

Phylogenetics

PHYLOViZ 2.0: providing scalable data integration and visualization for multiple phylogenetic inference methods

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Abstract

Summary: High Throughput Sequencing provides a cost effective means of generating high resolution data for hundreds or even thousands of strains, and is rapidly superseding methodologies based on a few genomic loci. The wealth of genomic data deposited on public databases such as Sequence Read Archive/European Nucleotide Archive provides a powerful resource for evolutionary analysis and epidemiological surveillance. However, many of the analysis tools currently available do not scale well to these large datasets, nor provide the means to fully integrate ancillary data. Here we present PHYLOViZ 2.0, an extension of PHYLOViZ tool, a platform independent Java tool that allows phylogenetic inference and data visualization for large datasets of sequence based typing methods, including Single Nucleotide Polymorphism (SNP) and whole genome/core genome Multilocus Sequence Typing (wg/cgMLST) analysis. PHYLOViZ 2.0 incorporates new data analysis algorithms and new visualization modules, as well as the capability of saving projects for subsequent work or for dissemination of results.

Availability and Implementation: <http://www.phyloviz.net/> (licensed under GPLv3).

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Supplementary information: [Supplementary data](#) are available at *Bioinformatics* online.

1 Introduction

DNA sequencing facilitated obtaining comparable and reproducible microbial typing data, effectively replacing other molecular and phenotypic techniques. Although single-gene approaches exist, MultiLocus Sequence Typing (MLST) (Maiden *et al.*, 2013; Spratt, 1999) remains the most popular. While traditional MLST relies on a few genes for discriminating bacterial isolates, the advent of High-Throughput Sequencing (HTS) allowed analyzing thousands of loci and is being presented as the ultimate tool for defining bacterial clones with application in clinical settings (Carriço *et al.*, 2013; Maiden *et al.*, 2013). On the other hand, traditional algorithms and

software are proving inadequate to handle the increase in number of loci and strains to be analyzed, which is going from tens to thousands given the decrease in HTS costs.

Several tools are available for data analysis and visualization of microbial typing data, such as START (Jolley, 2001), eBURST (Feil *et al.*, 2004) and goeBURST (Francisco *et al.*, 2009). However, these tools lack the capacity to integrate ancillary epidemiological data. Several well known tools (Suderman and Hallett, 2007) allow network visualization and data integration. However, these are of generic use and are not specifically directed towards population or evolutionary analysis, depending on

other software for inferring trees and requiring non-trivial customization.

PHYLOViZ (Francisco *et al.*, 2012) is a flexible and expandable plugin based tool, able to handle large datasets, both in number of analyzed samples and loci. PHYLOViZ includes data integration and visualization capabilities for molecular epidemiological data (such as SNP or cg/wgMLST data), allowing a visual analytics approach. However, the current version lacks important features such as storing data manipulations (projects) for sharing or later work. Moreover, PHYLOViZ offered limited clustering methods for the creation of trees, lacking widely used methods in the context of microbial population and epidemiological analyses such as Neighbor-Joining (Saitou and Nei, 1987) and Hierarchical Clustering methods (Sneath and Sokal, 1973).

We developed PHYLOViZ 2.0 to meet needs identified by users of PHYLOViZ, including new data analysis algorithms and visualization modules, namely a dendrogram view and a weighted tree view. PHYLOViZ 2.0 is also now capable of saving ongoing projects and of dynamically updating the saved projects, a time-saving feature when working with large datasets and essential for efficiently sharing results.

2 Methods

PHYLOViZ is based on the NetBeans Platform and it includes revisions of existing plugins and six new plugins (see Table 1).

PHYLOViZ now includes implementations of hierarchical clustering methods, namely methods that belong to a common class defined as Globally Closest Pair (GPC) clustering algorithms (Gronau and Shlomo, 2007). In each step of a GPC algorithm, one pair of clusters is selected such that it satisfies a criterion of minimal dissimilarity. The selected clusters are merged and the next step will consider a new cluster that corresponds to their union. We have implemented three variants of GPC algorithms, namely unweighted and weighted pair group method with arithmetic mean (UPGMA and WPGMA, respectively), Single Linkage and Complete Linkage. These methods are distinguished by the dissimilarity condition considered, so we have implemented a generic method where this is given as parameter. By using the lookup mechanism implemented in the NetBeans platform, dissimilarity conditions are provided as services and remain independent of the algorithm. Hence, new dissimilarity conditions can be made available through independent plugins, which may be developed and added at any time. We have also added to PHYLOViZ the Neighbor-Joining method with two different branch length estimators (Saitou and Nei, 1987; Studier and Kepler, 1988).

The new version includes two new visualization modules: a dendrogram view and a weighted tree view. In order to make these modules generic, we defined different types of abstractions associated to each visualization, including specific JSON schemas. The main goal is to allow reusing visualizations by other plugins. In order to visually emphasize the hierarchical groups within some pre-defined distance, we also implemented a visual cutoff functionality. Together with the ability of integrating ancillary data, this provides a unique and user friendly platform for visual analytics in microbial typing and phylogenetics.

In previous PHYLOViZ version, users could analyze and visualize their data and export results in several commonly used graphic formats. However, it was not possible to save studies, for

Table 1. New plugins in PHYLOViZ 2.0

Plugin	Description
Clustering Tree Viewer	Hierarchical clustering tree viewer
Dendrogram Viewer	UPGMA dendrogram/tree viewer
GPC Commons	Globally Closest Pair clustering utilities
Neighbor-Joining Projects	Neighbor-Joining algorithm implementation
UPGMA	Save and load features for Projects
	UPGMA algorithm implementation

subsequent work or for sharing with others. This limitation is of particular importance when working with large datasets, for which running algorithms and optimizing visualizations can take considerable time. In version 2.0 it is possible to save each study as a project. Each project includes the data under analysis, results of inference algorithms, visualization serializations and related graphical layout customizations.

Tutorial screencasts on new functionalities of PHYLOViZ 2.0 are available at <http://www.phyloviz.net/tutorials.html>, and its documentation is available at <http://phyloviz.readthedocs.org>. An example of the novel algorithms visualizations can be found in supplemental material.

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