Mathematical and Statistical Methods
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Dr. Di Cook and Dr. Catherine Hurley,
The R Journal Editor-in-Chief and Executive Editor,

Date: 22/10/2020

Subject: Manuscript on the R-package **netgwas** for submission to *The R Journal*

Dear Dr. Di Cook and Dr. Catherine Hurley,

Included please find the manuscript, entitled "netgwas: An R Package for Network-Based Genome Wide Association Studies". Please accept it as a candidate for publication in The R Journal.

In this paper we introduce the R package **netgwas**, which has been designed to accomplish three important and interrelated goals in genetics and genomics:
1. linkage map construction,
2. reconstructing linkage disequilibrium networks from multi-locus genotype data,
3. and exploring high-dimensional genotype-phenotype networks.

The novelty of the underlying methodology is to use graphical models to accomplish these three tasks in a unified way compared with conventional ways of studying them separately, each with different methods. Using the pairwise Markov property allows the **netgwas** for a more powerful interpretation of findings where it controls for spurious associations between variables that can arise from conventional approaches in a biological sense. Moreover, the **netgwas** package can deal with species of any ploidy level. We illustrate the package functionality with real biological examples.

Furthermore, the R-package **netgwas** on which this manuscript is based
*   has been available on CRAN for over two years,
*   has been updated 13 times since Dec 2017,
*   is recently receiving over 650 monthly downloads.

All the analyses we have performed in the paper can be replicated. We are committed to maintaining and developing the **netgwas** package in the future. This manuscript is original unpublished work and it has not been submitted to any other journal for review. The netgwas package is freely available at https://cran.r-project.org/web/packages/netgwas.

With best regards, also on behalf of my co-authors Ernst C. Wit and Danny Arends,

Pariya Behrouzi