

Genetics and Population Analysis

# skater: An R package for SNP-based Kinship Analysis, Testing, and Evaluation

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## Abstract

**Motivation:** SNP-based kinship analysis with genome-wide relationship estimation and IBD segment analysis methods produce results that often require further downstream manipulation and analysis. A software package with a consistent design and implementation that offers this downstream analysis functionality is needed.

**Results:** Here we present the skater package for SNP-based kinship analysis, testing, and evaluation as an R package. The skater package contains a suite of well-documented tools for importing, parsing, and analyzing pedigree data, performing relationship degree inference, benchmarking relationship degree classification, and summarizing IBD segment data.

**Availability:** The skater package is implemented as an R package and is released under the MIT license at <https://github.com/signaturescience/skater>. Documentation is available at <https://signaturescience.github.io/skater>.

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**Supplementary information:** Supplementary data are available at Bioinformatics Online.

## 1 Introduction

Inferring familial relationships between individuals using genetic data is a common problem in population genetics, medical genetics, and forensics. There are multiple approaches to estimating the relatedness between samples, including genome-wide relatedness measures such as those implemented in Plink (Purcell *et al.*, 2007) or KING (Manichaikul *et al.*, 2010), and methods that rely on identity by descent (IBD) segment detection such as GERMLINE (Gusev *et al.*, 2009), hap-IBD (Zhou *et al.*, 2020), and IBIS (Seidman *et al.*, 2020). Recent efforts have focused on benchmarking these methods (Ramstetter *et al.*, 2017; de Vries *et al.*, 2021) aided by tools for simulating pedigrees and genome-wide SNP data (Caballero *et al.*, 2019). Analyzing results from genome-wide SNP-based kinship analysis or comparing analyses to simulated data for benchmarking have to this point required writing one-off analysis functions or utility scripts that are rarely shared and/or poorly documented. There is a need in the field for a well-documented software package with a consistent design and API that contains functions to assist with downstream manipulation,

benchmarking, and analysis of SNP-based kinship assessment methods. Here we present the skater R package for SNP-based kinship analysis, testing, and evaluation.

## 2 The skater package

The skater package provides a tidyverse-friendly collection of analysis and utility functions for SNP-based kinship analysis, testing, and evaluation as an R package. Functions in the package include tools for importing, parsing, and analyzing pedigree data, performing relationship degree inference, benchmarking relationship degree classification, and summarizing IBD segment data.

### 2.1 Pedigree parsing, manipulation, and analysis

The skater package has several functions for importing, parsing, and analyzing pedigree data. Pedigrees define familial relationships in a hierarchical structure. Many genomics tools for working with pedigrees start with a .fam file, which is a tabular format with one row per individual

and columns for unique IDs of the mother, father, and the family unit. The skater package contains the functions `read_fam()` to read in a PLINK-formatted .fam file, and another function `fam2ped()` to convert these into an internal pedigree object as a nested tibble with one row per family. Further functions such as `plot_pedigree()` produce a multi-page PDF drawing a diagram of the pedigree for each family, while `ped2kinpair()` produces a pairwise list of relationships between all individuals in the data with the expected kinship coefficients for each pair.

## 2.2 Relationship degree inference and benchmarking

The skater package includes functions to translate kinship coefficients to relationship degrees. The kinship coefficients could come from `ped2kinpair()` or other kinship estimation software.

The `dibble()` function creates a **degree inference tibble**, with degrees up to the specified maximum degree resolution, expected kinship coefficient, and lower and upper inference ranges as defined in Manichaikul *et al.* (2010). The `kin2degree()` function infers the relationship degree given a kinship coefficient and a maximum degree resolution (e.g., 7th-degree relatives) up to which anything more distant is treated as unrelated.

Once estimated kinship is converted to degree, it may be of interest to compare the inferred degree to truth. When aggregated over many relationships and inferences, this can help benchmark performance of a particular kinship analysis method. The skater package adapts a `confusion_matrix()` function from Clark (2021) to provide standard contingency table metrics (e.g. sensitivity, specificity, PPV, precision, recall, F1, etc.) with a new reciprocal RMSE (R-RMSE) metric. The R-RMSE metric is defined more thoroughly in the skater package vignette (see Supplementary Material), and is a superior measure to classification accuracy when benchmarking relationship degree estimation. Taking the reciprocal of the target and predicted degree in a typical RMSE calculation results in larger penalties for more egregious misclassifications (e.g., classifying a first-degree relative pair as second degree) than misclassifications at more distant relationships (e.g., misclassifying a fourth-degree relative pair as fifth-degree).

## 2.3 IBD segment analysis

Tools such as hap-IBD (Zhou *et al.*, 2020), and IBIS (Seidman *et al.*, 2020) detect shared IBD segments between individuals. The skater package includes functionality to take those IBD segments, compute shared genomic centimorgan (cM) length, and convert that shared cM to a kinship coefficient. In addition to inferred segments, these functions can estimate "truth" kinship from simulated IBD segments (Caballero *et al.*, 2019). The `read_ibd()` function reads pairwise IBD segments from IBD inference tools and from simulated IBD segments. The `read_map()` function reads in genetic map in a standard format which is required to translate the total centimorgans shared IBD to a kinship coefficient using the `ibd2kin()` function.

## 3 Conclusion

The skater R package provides a thoroughly-documented software package for common data import, manipulation, and analysis tasks typically encountered when working with common SNP-based kinship analysis tools. All package functions are internally documented with examples, and the package contains a vignette demonstrating usage, inputs, outputs, and interpretation of all key functions (see Supplementary Material). The package contains internal tests which are automatically run with continuous integration via GitHub Actions whenever the package code is updated. The skater package is permissively licensed (MIT) and is easily

extensible to accommodate outputs from new genome-wide relatedness and IBD segment methods as they become available.

## Funding

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- The sentence should begin: 'This work was supported by ...' -
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An example is given here: 'This work was supported by the National Institutes of Health [AA123456 to C.S., BB765432 to M.H.]; and the Alcohol & Education Research Council [hfygr667789].'

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