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SPECIAL ISSUE: POPULATION GENOMICS WITH R

## **Towards an integrated ecosystem of R packages for the analysis of population genetic data**

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## Introduction

As a scientific field, population genetics, despite its relatively young age, occupies a central place in biology. It was considered early on, well before the foundation of molecular genetics, as the way forward to solve the forces behind the evolution of species (Fisher 1930). Today, many pressing issues in understanding or predicting biological responses are investigated through population genetics approaches, for example the adaptation of populations of animals or plants facing human-mediated global changes such as habitat destruction or climate warming (Fordham *et al.* 2014; Merilä & Hendry 2014). Addressing these and other applied questions benefits greatly from an integrative approach that combines analyses of genetic data with geographical and/or ecological data.

The ongoing revolution in sequencing technologies has had a dramatic impact on the questions population geneticists and molecular ecologists can tackle. Genotypic data are now readily available for many loci for many individuals from many microbe, plant, or animal species (Luikart *et al.* 2003; Ellegren 2014). However, acquiring massive amounts of data without an interoperating ecosystem of tools to manipulate, explore, and analyse them properly for a wide variety of research questions results in – paraphrasing John Naisbitt (1984) – “drowning under data and starving from knowledge”. Much progress in addressing this challenge for population genetics has arguably been facilitated through the de facto convergence on a single computer language: the open-source statistical analysis and programming platform R (Ihaka & Gentleman 1996). The main advantages of R for users as well as for developers of analytical methods in population genetics are described elsewhere in this special issue (Kamvar *et al.* 2017; Paradis *et al.* 2017).

Evolutionary ecologists have been among the earliest adopters of R for analysing molecular data: APE (Paradis *et al.* 2004) was first released on CRAN in August 2002, and ADE4 (Dray *et al.* 2007) followed in December of the same year. These and other early adopters, such as ADEGENET, first released in April 2007 (Jombart 2008), created the beginning of an ecosystem that made it increasingly attractive for population geneticists to continue enriching it with packages implementing new methods.

Recognizing the importance of nurturing this ecosystem, and that it faces challenges

from its rapid yet mostly organic growth, the National Evolutionary Synthesis Center (NESCent) held the Population Genetics in R Hackathon on March 16–20, 2015, in  
33 Durham (USA) at the Center’s headquarters. Hackathons are intensive coding events that bring together groups of people who normally do not meet, to work collaboratively and face-to-face on a shared objective (Lapp *et al.* 2007; Groen & Calderhead 2015). For  
36 the event held at NESCent, the objective was to address interoperability, scalability, and workflow building challenges for users and developers of R packages for population genetics. Such work usually receives little reward in the academic incentive system, and  
39 thus tends to fall behind without dedicated initiatives (Howison & Herbsleb 2013; Prins *et al.* 2015). In order to promote the corresponding efforts of not only the participants of the event but also the community as a whole, and to raise awareness of the importance  
42 of a high-quality, interoperable, and well-documented ecosystem of analysis tools, this special issue “Population Genomics in R” highlights several products of the hackathon in combination with similar recent works from others in the population genetics community.

45 Hackathons have become increasingly popular, including in scientific computing, to facilitate a range of objectives such as resource adoption, community building, or tool innovation (Trainer *et al.* 2014). Of note, the NESCent hackathon was among those  
48 chosen by a Carnegie Mellon University-based research group for studying how and with what success such events use different mechanisms to balance their different objectives. Their results are outside the scope of this special issue and have been reported  
51 separately (Trainer *et al.* 2016).

### Summary of special issue “Population Genomics in R”

Most papers in this special issue present new packages or significant improvements over  
54 existing ones. Two papers deviate from this theme. Kamvar *et al.* (2017) present how new internet-based development platforms enable the community to collaborate on promoting teaching of and education in population genetics methods. Paradis *et al.*  
57 (2017) synthesize the recent progress in analysing genomic data for population genetics, and present an overview of the available packages and how they integrate into a common programming environment.

60 A motivation shared by several packages presented in this issue is to provide tools  
that better facilitate users' work, particularly handling their data, which may involve  
complex sampling designs. STRATAG provides user-friendly tools to handle allelic data  
63 from stratified populations, including the possibility to read a variety of data file formats  
and perform a series of different analyses (Archer *et al.* 2017). APEX facilitates the  
manipulation of sequence data from multiple genes with tools to display them and  
66 explore incongruence among them (Jombart *et al.* 2017). GENEPOPEDIT is a collection of  
tools which helps in the manipulation of large multilocus molecular data sets and  
integrates with a variety of other packages (Stanley *et al.* 2017).

69 Another difficult task users often face, especially with multilocus data sets, is data  
visualization, which is one of the chief objectives of two packages presented in this issue.  
MINOTAUR implements several measures of outliers calculated from high-dimensional  
72 genomic data and their visualization with a user-friendly interface (Verity *et al.* 2017).  
POPHELPER, which is both an R package and a web server, provides tools for the  
visualization of population structure, including the outputs of external applications  
75 (Francis 2017).

Handling or analysing (very) big data sets in a scalable manner is increasingly a  
challenge with the exponential growth in available data. Addressing this challenge is a  
78 common goal among several papers. Knaus & Grünwald (2017) present VCFR, a package  
for handling variant call format (VCF) files (Danecek *et al.* 2011), including tools to  
read, write and visualize VCF as well as FASTA (DNA sequences) and GFF  
81 (annotation) files. Paradis *et al.* (2017) present tools from the PEGAS package (Paradis  
2010) to scan VCF files, select the loci to read, and analyse them using basic R  
operations. To handle large quantities of data efficiently, both packages use optimized  
84 C/C++ code interfaced with R. Wringe *et al.* (2017) use parallel code execution to  
efficiently detect hybrids from multilocus data in their package PARALLELNEWHYBRID.

The many different file formats used by population genetics software has been an  
87 ongoing interoperability difficulty (discussed in, e.g., Lischer & Excoffier 2012). Many of  
the packages presented in this issue have the ability to read many different file formats  
(Archer *et al.* 2017; Francis 2017; Paradis *et al.* 2017). However, the general trend  
90 among R packages, and other software as well, has been to address the data exchange

format issue by adopting unified file formats: FASTA for DNA sequences and VCF for genotypic data.

93     Testing for or quantifying natural selection in populations is one of the main  
objective of population genetics. Two of the papers in this special issue present packages  
that test for selection from genomic data, and use innovative algorithmic and  
96     implementation approaches to achieve substantial performance improvements over  
previous releases. PCADAPT (Luu *et al.* 2017) uses new algorithms for multivariate  
analysis in high-dimensional tables (see also Paradis *et al.* 2017), whereas REHH (Vitalis  
99     *et al.* 2017) uses multi-threading (light-weight parallelism) for the analysis of SNP data.

      Data simulation under more or less complex scenarios has become an increasingly  
important task in population genetics. Two papers in this special issue present packages  
102     designed for making this task easier. SKELESIM simulates genetic data with a  
user-friendly interface to help users to set parameters or choose sample sizes, as well as  
tools to summarize outputs (Hoban *et al.* 2017); it uses a similar user interface as  
105     MINOTAUR. PHYLODYN provides functions to simulate phylogenies under a wide range of  
coalescent models including heterogeneous sampling (Palacios *et al.* 2017). This package  
also implements a variety of inference tools under Bayesian nonparametric coalecent.

108     Finally, Rousset *et al.* (2017) present the summary likelihood method of statistical  
inference as an alternative to the approximate Bayesian computation (ABC) method,  
which is also based on summary statistics when the full likelihood cannot be computed.  
111     However, for the summary likelihood method of Rousset *et al.* the user does not need to  
formulate priors on the distribution of the parameters. The package INFUSION provides a  
generic implementation of this method, and Rousset *et al.* illustrate its use with a  
114     coalescent model of population change.

## **Impacts of the hackathon and this special issue**

      The NESCent hackathon that gave rise to many of the tools and products reported in  
117     this special issue was held with the kind of non-tangible objectives in nurturing the  
community and fostering collaboration whose achievement will only truly manifest in the  
long term. The collection of articles in this special issue will, hopefully, be a milestone

120 for the future progress of R in population genetics.

It is obviously too soon to pinpoint any such long-term successes. In addition to the tangible outcomes reported by Trainer *et al.* (2016) and the products described in this special issue, the hackathon nonetheless had a variety of impacts, some smaller and some larger. It helped create new collaborations on open source tools for population genetics, as evidenced by the author teams of the hackathon-related papers in this special issue; it introduced tools (such as the package HIERFSTAT) and their developers and users for the first time to collaborative code development and public version control on GitHub; and allowed participants to share knowledge and know-how. It also resulted in the revival of a previously existing but barely used community mailing list for population genetics in R (https://stat.ethz.ch/mailman/listinfo/r-sig-genetics).

It will remain to be seen whether these outcomes will have a lasting impact on population genetics as a field. However, the field will continue to face challenges – and opportunities – from the deluge of yet more massive amounts of genetic data, and these are likely to be addressed more effectively by a community well equipped to collaborate, whether across projects, institutions, or continents.

## Open questions and future prospects

Population genetics is facing a number of challenges and opportunities from the next-generation sequencing revolution, both technical and scientific. On the technical side, how to efficiently deal with the massive amounts of data generated by next-generation sequencing will remain an ongoing problem. This includes the question of how data generated by different technologies are best analysed in combination. On the scientific side, the different drivers of genomic selection in different scenarios of population evolution have traditionally been investigated separately, using different genetic markers. Today's possibilities for genetic data collection offer the opportunity to assess how different portions of a genome are linked and evolve under different selective pressures in different environments. It will be particularly exciting to see how R and its packages will evolve to meet these challenges in the years to come.

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