Package 'skater'

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Title Utilities for SNP-Based Kinship Analysis

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Description Utilities for single nucleotide polymorphism (SNP) based kinship analysis testing and evaluation. The 'skater' package contains functions for importing, parsing, and analyzing pedigree data, performing relationship degree inference, benchmarking relationship degree classification, and summarizing identity by descent (IBD) segment data. Package functions and methods are described in Turner et al. (2021) ``skater: An R package for SNP-based Kinship Analysis, Testing, and Evaluation'' <doi:10.1101/2021.07.21.453083>.

```
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```

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arrange_ids

Order IDs across two columns

Description

Some types of data or results are indexed by two identifiers in two different columns corresponding to data points for *pairs* of observations. E.g., you may have columns called id1 and id2 that index the tibble for all possible pairs of results between samples A, B, and C. If you attempt to join two tibbles with by=c("id1", "id2"), the join will fail if samples are flipped from one dataset to another. E.g., one tibble may have id1=A and id2=B while the other has id1=B and id2=A. This function ensures that id1 is alphanumerically first while id2 is alphanumerically second. See examples.

Usage

```
arrange_ids(.data, .id1, .id2)
```

Arguments

.data	A tibble with two ID columns to arrange.
.id1	Unquoted name of the "id1" column. See examples.
.id2	Unquoted name of the "id2" column. See examples.

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Value

A tibble with id1 and id2 rearranged alphanumerically.

Examples

```
d1 <- tibble::tribble(</pre>
  ~id1, ~id2, ~results1,
  "a", "b",
                   10L,
  "a", "c",
                   20L,
  "c", "b",
                   30L
)
d2 <- tibble::tribble(</pre>
  ~id1, ~id2, ~results2,
  "b", "a",
                   101L,
  "c", "a",
                   201L,
  "b", "c",
                   301L
)
# Inner join fails because id1!=id2.
dplyr::inner_join(d1, d2, by=c("id1", "id2"))
# Arrange IDs
d1 %>% arrange_ids(id1, id2)
d2 %>% arrange_ids(id1, id2)
# Inner join
dplyr::inner_join(arrange_ids(d1, id1, id2), arrange_ids(d2, id1, id2), by=c("id1", "id2"))
# Recursively, if you had more than two tibbles
list(d1, d2) %>%
  purrr::map(arrange_ids, id1, id2) %>%
  purrr::reduce(dplyr::inner_join, by=c("id1", "id2"))
```

calc_accuracy

Calculate Accuracy

Description

Calculates accuracy and related metrics.

Usage

```
calc_accuracy(tabble)
```

Arguments

tabble

A frequency table created with table

Details

Calculates accuracy, lower and upper bounds, the guessing rate and p-value of the accuracy vs. the guessing rate. This function is called by confusion_matrix, but if this is all you want, you can simply supply the table to this function.

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Value

A tibble with the corresponding statistics

Author(s)

Michael Clark (see m-clark/confusion_matrix).

See Also

binom.test

calc_stats

Calculate various statistics from a confusion matrix

Description

Given a frequency table of predictions versus target values, calculate numerous statistics of interest.

Usage

```
calc_stats(tabble, prevalence = NULL, positive, ...)
```

Arguments

tabble A frequency table created with table prevalence Prevalence value. Default is NULL

positive Positive class

... Other, not currently used

Details

Used within confusion_matrix to calculate various confusion matrix metrics. This is called by confusion_matrix, but if this is all you want you can simply supply the table.

Suppose a 2x2 table with notation

	target	
Predicted	Event	No Even
Event	A	В
No Event	C	D

The formulas used here are:

$$Sensitivity = A/(A+C)$$

$$Specificity = D/(B+D)$$

$$Prevalence = (A+C)/(A+B+C+D)$$

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Positive Predictive Value = (sensitivity*prevalence) / ((sensitivity*prevalence) + ((1-specificity)*(1-prevalence)) / ((1-sensitivity*prevalence) + ((1-specificity)*(1-prevalence)) / ((1-sensitivity)*prevalence) + ((1-specificity)*(1-prevalence)) / ((1-specificity)*(1-pre

$$DetectionRate = A/(A+B+C+D)$$

DetectionPrevalence = (A + B)/(A + B + C + D)

BalancedAccuracy = (sensitivity + specificity)/2

$$Precision = A/(A+B)$$

$$Recall = A/(A+C)$$

 $F1 = harmonic mean of precision and recall = (1+beta^2)*precision*recall/((beta^2*precision)+recall) \\ \text{where beta = 1 for this function.}$

False Discovery Rate = 1 - Positive Predictive Value

False Omission Rate = 1 - Negative Predictive Value

False Positive Rate = 1 - Specificity

FalseNegativeRate = 1 - Sensitivity

D' = qnorm(Sensitivity) - qnorm(1 - Specificity)

AUC = pnorm(D'/sqrt(2))

See the references for discussions of the first five formulas. Abbreviations:

Positive Predictive Value: PPV
Negative Predictive Value: NPV
False Discovery Rate: FDR
False Omission Rate: FOR
False Positive Rate: FPR
False Negative Rate: FNR

Value

A tibble with (at present) columns for sensitivity, specificity, PPV, NPV, F1 score, detection rate, detection prevalence, balanced accuracy, FDR, FOR, FPR, FNR. For more than 2 classes, these statistics are provided for each class.

Note

Different names are used for the same statistics.

Sensitivity: True Positive Rate, Recall, Hit Rate, Power

Specificity: True Negative Rate
Positive Predictive Value: Precision

False Negative Rate: Miss Rate, Type II error rate, beta False Positive Rate: Fallout, Type I error rate, alpha

This function is called by confusion_matrix, but if this is all you want, you can simply supply the table to this function.

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Author(s)

Michael Clark (see m-clark/confusion_matrix).

References

Kuhn, M. (2008), "Building predictive models in R using the caret package," *Journal of Statistical Software*, (https://www.jstatsoft.org/article/view/v028i05).

Altman, D.G., Bland, J.M. (1994) "Diagnostic tests 1: sensitivity and specificity", *British Medical Journal*, vol 308, 1552.

Altman, D.G., Bland, J.M. (1994) "Diagnostic tests 2: predictive values," *British Medical Journal*, vol 309, 102.

Velez, D.R., et. al. (2008) "A balanced accuracy function for epistasis modeling in imbalanced datasets using multifactor dimensionality reduction.," *Genetic Epidemiology*, vol 4, 306.

confusion_matrix

Calculate various statistics from a confusion matrix

Description

Given a vector of predictions and target values, calculate numerous statistics of interest. Modified from m-clark/confusion_matrix.

Usage

```
confusion_matrix(
  prediction,
  target,
  positive = NULL,
  prevalence = NULL,
  dnn = c("Predicted", "Target"),
  longer = FALSE,
  ...
)
```

Arguments

 $\begin{array}{ll} \hbox{prediction} & A \ \hbox{vector of predictions} \\ \hbox{target} & A \ \hbox{vector of target values} \end{array}$

positive The positive class for a 2-class setting. Default is NULL, which will result in

using the first level of target.

prevalence Prevalence rate. Default is NULL.

dnn The row and column headers for the contingency table returned. Default is 'Pre-

dicted' for rows and 'Target' for columns.

longer Transpose the output to long form. Default is FALSE (requires tidyr 1.0).

.. Other parameters, not currently used.

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Details

This returns accuracy, agreement, and other statistics. See the functions below to find out more. Originally inspired by the confusionMatrix function from the caret package.

Value

A list of tibble(s) with the associated statistics and possibly the frequency table as list column of the first element. If classes contain >1 numeric class and a single non-numeric class (e.g., "1", "2", "3", and "Unrelated", the RMSE of the reciprocal of the Targets + 0.5 will also be returned.)

References

Kuhn, M., & Johnson, K. (2013). Applied predictive modeling.

See Also

```
calc_accuracy calc_stats
```

Examples

```
prediction = c(0,1,1,0,0,1,0,1,1,1)
          = c(0,1,1,1,0,1,0,1,0,1)
confusion_matrix(prediction, target, positive = '1')
set.seed(42)
prediction = sample(letters[1:4], 250, replace = TRUE, prob = 1:4)
         = sample(letters[1:4], 250, replace = TRUE, prob = 1:4)
confusion_matrix(prediction, target)
prediction = c(rep(1, 50), rep(2, 40), rep(3, 60))
          = c(rep(1, 50), rep(2, 50), rep(3, 50))
confusion_matrix(prediction, target)
confusion_matrix(prediction, target) %>% purrr::pluck("Table")
confusion_matrix(prediction, target, longer=TRUE)
confusion_matrix(prediction, target, longer=TRUE) %>%
 purrr::pluck("Other") %>%
 tidyr::spread(Class, Value)
# Prediction with an unrelated class
prediction = c(rep(1, 50), rep(2, 40), rep(3, 60), rep("Unrelated", 55))
          = c(rep(1, 50), rep(2, 50), rep(3, 55), rep("Unrelated", 50))
confusion_matrix(prediction, target)
# Prediction with two unrelated classes
prediction = c(rep(1, 50), rep(2, 40), rep("Third", 60), rep("Unrelated", 55))
          = c(rep(1, 50), rep(2, 50), rep("Third", 55), rep("Unrelated", 50))
confusion_matrix(prediction, target)
```

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dibble

Degree tibble

Description

Creates a tibble with degree, expected kinship coefficient, and inference boundaries.

Rows will be created up to the max_degree, with an additional row for any relationship more distant than max_degree. The degree value for the final row will be NA. This represents inference criteria for "unrelated" individuals. See examples.

Usage

```
dibble(max_degree = 3L)
```

Arguments

max_degree

The most distant degree you want to measure (usually between 3-9, default 3).

Value

A tibble containing the degree, expected kinship coefficient (k), lower (1) and upper (u) inference bounds.

Examples

dibble(3)
dibble(10)

fam2ped

Fam to pedigree

Description

Converts a PLINK-formatted fam file to a pedigree object using kinship2::pedigree.

Usage

```
fam2ped(fam)
```

Arguments

fam

A tibble with six columns of PLINK .fam data as read in by read_fam.

Value

A tibble with new listcol ped containing pedigrees from kinship2::pedigree.

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Examples

```
famfile <- system.file("extdata", "3gens.fam", package="skater", mustWork=TRUE)
fam <- read_fam(famfile)
fam2ped(fam)</pre>
```

ibd2kin

Compute kinship coefficient from IBD segments

Description

This function is used to retrieve a relatedness measure from IBD segments. The relatedness value returned is the kinship coefficient.

Usage

```
ibd2kin(.ibd_data, .map, type = NULL)
```

Arguments

. ibd_data Tibble with IBD segments created using the read_ibd function

map Tibble with the genetic map data created using the read_map function

type Type of IBD to use for kinship coefficient calculation; must be 'IBD1', 'IBD2', or NULL (both IBD1 and IBD2 will be treated the same); default is NULL

Details

The input data should be pairwise IBD segments prepared via read_ibd. The function will internally loop over each chromosome, and use a specified genetic map to convert shared segments to genetic units. After doing so, the function converts the shared length to a kinship coefficient by summing 0.5*IBD2+0.25*IBD1.

Note that the data read in by read_ibd when source="pedsim" returns a list with separate tibbles for IBD1 and IBD2 segments. The current implementation of this function requires running this function independently on IBD1 and IBD2 segments, then summarizing (adding) the corresponding proportions. See examples.

Value

Tibble with three columns:

- 1. id1 (sample identifier 1)
- 2. id2 (sample identifier 2)
- 3. kinship (kinship coefficent derived from shared segments)

References

http://faculty.washington.edu/sguy/ibd_relatedness.html

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Examples

```
pedsim_fp <- system.file("extdata", "GBR.sim.seg.gz", package="skater", mustWork=TRUE)
pedsim_seg <- read_ibd(pedsim_fp, source = "pedsim")
gmapfile <- system.file("extdata", "sexspec-avg-min.plink.map", package="skater", mustWork=TRUE)
gmap <- read_map(gmapfile)
ibd1_dat <- ibd2kin(.ibd_data=pedsim_seg$IBD1, .map=gmap, type="IBD1")
ibd2_dat <- ibd2kin(.ibd_data=pedsim_seg$IBD2, .map=gmap, type="IBD2")
dplyr::bind_rows(ibd1_dat,ibd2_dat) %>%
    dplyr::group_by(id1,id2) %>%
    dplyr::summarise(kinship = sum(kinship), .groups = "drop")
```

interpolate

Interpolate over segments

Description

This is an unexported helper used in in ibd2kin. The function interpolates over segments to apply genetic length to the segment. It is inspired by Python code distributed by the Browning lab (documentation).

Usage

```
interpolate(ibd_bp, chromgpos)
```

Arguments

ibd_bp Base pair for the IBD segment over which to interpolate

chromgpos Genetic map data for a specific chromosome

Value

Numeric vector with the genetic distance shared at the segment.

References

http://faculty.washington.edu/sguy/ibd_relatedness.html

kin2cm

kin2cm

Kinship coefficient to cM

Description

"Converts" a kinship coefficient to put on the same scale as shared cM using the formula cm < -pmin(3560, 4*pmax(0, k)*3560).

Usage

kin2cm(k)

Arguments

k

Kinship coefficient (numeric, typically between 0 and .5, although KING can produce values <0).

Value

A vector of numeric estimated cM, ranging from 0-3560.

References

```
https://dnapainter.com/tools/sharedcmv4.
https://www.ancestry.com/dna/resource/whitePaper/AncestryDNA-Matching-White-Paper.
pdf.
https://verogen.com/wp-content/uploads/2021/03/snp-typing-uas-kinship-estimation-gedmatch-pro-techpdf.
```

Examples

```
kin2cm(.25)
kin2cm(.125)
kin2cm(.0625)
dibble(9) %>% dplyr::mutate(cm=kin2cm(k))
```

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Kinship coefficient to degree

Description

Infers relationship degree given a kinship coefficient.

Usage

```
kin2degree(k, max_degree = 3L)
```

Arguments

k Kinship coefficient (numeric, typically between 0 and .5, although KING can

produce values <0).

max_degree Max degree resolution (default 3). Used to seed dibble. Anything below the

inference range of max_degree will report NA. See dibble.

Value

A vector with inferred degree, up to the maximum degree in dibble (anything more distant is NA, i.e., unrelated).

Examples

```
kin2degree(0.5)
kin2degree(0.25)
kin2degree(0.125)
kin2degree(0.0625)
kin2degree(0.03125)
kin2degree(0.03125, max_degree=5)
kin2degree(-0.05)
k <- seq(.02, .5, .03)
kin2degree(k)
kin2degree(k, max_degree=5)
tibble::tibble(k=k) %>% dplyr::mutate(degree=kin2degree(k))
```

ped2kinpair

Pedigree to pairwise kinship

Description

Converts a pedigree class object from fam2ped to a pairwise list of relationships and their expected/theoretical kinship coefficient.

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Usage

```
ped2kinpair(ped)
```

Arguments

ped

A "pedigree" class object from fam2ped.

Value

A tibble containing all pairwise kinship coefficients from the input pedigree.

Examples

```
famfile <- system.file("extdata", "3gens.fam", package="skater", mustWork=TRUE)
famfile %>%
    read_fam() %>%
    fam2ped() %>%
    dplyr::mutate(kinpairs=purrr::map(ped, ped2kinpair)) %>%
    dplyr::select(fid, kinpairs) %>%
    tidyr::unnest(cols=kinpairs)
```

plot_pedigree

Plot pedigree

Description

Plot pedigree

Usage

```
plot_pedigree(ped, file = NULL, width = 10, height = 8)
```

Arguments

ped List of pedigree objects from fam2ped file Output file path (must end in ".pdf")

width Width of output PDF height Height of output PDF

Value

No return value, called for side effects.

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read_akt

Read AKT kin output file

Description

Reads in an akt kin results file. Input file must have seven columns, whitespace delimited:

- 1. id1 (member 1)
- 2. id2 (member 2)
- 3. IBD0 (ratio of IBD0/All SNPS)
- 4. IBD1 (ratio of IBD1/All SNPS)
- 5. Kinship Coefficient
- 6. NSNPS

Usage

```
read_akt(file)
```

Arguments

file

Input file path

Value

A tibble containing the 7 columns from the akt file.

Examples

```
\label{lem:aktFile} $$ aktFile <- system.file("extdata", "3gens.akt", package="skater", mustWork=TRUE) $$ akt <- read_akt(aktFile) $$ akt $$
```

read_fam

Read PLINK-formatted .fam file

Description

Reads in a PLINK-formatted .fam file. Input file must have six columns:

- 1. Family ID
- 2. Individual ID
- 3. Father ID
- 4. Mother ID
- 5. Sex
- 6. Affected Status

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Usage

```
read_fam(file)
```

Arguments

file

Input file path

Value

A tibble containing the 6 columns from the fam file.

Examples

```
famfile <- system.file("extdata", "3gens.fam", package="skater", mustWork=TRUE)
fam <- read_fam(famfile)
fam</pre>
```

read_ibd

Read IBD segment file

Description

Reads in the inferred IBD segments from hapibd (documentation) or IBD segment file generated by ped-sim (documentation).

If reading a hapibd segment file, the input data should have the following columns:

- 1. First sample identifier
- 2. First sample haplotype index (1 or 2)
- 3. Second sample identifier
- 4. Second sample haplotype index (1 or 2)
- 5. Chromosome
- 6. Base coordinate of first marker in segment
- 7. Base coordinate of last marker in segment
- 8. cM length of IBD segment

If read a pedsim segment file, the input data should have the following columns:

- 1. First sample identifier
- 2. Second sample identifer
- 3. Chromosome
- 4. Physical position start
- 5. Physical position end
- 6. IBD type
- 7. Genetic position start
- 8. Genetic position end
- 9. Genetic length (end start)

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Usage

```
read_ibd(file, source)
```

Arguments

file Input file path

source Source of the input file; must be one of "hapibd" or "pedsim"

Value

if source="hapibd", a tibble is returned. If source="pedsim", a list with two tibble elements, IBD1 and IBD2 is returned. Both the hapibd tibble, and the two pedsim tibbles contain six columns:

- 1. id1 (sample identifier 1)
- 2. id2 (sample identifier 2)
- 3. chr (chromosome)
- 4. start (segment bp start coordinate)
- 5. end (segment bp end coordinate)
- 6. length (shared segment length in genetic units, cM)

References

```
https://github.com/browning-lab/hap-ibd#output-files
https://github.com/williamslab/ped-sim#output-ibd-segments-file
```

Examples

```
hapibd_fp <- system.file("extdata", "GBR.sim.ibd.gz", package="skater", mustWork=TRUE)
hapibd_seg <- read_ibd(hapibd_fp, source = "hapibd")
pedsim_fp <- system.file("extdata", "GBR.sim.seg.gz", package="skater", mustWork=TRUE)
pedsim_seg <- read_ibd(pedsim_fp, source = "pedsim")</pre>
```

read_ibis

Read IBIS coef output file

Description

Reads in an ibis results file. Input file must have six columns, whitespace delimited:

- 1. id1 (member 1)
- 2. id2 (member 2)
- 3. Kinship Coefficient
- 4. IBD2 (ratio of IBD2/All SNPS)
- 5. Segment count
- 6. Kinship Degree

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Usage

```
read_ibis(file)
```

Arguments

file

Input file path

Value

A tibble containing the 6 columns from the ibis file.

Examples

```
ibisFile <- system.file("extdata", "3gens.ibis.coef", package="skater", mustWork=TRUE)
ibis <- read_ibis(ibisFile)
ibis</pre>
```

read_map

Read genetic map file

Description

This function reads in the content from a genetic map file to translate physical distance to genetic units (i.e. cM). Regardless of the source, the input file must be sex-averaged and in a tab-separated "Plink" format (documentation) with the following four columns and no header (i.e. no column names):

- 1. Chromosome
- 2. Identifier (ignored in read_map())
- 3. Length (genetic length within the physical position boundary)
- 4. Position (physical position boundary)

The columns must be in the order above. Note that only the first, third, and fourth columns are used in the function.

Usage

```
read_map(file)
```

Arguments

file

Input file path

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Details

The genetic map could come from different sources. One source is the HapMap map distributed by the Browning Lab (documentation). If this map file is used, the non-sex chromosomes can be downloaded and concatenated to a single file as follows:

```
wget https://bochet.gcc.biostat.washington.edu/beagle/genetic_maps/plink.GRCh37.map.zip
unzip plink.GRCh37.map.zip
cat *chr[0-9]*GRCh37.map | sort -k1,1 -k4,4 --numeric-sort > plink.allchr.GRCh37.map
```

Another source is a sex-specific map ("bherer") originally published by Bherer et al and recommended by the developers of ped-sim for simulating IBD segments (documentation). To retrieve and prep this map file for simulation:

After this, the sexspec.pedsim.map file is ready for use in simulation. However, it must be averaged and reformatted to "Plink format" to use here:

```
cat sexspec.pedsim.map | grep -v "^#" | awk -v OFS="\t" '{print $1,".",($3+$4)/2,$2}' > sexspec-avg.pli
```

#' The genetic maps created above are in the tens of megabytes size range. This is trivial to store for most systems but a reduced version would increase portability and ease testing. This "minimum viable genetic map" could be used for testing and as installed package data in an R package for example analysis. Read more about minimum viable genetic maps at:

- Blog post: https://hapi-dna.org/2020/11/minimal-viable-genetic-maps/
- Github repo with python code: https://github.com/williamslab/min_map

The code as written below reduces the averaged sex-specific genetic map from 833776 to 28726 positions (~30X reduction!).

```
# Get minmap script from github
wget https://raw.githubusercontent.com/williamslab/min_map/main/min_map.py
# Create empty minmap
```

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```
# For each autosome...
for chr in {1..22}; do
    echo "Working on chromosome $chr..."
    # First pull out just one chromosome
    grep "^${chr}[[:space:]]" sexspec-avg.plink.map > tmp.${chr}
    # Run the python script on that chromosome.

# The genetic map column is 3rd column (2nd in 0-start). Physical position is last column (3 in 0-based)
python3 min_map.py -mapfile tmp.${chr} -chr ${chr} -genetcol 2 -physcol 3 -noheader -error 0.05
# Strip out the header and reformat back to plink format, and append to minmap file
cat min_viable_map${chr}.txt | grep -v "^#" | awk -v OFS="\t" '{print $1,".",$4,$2}' >> sexspec-avg-mi
# Clean up
rm -f min_viable_map${chr}.txt tmp.${chr}
```

This averaged version of the Bherer sex-specific map, reduced to a minimum viable genetic map with at most 5% error, in Plink format, is available as installed package data (see examples). This is useful for testing code, but the full genetic map should be used for most analysis operations.

Value

A tibble containing 3 columns:

- 1. chr (chromosome)
- 2. value (genetic length within the physical position boundary)
- 3. bp (physical position boundary)

References

```
https://www.cog-genomics.org/plink/1.9/formats#map
https://bochet.gcc.biostat.washington.edu/beagle/genetic_maps/
https://github.com/williamslab/ped-sim#map-file
https://www.nature.com/articles/ncomms14994
https://www.nature.com/articles/ncomms14994
https://github.com/cbherer/Bherer_etal_SexualDimorphismRecombination
```

Examples

```
gmapfile <- system.file("extdata", "sexspec-avg-min.plink.map", package="skater", mustWork=TRUE)
gmap <- read_map(gmapfile)</pre>
```

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read_plink2_king

Read PLINK KING table

Description

Reads in the output from plink2 --make-king-table (documentation). Input file must have six columns, tab delimited:

- 1. id1 (member 1)
- 2. id2 (member 2)
- 3. nsnps
- 4. hethet: proportion of sites where both are heterozygous
- 5. k: Kinship Coefficient

Usage

```
read_plink2_king(file)
```

Arguments

file

Input file path

Value

A tibble containing the 6 columns from the plink2 --make-king-table output.

References

```
https://www.cog-genomics.org/plink/2.0/distance#make_king
```

Examples

```
plink2kingFile <- system.file("extdata", "plink2-king-table.tsv", package="skater", mustWork=TRUE)
plink2king <- read_plink2_king(plink2kingFile)
plink2king
plink2king %>% dplyr::filter(k>0.01)
```

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