframe with draft haplotype information
`minDistance`	a numeric value of the distance between two genomic positions with cv-links. Default is `1000000`
`cvlink`	a numeric value of number of cvlinks. Default is `2`

Value

a dataframe of regions to be filtered out

Author(s)

Ruidong Li

Examples

```
ref <- rep(0,500)
alt <- rep(1,500)

imputedFrame <- data.frame(gmt1=ref, gmt2=alt, gmt3=ref,
gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
stringsAsFactors = FALSE)

draftHap <- hapiPhase(imputedFrame)
cvCluster <- hapiCVCluster(draftHap = draftHap, cvlink=2)
```

---

hapiCVDistance *Histogram of crossover distance*

Description

Histogram of crossover distance

Usage

```
hapiCVDistance(cv)
```

Arguments

cv	a dataframe of crossover information

Value

a histogram

Author(s)

Ruidong Li

Examples

```
data(crossover)
hapiCVDistance(cv=crossover)
```

hapiCVMap *Visualization of crossover map*

Description

Visualization of crossover map

Usage

```
hapiCVMap(cv, chr = hg19, step = 5, gap = gap.hg19, x.limits = 6,
  y.breaks = NULL, y.labels = NULL)
```

Arguments

cv	a dataframe of crossover information
chr	a dataframe of chromosome information, including length, and centrometric regions
step	a numeric value of genomic interval in Mb. Default is 5
gap	a dataframe of unassembled regions with the first column is chromosme, the second column is start position, and third column is the end position of the gap. Default is gap for hg19. If no gap region is provided, use gap=NULL
x.limits	a numeric value of limits on x axis
y.breaks	a vector of positions to show labels on y axis. Default is NULL
y.labels	a vector of labels on the y axis. Default is NULL

Value

a plot of crossover map on all the chromosomes

Author(s)

Ruidong Li

Examples

```
data(crossover)
hapiCVMap(cv=crossover)
```

hapiCVResolution *Histogram of crossover resolution*

Description

Histogram of crossover resolution

Usage

```
hapiCVResolution(cv)
```

Arguments

cv	a dataframe of crossover information

Value

a histogram

Author(s)

Ruidong Li

Examples

```
data(crossover)
hapiCVResolution(cv=crossover)
```

hapiFilterError *Filter out hetSNPs with potential genotyping errors*

Description

Filter out hetSNPs with potential genotyping errors

Usage

```
hapiFilterError(gmt, hmm = NULL)
```

Arguments

gmt	a dataframe of genotype data of gamete cells
hmm	a list containing probabilities of a HMM. Default is NULL

Value

a dataframe of genotype data of gamete cells

Author(s)

Ruidong Li

Examples

```
ref <- rep(0,500)
alt <- rep(1,500)

gmt <- data.frame(gmt1=ref, gmt2=alt, gmt3=ref,
    gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
    stringsAsFactors = FALSE)

idx <- sort(sample(seq_len(500), 10, replace = FALSE))
gmt[idx,1] <- 1

gmtDa <- hapiFilterError(gmt = gmt)
```

---

hapiFrameSelection *Selection of hetSNPs to form a framework*

Description

Selection of hetSNPs to form a framework

Usage

```
hapiFrameSelection(gmt, n = 3)
```

Arguments

gmt	a dataframe of genotype data of gamete cells
n	a numeric value of the minumum number of gametes with observed genotypes at a locus

Value

a dataframe of genotype data of gamete cells

Author(s)

Ruidong Li

Examples

```
ref <- rep(0,500)
alt <- rep(1,500)

gmt <- data.frame(gmt1=ref, gmt2=alt, gmt3=ref,
gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
stringsAsFactors = FALSE)

idx <- sort(sample(seq_len(500), 10, replace = FALSE))

gmt[idx,1] <- NA
gmt[idx,2] <- NA
gmt[idx,3] <- NA

gmtFrame <- hapiFrameSelection(gmt = gmt, n = 3)
```

---

hapiGameteView *Visualization of haplotypes in a single gamete cell*

Description

Visualization of haplotypes in a single gamete cell

Usage

```
hapiGameteView(hap, chr = hg19, hap.color = c("deepskyblue2",
  "darkorange2"), centromere.fill = "black", x.breaks = NULL,
  x.labels = NULL, y.breaks = NULL, y.labels = NULL)
```

Arguments

hap	a dataframe of all the phased hetSNPs in all chromosomes
chr	a dataframe of chromosome information, including length, and centrometric regions
hap.color	a vector of colors for the two haplotypes. Default is c('deepskyblue2','darkorange2')
centromere.fill	a character of the color for the centromeres. Default is 'black'
x.breaks	a vector of positions to show labels on x axis. Default is NULL
x.labels	a vector of labels on the x axis. Default is NULL
y.breaks	a vector of positions to show labels on y axis. Default is NULL
y.labels	a vector of labels on the y axis. Default is NULL

Value

a plot of haplotypes in a single gamete cell

Author(s)

Ruidong Li

Examples

```
data(gamete11)
hapiGameteView(hap=gamete11)
```

---

hapiIdentifyCV *Indentify crossovers in gamete cells*

Description

Indentify crossovers in gamete cells

Usage

```
hapiIdentifyCV(hap, gmt, hmm = NULL)
```

Arguments

hap	a dataframe of the two haplotypes
gmt	a dataframe of genotype data of gamete cells
hmm	a list containing probabilities of a HMM. Default is NULL

Value

a dataframe containing crossover information in each gamete cell

Author(s)

Ruidong Li

Examples

```
ref <- sample(c('A','T'),500, replace=TRUE)
alt <- sample(c('C','G'),500, replace=TRUE)

hap <- data.frame(hap1=ref, hap2=alt, stringsAsFactors = FALSE)
rownames(hap) <- seq_len(500)

gmt <- data.frame(gmt1=ref, gmt2=alt, gmt3=ref,
    gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
    stringsAsFactors = FALSE)

cvOutput <- hapiIdentifyCV(hap=hap, gmt=gmt)
```

hapiImupte *Imputation of missing genotypes in the framework*

Description

Imputation of missing genotypes in the framework

Usage

```
hapiImupte(gmt, nSPT = 2, allowNA = 0)
```

Arguments

gmt	a dataframe of genotype data of gamete cells in the framework
nSPT	a numeric value of the minumum number of supports for an imputation
allowNA	a numeric value of the maximum number of gametes with NA at a locus

Value

a dataframe of imputed genotypes in the framework

Author(s)

Ruidong Li

Examples

```
ref <- rep(0,500)
alt <- rep(1,500)

gmtFrame <- data.frame(gmt1=ref, gmt2=alt, gmt3=ref,
gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
stringsAsFactors = FALSE)

idx1 <- sort(sample(seq_len(500), 30, replace = FALSE))
idx2 <- sort(sample(seq_len(500), 30, replace = FALSE))
idx3 <- sort(sample(seq_len(500), 30, replace = FALSE))

gmtFrame[idx1,1] <- NA
gmtFrame[idx2,2] <- NA
gmtFrame[idx3,3] <- NA
imputedFrame <- hapiImupte(gmtFrame, nSPT=2, allowNA=0)
```

hapiPhase *Phase draft haplotypes by majority voting*

Description

Phase draft haplotypes by majority voting

Usage

```
hapiPhase(gmt)
```

Arguments

gmt	a dataframe of imputed genotype data of gamete cells

Value

a dataframe of inferred draft haplotypes

Author(s)

Ruidong Li

Examples

```
ref <- rep(0,500)
alt <- rep(1,500)
imputedFrame <- data.frame(gmt1=ref, gmt2=alt, gmt3=ref,
gmt4=ref, gmt5=c(alt[1:250], ref[251:500]),
stringsAsFactors = FALSE)
draftHap <- hapiPhase(gmt=imputedFrame)
```

hg19 *Chromosome information of hg19*

Description

Chromosome information of hg19

num2base *Convert genotype coded in 0/1 to A/T/C/G*

Description

Convert numeric (0/1) coded genotype to base (A/T/C/G) coded

Usage

```
num2base(hap, ref, alt)
```

Arguments

hap	a dataframe of consensus haplotypes
ref	a character represents reference allele
alt	a character represents alternative allele

Value

a dataframe containing converted haplotypes

Author(s)

Ruidong Li

Examples

```
ref <- sample(c('A','T'),500, replace=TRUE)
alt <- sample(c('C','G'),500, replace=TRUE)

consensusHap <- data.frame(hap1=rep(0,500),hap2=rep(1,500),
    total=rep(5,500),rate=rep(1,500),
    confidence=rep('F',500),
    stringsAsFactors = FALSE)
rownames(consensusHap) <- seq_len(500)

hap <- num2base(hap=consensusHap, ref=ref, alt=alt)
```

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