

# Modification of PrimeTV2 and Implementation of a Web Application

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Bachelor's Thesis in Computer Science (15 ECTS credits)

Bachelor's Programme in Computer Science

Stockholm University year 2018

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# Abstract

## **Modification of PrimeTV2 and implementation of a Web Application**

Evolutionary trees of genes are called gene trees. Gene tree evolution is constrained by how the species tree has evolved. To visualize this as a gene tree into a species tree, a reconciliation can be used. PrimeTV, written by Lars Arvestad and colleagues, is a program for visualizing reconciled (evolutionary) trees.

There exists a successor to PrimeTV called PrimeTV2. PrimeTV2 has a Graphical User Interface and has more features than the predecessor has.

This degree project is about making PrimeTV2 accessible as a web application. The web application PrimeTV2-ForWeb acts as a Graphical User Interface for the program PrimeTV2 and makes it easier for the user to visualize gene trees. It does not require any download of software when the program runs through the web. PrimeTV2ForWeb runs PrimeTV2 directly from the web through a web server.

# Referat

## **Modifering av PrimeTV2 samt implementation av en webbtjänst**

Evolutionära träd av gener kallas geneträd. Genträdens utveckling begränsas av hur arträden har utvecklats. För att visualisera detta som ett geneträd i ett arträd kan en mappning användas. PrimeTV, skrivet av Lars Arvestad med kollegor, är ett program för visualisering av evolutionära träd.

Det finns en uppföljare till PrimeTV som kallas PrimeTV2. PrimeTV2 har ett grafiskt användargränssnitt och har flera funktioner än föregående program.

Detta examensarbete handlar om att göra PrimeTV2 tillgänglig som en webbtjänst. Webbtjänsten PrimeTV2-ForWeb fungerar som ett grafiskt användargränssnitt för programmet PrimeTV2 och gör det enklare för användaren att visualisera geneträd. Det krävs ingen nedladdning av programvara när programmet körs via en webbtjänst. PrimeTV2ForWeb kör PrimeTV2 direkt på en server via en hemsida.

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# 1 Introduction

The purpose of this project is to develop a web application called PrimeTV2ForWeb, which will work as a Graphical User Interface for the reconciliation program PrimeTV2. PrimeTV2 is a program that visualizes gene trees (see Fig 1). PrimeTV2ForWeb integrates with a web server for sending and receiving data from PrimeTV2.

The intention of this web application is to make visualization of gene trees easier, and it does not require any download of software. This project will make it easier to use PrimeTV2.

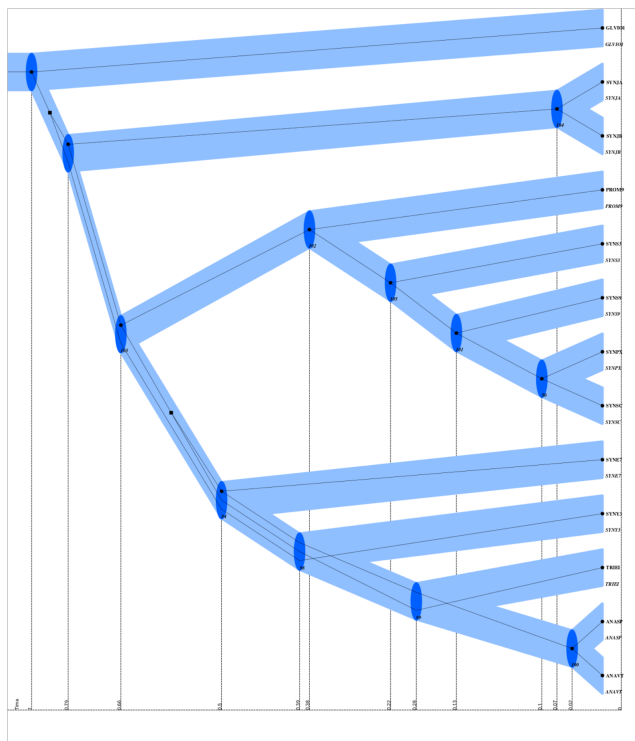


Figure 1: Output from PrimeTV2.

## 1.1 Background

The word evolution means gradually growing from something or gradually changing with time. Evolution is the process in which behavior and appearance for species changes over time. The study of gene evolution is one of the most fast developing fields of biology [1]. Illustrating evolution using phylogenetic (evolutionary) trees is a natural way of describing evolutionary processes [2]. A gene tree is an evolutionary tree, which is a branching diagram showing the evolutionary relationships within species [3]. Evolutionary trees can sometimes be represented as tree-within-trees. Tree-within-tree representation is the relation between a gene tree into the species tree, also called a reconciliation (see Fig 1 for example). Reconciliations can be used to understand the history of a specific gene family [4]. A reconciliation allows the prediction and dating of evolutionary events (e.g. gene duplication) corresponding to vertices of gene tree  $G$  with respect to species tree  $S$  [2]. Illustration of reconciliations requires a lot of work if created by hand. Visualization of gene evolution with computer programs facilitates the work for biologists.

The program PrimeTV was created by Lars Arvestad and colleagues to facilitate the work of visualizing reconciled trees. It is a command-line based reconciliation viewer program.

Input to PrimeTV is a host tree  $S$ , gene tree  $G$  and (optionally) a reconciliation between  $G$  and  $S$ . The reconciliation between  $G$  and  $S$  is a mapping between vertices in  $G$  and the edges in  $S$  on which they evolve [2]. A reconciliation is given directly in the gene tree  $G$  or as a map file. Without a map file the program can reconcile by itself. The tree input to PrimeTV is in Newick format, which is a way of representing trees using parentheses and commas [5]. The output of PrimeTV is an illustration of  $S$ ,  $G$  and the reconciliation which has  $G$  nested in  $S$  (see Fig 1 for example output). The species tree  $S$  is illustrated using wide edges, the gene tree  $G$  is illustrated using narrow edges.

The successor to PrimeTV is called PrimeTV2 and was created as an earlier student project [6]. PrimeTV2 has a Graphical User Interface (GUI) which is developed in Qt. The GUI program Qt is a framework and toolkit that helps to build applications and graphical user interfaces [7]. PrimeTV2 has also more features than PrimeTV has. The program PrimeTV2 is based on Cairo (which is a 2D graphics library [8]).

This project is about creating a web application for the program PrimeTV2. The web application will work as a Graphical User Interface instead of having a Graphical User Interface with Qt. A web application makes it easier to use PrimeTV2 because no download of software is required.

## 1.2 Problem Statement

This degree project is about creating the web application called PrimeTV2ForWeb with a user friendly graphical design, because there is no one created for the web application from the beginning. The design of the application is user-centered. The web application needs to improve the usability, accessibility and also needs to look beautiful with a color-scheme. These parts are called User Experience (UX) and User Interface (UI) design, more about UI/UX design in [subsection 3.1](#)

The fundamental part of the project is to create a web application. The web application is implemented with a user friendly Graphical User Interface instead of, as it is now, having a Graphical User Interface built into PrimeTV2. A web application is desirable because there is no requirement to download any software tools or data files in order to run the program. Everyone having a device with a web browser, no matter what operating system used, can use the program because it is platform independent. The web application is also desirable because it is easy to update and maintain the web application, for getting the updated version of the program for all clients, a developer only has to update on the server side. To update a program that is not running through a web application, a new version of the program must be downloaded and installed and the developer can not be sure that every client has the newest version.

The existing reconciliation program PrimeTV2 must be downloaded and installed on the computer in order to run it. The program is based on Cairo and has a Graphical User Interface with Qt, which was an add-on. Cairo is used for graphic output, while Qt is used for Graphical User Interface. Qt:s interaction with Cairo has changed since the program was written. PrimeTV2 is therefore hard to compile.

The web application is only using open source software, so it is free to use. PrimeTV2ForWeb is running the reconciliation program PrimeTV2 directly from the web through a web server.

The web application facilitates visualization of reconciled trees for the user, and will work as a Graphical User Interface instead of using Qt as a GUI to PrimeTV2.



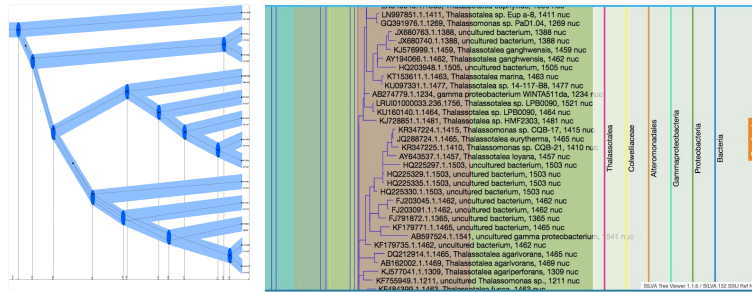
## 2 Related Work

PrimeTV2 [6] is a successor to PrimeTV. PrimeTV2 is a tool for gene visualization and how they evolve with respect to species evolution. PrimeTV is command-line based while PrimeTV2 can either be run using a Graphical User Interface or from the command-line. PrimeTV2 also has more features than PrimeTV. PrimeTV2ForWeb [9], which is created in this project, is the successor to PrimeTV2. PrimeTV2ForWeb is a web application for reconciliation trees, which means it does not require any software downloads. The web application uses a simplified command-line version of PrimeTV2 instead of having a Graphical User Interface [10]. The program PrimeTV2 creates a graphical representation of a tree-within-tree visualization (see Fig 2a). This kind of representation of trees is used in a similar program called SylvX [11]. SylvX is a reconciliation viewer which implements graphic operators (color, highlighting etc.) and uses new methods for comparison of reconciliations [11]. SylvX gives a good overview over how gene- and species trees relates (see Fig 2c). SylvX does not represent the gene evolution as a tree evolving inside another tree. The evolutionary processes of species are represented as nested trees in both PrimeTV2 and SylvX. SylvX needs to be downloaded from their web page (<http://www.sylvx.org>), while PrimeTV2ForWeb is a web application and is designed for visualizing trees without requiring to download any software.

There exists many tree viewers for non-reconciled trees.

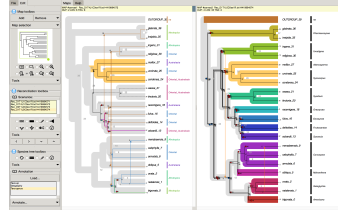
Another tree viewer program is SILVA [12] and can be found at ([http://treeviewer.mpi-bremen.de/tree\\_viewer\\_public/](http://treeviewer.mpi-bremen.de/tree_viewer_public/)). SILVA is a web application like PrimeTV2ForWeb and is designed for visualizing large trees without requiring the download of any software tools or data files [12]. SILVA does not allow user input. Files can not be submitted like in PrimeTV2 where gene tree, species tree and map file can be submitted as input and a tree-within-tree visualization appear as output. SILVA provides tree navigation, search and browse tools but not uploading files from computer (see Fig 2b for an example of how SILVA looks). Through SILVA rRNA database, SILVA provides direct access to the evolutionary trees. SILVA represent large data from

a database, the program provides search and browsing functions for finding the data of interest. The viewer does not provide editing of the trees, only visualization tools is supported in version 1.1 of SILVA [12].



(a) PrimeTV2

(b) SILVA



(c) SylvX

**Figure 2:** Different layouts for different programs.

There exists other viewers for phylogenetic trees, for instance:

- Dendroscope, which is an interactive viewer for rooted evolutionary trees and networks [13]. Dendroscope is open source and can view large trees which easily can be browsed and edited. This program has seven different layouts for the output: Rectangular Phylogram, Rectangular Cladogram, Slanted Cladogram, Circular Phylogram, Circular Cladogram, Radial Phylogram and Radial Cladogram [13].
- Notung [14] is another reconciliation program that supports phylogenomic analysis. Although it doesn't visualize results as tree-within-tree, it is still worth mentioning. Through its integrated results from reconciled gene families it enables a multitude of analysis, e.g. gene age relative to the species tree [14].

Another frequently used program is FigTree which is a graphical viewer of phylogenetic trees for producing figures [15].

PrimeTV2ForWeb is a mix between SvlvX and SILVA. It does not require any downloading of software just like SILVA. These programs are more user friendly because it is convenient to avoid installation of software. The representation of the trees in PrimeTV2 and how to run the program is more in line with SvlvX, because SILVA views large trees directly when browsing to the web application. In PrimeTV2 and SvlvX some input files are required, the input files consists of gene tree and host tree and creates output after the users input. SILVA does not allow input from the user, it only shows trees where the user can browse and search through.

## 3 Method

In the beginning of the project some decisions were made, these decisions lays the foundation for the entire project. These decisions includes choices of front-end and back-end languages, which frameworks to use and how to design the web application.

### 3.1 Design

The design has taken into account both User Experience (UX) and User Interface (UI) design. UX is about improving the usability and accessibility, UX design is how easy the users understand how to use the web application [16]. The web application has a menu, from where to navigate to the Upload files section which is the main area in the application. In the menu there only exists Upload files, About and Contact us sections so there should be no confusion on which section to use for uploading files and running the program.

After implementing all parts in the web application and the components have been placed strategically, the usability and accessibility was tested by some users to see if the website is fulfilling the demands and how easy it is to use and understand.

UI design is about making the interfaces created in the UX part look beautiful, like color scheme to make it easy to use [16]. The main output picture from the reconciliation program, without changing options, is used as header image on the web page. Color on the output picture is blue, the color scheme was therefore created after this. The UI design was tested on the same group of users as the UX design to see so it is fulfilling the demands on the design.

### 3.2 Technologies

For creating a project a specific technology and programming languages needs to be chosen. As an owner of the project, the technology and language selected will last for many years beyond the project's schedule.

A web application is a program that is accessed through a web server using a web browser. The web application usually consists of two parts:

- A client that is shown in the browser as HTML and presents dynamic content.
- A web server that provides and stores data.

There are several advantages with a web application:

- Almost every modern device has a browser.
- Update and maintain web applications without having to install any software. A developer only has to update on the server side for getting the updated version of a program for all clients.
- Software is not platform dependent.

The web application is built using the web technologies HTML5, CSS and JavaScript/jQuery. Developing the application in this environment was a natural choice because they are the main parts for creating a website. There is no way to create a website without HTML. HTML is the foundational structure of all websites and web applications. For designing the web application, a framework called bootstrap is used.

Server side technology was harder to decide due to more choices. Here a research phase begun. Some previous experience of web development existed, but the decision about which technology to use was based on the research part. Three books was used [17], [18] and [19] and several scientific articles were downloaded.

### 3.2.1 Program and development tools used

The program developed is tested on an Apache server on the local computer. Apache is free to use, open source and suits all needs [20].

The development environment used for this project is Sublime Text, it is a text editor for code and markup [21]. Sublime Text is used because it is easy to use and is a favorite for coding.

For version control git is used. Git is also used by the supervisor of the project to keep track of how the project is going based on the timetable that needs to be followed. The code is uploaded on the website GitHub who provides git and remote repository. GitHub is a program to safely save the code in the cloud, to be safe if the computer breaks [22].

### 3.3 Building a web application

A web page foundational structure is HTML. This project uses HTML5, CSS, JavaScript and jQuery as front-end language, PHP as back-end language and the framework bootstrap for Graphical User Interface. Next is a description of the techniques used in the implementation of the user friendly Graphical User Interface web application.

#### 3.3.1 HTML5

HTML5 stands for Hypertext Markup Language. HTML5 is the language of the Browser and is the latest version of HTML, its elements is the main part for the web application. HTML is a standard for the World Wide Web (WWW) and support for HTML is implemented in all web browsers e.g., Safari, Chrome and Firefox [23].

#### 3.3.2 CSS

CSS stands for Cascading Style Sheets and is used for describing the presentation style of a HTML-element [24]. CSS is used to visually present image, text and other elements.

#### 3.3.3 JavaScript

JavaScript is a scripting language executing on the client side. JavaScript is used for controlling the content of a web page and for dynamically script web pages. The purpose of JavaScript is to increase client flexibility. All modern browsers support it without plug-ins [25].

#### 3.3.4 jQuery

jQuery is a JavaScript library and is used to simplify HTML and CSS modification to speed up web development. jQuery is designed to make it easier to navigate a document, select DOM<sup>1</sup> elements, create animations, handle events, and develop Ajax applications [27].

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<sup>1</sup>An interface that allow programs to dynamically update the content of a document [26].

### 3.3.5 PHP

PHP stands for PHP: Hypertext Preprocessor and is a scripting language. PHP primarily runs on web servers to run the web application with dynamic content. PHP code can be embedded into HTML or HTML5 markup [28].

### 3.3.6 Bootstrap

Bootstrap is a framework for front-end programming. Bootstrap is used for designing websites and web applications. It is a design template for typography, forms, buttons, navigation etc. The design template is HTML-, CSS- and JavaScript based. Bootstrap is used to create a simple and good-looking web page, it makes it easier to create a design [29]. Bootstrap provides an API through a plugin which makes the interaction very easy. There is no need for writing any JavaScript lines [30].

## 3.4 Server side language

Server side language is used in web development. A web application runs through a web server which sends and receives data for each user to the website [31].

This section compares a certain number of server side languages and selects the best fitted for this project.

### 3.4.1 Previous web application - Perl

There existed a web page for PrimeTV before, but it did not work and was old. The web page was developed in the programming scripting language Perl (Practical Extraction and Reporting Language).

### 3.4.2 PHP vs Ruby on Rails vs Perl

PHP is described on their official website as “PHP (recursive acronym for PHP: Hypertext Preprocessor) is a widely-used open source general-purpose scripting language that is especially suited for web development and can be embedded into HTML” [32]. PHP is a script language embedded in the HTML code, and is used to create web applications. PHP is written especially for the web and provides a tool for dynamic content on a web page. The

language is server side, namely back-end programming. An external web server is required for running PHP (e.g. Apache), but Ruby on Rails contains its own web server [33].

Ruby is described on their official website as “A dynamic, open source programming language with a focus on simplicity and productivity. It has an elegant syntax that is natural to read and easy to write” [34]. Ruby on Rails is a web framework, based on Ruby, and by that not directly comparable to PHP.

Perl has hundreds of modules that can be added easily to extend their capabilities [35]. The program is used for creating Common Gateway Interface (CGI) applications, although writing CGI programs can be done in any programming language. [35]. CGI is used for transmit information between a web page and a program designed to accept and return data (like PrimeTV2).

#### **Ruby on Rails advantages:**

1. Easily used for web applications [19].
2. Integration: Communicate with other language, e.g., C/C++, Java and Matlab [19].
3. Easy to start script on the web server for testing.

#### **PHP advantages:**

1. One of the fastest scripting languages [36].
2. Easy to use. PHP is simple, fluent, clean and organized.
3. Most commonly used.[37].
4. Easy to find cheap web hosting. [38].

#### **Perl advantages:**

1. Easy to learn.
2. Built in debugging [39].
3. Easy integration with C.



### Statistics over which programming back-end language most used on websites:

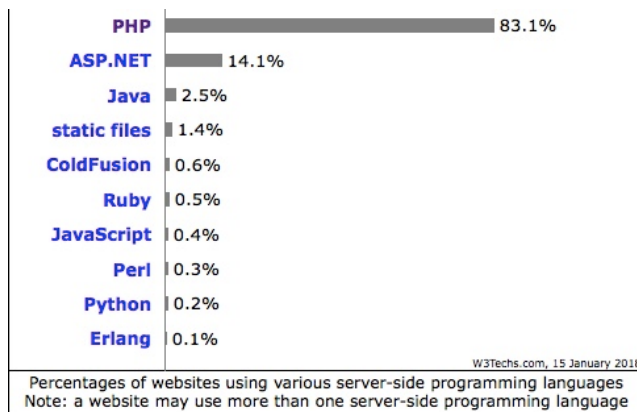


Figure 3: PHP is definitely the most used language – Picture from [40].

The statistic from Fig 3 shows that PHP is by far the server-side programming language that is used by most websites. PHP is used by facebook, wikipedia and Yahoo among others [41].

PHP, Perl and Ruby on Rails are all open source. All these also have powerful database connection abilities. Ruby on Rails is slow (because it is a web framework), while PHP is one of the fastest scripting languages [42]. PHP and Perl has a shorter learning curve than Ruby on Rails and since this project has quite short time frame, Ruby on Rails was not chosen for this project [38]. PHP is especially created for the web, which means scripts will run faster and can handle more simultaneous users on the website. Since Perl is older and only 0.3 % of all websites uses it, PHP was chosen as the back-end language [40]. Some previous experience existed in PHP before the project. PHP is used as server-side language by 83.1 % of all websites, it is the most popular web application language at this time (year 2017) [40]. For this project, PHP was chosen due to the short learning curve, previous experience, open source and because it is one of the most widespread programming language used on web pages.

## 3.5 Implementation

Below is a description of the developed web application specification and functionality.

### 3.5.1 Specification

Before the web application development could start a project specification of what the application should contain was made.

- Uploading files to the program PrimeTV2.
- Getting data from PrimeTV2 with the output picture.
- Optional choices – color on the output, which fonts used, show time etc.
- Creating a user friendly Graphical User Interface.

This was the main things in the specification that needed to be implemented, in order to get the same functionality as the existing program.

### 3.5.2 Functionality

The functionality of the web application is the one specified in the beginning of the project. The main things implemented in PrimeTV2ForWeb are:

- Uploading files to the server, this is made with PHP script for accessing the files.
- Accessing the files from the server with JavaScript and sending to the program using PHP.
- Getting data from PrimeTV2 with the output file. This is done with PHP, accessing the file that the program has created.
- Example data – the user can test the program without knowing so much about the program.
- Creating a Graphical User Interface with bootstrap.

Some features were implemented as optional input selections to the program:

- Color scheme of the output file – Can choose between KTH, SU, Yellow, Mono, Blue, Grey.
- Time scale on the output file – E.g., no time scale, no time at all.
- Fonts on the output file – E.g., guest tree font, host tree font.
- Font size – E.g., size of font for gene nodes, size of font for species nodes.
- Activate – E.g., activate the legend, activate the header, include the text on the top of the image.
- LGT cost – Show the number of duplication's and transfers used in the computed reconciliation.
- Output format – Can choose between SVG, PDF and PNG.
- Activate the legend, the header and include text on top of the image.

All these features existed in the program PrimeTV2. Almost all options in the existing program was implemented in the web application, at least all the options desired from the project commissioner.

### 3.6 Source code

The source code for the web application can be found at: <https://github.com/alexandraone/PrimeTV2Forweb>

The source code for the reconciliation program PrimeTV2 can be found at: <https://github.com/alexandraone/PrimeTV2>

## 4 Conclusions and Furture Work

The main purpose of this project has been to create a link between the program PrimeTV2 and a web page, in other words – a web application. The web application is created to make it easier for the user to run the program, because no downloading is required. The program PrimeTV2 that needs to be installed, is replaced with a web-based alternative with similar functionality.

The conclusion that can be drawn from this project is that the web-based program implementation of this project came out well. The functionality of the web application fulfills the expectations of what it should contain, the most used options in the program are implemented as input from the web application. The design of the web page seems to be good and user friendly since some users have tried it. The user testing was about asking them to use the website (e.g. upload files, changes options, run program) and see if they understands how to do it. There was no confusion of how to use the main page of the web application to run the program with the input required by the user. The result is a web application that is easy to use and understand. The choices made from the possible front-end and back-end languages that were compared worked excellent, the web application could be developed with these languages without any problems.

Possible future work on this project includes creating more options to the program. The web application should be tested on more browsers, it has only been tested on Google Chrome and Safari. Since the application has been tested on a local server, mobile devices have not been tested. It should therefore also be tested on mobile devices to see if it works and how it looks. Another thing that was considered in this project was to change the input format for PrimeTV2 to recPhyloXML [4]. RecPhyloXML is designed to describe reconciled gene trees, it is designed so that every reconciliation program can use the same input so it is easy to use for all. Changing the input format to recPhyloXML is a thing that can be done in future work.

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