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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 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 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 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 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.

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 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 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 existing ones. Two papers deviate form 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. (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.
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 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 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).

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 genomic data and their visualization with a user-friendly interface (Verity et al. 2017). POPHELP, which is both an R package and a web server, provides tools for the visualization of population structure, including the outputs of external applications (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 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 (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 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 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 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.

Testing for or quantifying natural selection in populations is one of the main objectives 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 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 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 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 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 coalescent.

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. 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 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 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
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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