Phylogenetics

Genesis and Gappa: processing, analyzing and visualizing phylogenetic (placement) data

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Abstract

Summary: We present genesis, a library for working with phylogenetic data, and gappa, an accompanying command-line tool for conducting typical analyses on such data. The tools target phylogenetic trees and phylogenetic placements, sequences, taxonomies and other relevant data types, offer high-level simplicity as well as low-level customizability, and are computationally efficient, well-tested and field-proven.

Availability and implementation: Both genesis and gappa are written in modern C++11, and are freely available under GPLv3 at http://github.com/lczech/genesis and http://github.com/lczech/gappa.

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Supplementary information: Supplementary data are available at Bioinformatics online.

1 Introduction

The necessity of computation in biology, and in (metagenomic) sequence analysis in particular, has long been acknowledged. In phylogenetics, for example, there is a plethora of software for analyzing data, covering tasks, such as sequence alignment (Pervez et al., 2014), phylogenetic tree inference (Zhou et al., 2018) and diverse types of downstream analyses (Washburne et al., 2018). Furthermore, in metagenomics, a key task is the taxonomic identification of sequences obtained from microbial environments. An increasingly popular method for this is phylogenetic (or evolutionary) placement, which can classify large numbers of (meta-)genomic sequences with respect to a given reference phylogeny. Common tools for phylogenetic placement are pplacer (Matsen et al., 2010), RAxML-EPA (Berger et al., 2011) as well as the more recent and more scalable tools EPA-ng (Barbera et al., 2018), APPLES (Balaban et al., 2019) and RAPPAS (Linard et al., 2019). The result of a phylogenetic placement can be understood as a distribution of sequences over the reference tree, which allows to examine the composition of microbial communities, and to derive biological and ecological insights (Czech et al., 2019; Czech and Stamatakis, 2019).

Here, we introduce genesis, a library for working with phylogenetic data, as well as gappa, a command-line tool for typical analyses of such data. They focus on phylogenetic trees and phylogenetic placements, but also offer various additional functionality. Combined, they allow to analyze as well as visualize phylogenetic placement data with existing methods and to experiment with and develop novel ideas.

To maximize usability of our tools, our implementation is guided by the following design objectives: (i) most users require a fast and simple application for analyzing their data, (ii) some power users desire customization, for example, via scripting, (iii) developers require a flexible toolkit for rapid prototyping and (iv) with the on-going data growth, the implementation needs to be scalable and efficient with respect to memory and execution times. To this end, GENESIS and GAPPA are written in C++11, relying on a modern, modular and function-centric software design.

We evaluate the code quality, the runtime behavior and the memory requirements for conducting typical tasks, such as file parsing and data processing in the Supplementary Material. An exemplary benchmark for reading Newick files is shown in Figure 1. We find that GENESIS has the overall best code quality score compared to other scientific codes written in C or C++, using softwipe for the comparison (https://github.com/adrianzap/softwipe). It is also consistently faster than all evaluated Python and R libraries in our tests. Furthermore, GAPPA is faster and more memory efficient than its main competitor GUPPY in almost all tests and, most importantly, it scales better on larger datasets in all benchmarks.

2 Features of Genesis

GENESIS is a highly flexible library for reading, manipulating and evaluating phylogenetic data with a simple and straightforward application programming interface (API). Typical tasks, such as parsing and writing files, iterating over the elements of a data structure, and other frequently used functions are mostly one-liners that integrate well with modern C++. The library is multi-threaded, allowing for fully leveraging multi-core systems for scalable processing of large datasets. The functionality is divided into loosely coupled

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modules, which are organized in C++ namespaces. We briefly de-
scribe them in the following.

2.1 Phylogenetic trees
Phylogenetic trees are implemented via a pointer-based data struc-
ture that enables fast and flexible operations, and allows to store ar-
bitrary data at the nodes and at the edges. The trees may contain mul-
tifurcations and may have a designated root node. Trees can be
parsed from Newick files and be written to Newick, phylxml and nexus files, again including support for arbitrary edge and
node annotations. Traversing the tree starting from an arbitrary
node in, for example, post-order, pre-order, or level-order can be
accomplished via simple for loops:

```cpp
// Read a tree from a Newick file.
Tree tree = CommonTreeNewickReader().read(
    from_file("path/to/tree.newick")
);
// Traverse tree in pre-order, print node names.
for (auto it: preorder (tree)) {
    std::cout << it.node().data.name << "\n";
}
```

Functionality for manipulating trees, finding lowest common
ancestors of nodes (e. g. using the Euler tour technique of Berkman
and Vishkin (1993)) or paths between nodes, calculating distances
between nodes, testing monophyly of clades, obtaining a bitset rep-
resentation of the bipartitions/splits of the tree and many other
standard tasks are provided. Furthermore, functions for drawing
rectangular and circular phylograms or cladograms to svg files,
using individual custom edge colors and node shapes, are provided
for creating publication quality figures.

2.2 Phylogenetic placements
Handling phylogenetic placement data constitutes a primary focus of
GENESIS. Placement data are usually stored in so-called jplace files
(Matsen et al., 2012). Our implementation offers low-level functions
for reading, writing, filtering, merging and otherwise manipulating
these data, as well as high-level functions for distance calculations
(Evans and Matsen, 2012), edge PCA and squash clustering (Matsen
and Evans, 2011) and phylogenetic k-means clustering (Czech and
Stamatakis, 2019), among others. Advanced functions for analyzing
and visualizing the data are implemented as well, for instance, our
adaptation of phylofactorization to phylogenetic placement data (Czech
and Stamatakis, 2019; Washburne et al., 2017). Lastly, we offer a sim-
ple simulator for generating random placement data (e.g. for testing).

To the best of our knowledge, competing software that can parse
placement data in form of jplace files (BoSSA (Lefeuvre, 2018),
ggtree (Yu et al., 2017) or iTOL (Letunic and Bork, 2016) merely
offers some very basic analyses and visualizations, such as displaying
the distribution of placed sequences on the reference phylogeny, but
does not offer the wide functionality range of GENESIS.

2.3 Other features
Sequences and alignments can be efficiently read from and written
to fasta and phylip files; high-level functions for managing sequences
include several methods for calculating consensus sequen-
ties, the entropy of sequence sets and sequence re-labeling via hashes.
Taxonomies and taxonomic paths (e. g. ‘Bukaryota; Alveolata; Apicomplexa’)
can be parsed from databases, such as Silva (Quast et al., 2013; Yilmaz et al., 2014) or NCBI (Benson et al., 2009; Sayers et al., 2009), and stored in a hierarchical taxo-
nomic data structure, again with the ability to store arbitrary meta-
data at each taxon, and to traverse the taxonomy.

Furthermore, GENESIS supports several standard file formats, such as
json, csv and svg. All input methods automatically and
transparently handle gzip-compressed files. Moreover, a multitude of
auxiliary functions and classes is provided: matrices and dataframes to
store data, statistical functions and histogram generation to examine
such data, regression via the generalized linear model, multi-dimen-
sional scaling, k-means clustering, an efficient bitvector implementa-
tion (e. g. used for the bitset representation of phylogenetic trees
mentioned above), color support for handling gradients in plots, etc.
The full list of functionality is available via the online documentation.

Lastly, GENESIS offers a simple architecture for scripting-like de-
velopment, intended for rapid prototyping or small custom pro-
grams (e.g. convert some files or examine some data for a particular experiment).

3 Features of Gappa
The flexibility of a library, such as GENESIS is primarily useful for
method developers. For most users, it is, however, more convenient
for a simple interface for typical, frequent tasks. To this end, we
have developed the command line program GAPPA.

GAPPA implements and makes available the methods we presented
in Czech et al. (2019) and Czech and Stamatakis (2019), such as:
automatically obtaining a set of reference sequences from large data-
bases, which can be used to infer a reference tree for phylogenetic
placement; visualization tools to display the distribution of place-
ments on the tree or to visualize per-branch correlations with meta-
data features of environmental samples; analysis methods, such as
phylogenetic k-means and placement-factorization for environmen-
tal samples.

GAPPA also contains re-implementations of a few prominent meth-
ods of GUPPY (Matsen et al., 2010), as well as commands for sanitizing,
filtering, and manipulating files in formats, such as jplace, Newick
or fasta, and a command for conducting a taxonomic assignment of
phylogenetic placements (Kozlov et al., 2016).

As GAPPA internally relies on GENESIS, it is also efficient and scal-
able. Hence, GAPPA can also be considered as a collection of demo
programs for using GENESIS, which might be helpful as a starting
point for developers who intend to use our library. In comparison to
GUPPY, we have observed speedups of several orders of magnitude
and significantly lower memory requirements in general when pro-
cessing large data volumes; see the Supplementary Material and
Czech et al. (2019) for details.

4 Conclusion
We presented GENESIS, a library for working with phylogenetic
(placement) data and related data types, as well as GAPPA, a
command line interface for analysis methods and common tasks related to phylogenetic placements. **GENESIS** and **GAPPA** already formed an integral part in several of our previous publications and programs (Barbera et al., 2018; Czech et al., 2019; Czech and Stamatakis, 2019; Mahé et al., 2017; Zhou et al., 2017), proving their flexibility and utility.

In future **GENESIS** releases, we intend to offer API bindings to **Python**, thus making the library more accessible to developers. In **GAPPA**, we will implement additional commands, in particular for working with phylogenetic placements, as well as re-implement the remaining commands of **Guppy**, in order to facilitate analysis of larger datasets.

Both **GENESIS** and **GAPPA** are freely available under GPLv3 at [http://github.com/lczech/genesis](http://github.com/lczech/genesis) and [http://github.com/lczech/gappa](http://github.com/lczech/gappa).

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