Genome analysis

**CiVi: circular genome visualization with unique features to analyze sequence elements**

Lex Overmars¹,²,³,*, Sacha A. F. T. van Hijum¹,²,⁴, Roland J. Siezen¹,² and Christof Francke¹,²,⁵

¹CMBI, Radboud University Medical Centre, Nijmegen 6525GA, The Netherlands, ²Netherlands Bioinformatics Centre, Nijmegen 6500HB, The Netherlands, ³Institute for Biodiversity and Ecosystem Dynamics, University of Amsterdam, Amsterdam, The Netherlands, ⁴NIZO Food Research B.V., Ede, The Netherlands and ⁵Hogeschool Arnhem en Nijmegen BioCentre, 6525EM Nijmegen, The Netherlands

*To whom correspondence should be addressed.

Associate Editor: John Hancock

Received on November 28, 2014; revised on April 17, 2015; accepted on April 20, 2015

**Abstract**

Summary: We have developed CiVi, a user-friendly web-based tool to create custom circular maps to aid the analysis of microbial genomes and sequence elements. Sequence related data such as gene-name, COG class, PFAM domain, GC%, and subcellular location can be comprehensively viewed. Quantitative gene-related data (e.g. expression ratios or read counts) as well as predicted sequence elements (e.g. regulatory sequences) can be uploaded and visualized. CiVi accommodates the analysis of genomic elements by allowing a visual interpretation in the context of: (i) their genome-wide distribution, (ii) provided experimental data and (iii) the local orientation and location with respect to neighboring genes. CiVi thus enables both experts and non-experts to conveniently integrate public genome data with the results of genome analyses in circular genome maps suitable for publication.

Contact: L.Overmars@gmail.com

Supplementary information: Supplementary data are available at *Bioinformatics* online.

Availability and implementation: CiVi is freely available at http://civi.cmbi.ru.nl

---

**1 Introduction**

Circular genome representations provide an excellent way to comprehensively inspect genome-wide data. Various tools have been developed to generate these circular visualizations including CGView (Stothard and Wishart, 2005), GenomeVx (Conant and Wolfe, 2008), GeneWiz (Hallin et al., 2009) and DNAPlotter (Carver et al., 2009). Tools such as BRIG (Alikhan et al., 2011), CGView Comparison Tool (Grant et al., 2012), Circos (Krzywinski et al., 2009) and Circletator (Crabtree et al., 2014) can also visualize genome comparisons and in some cases, visualize links between genome sequence and other types of information. The tools described above are well-suited for the visualization of high-throughput genomic data like sequence-similarities or read counts, but have limited functionality in relation to smaller-scale activities such as reconstructing transcription networks and finding gene functions associated to genetic elements. Moreover, with the exception of GeneWiz (Hallin et al., 2009), they require laborious and sometimes complex uploads of genome and annotation data. In 2013 we published MGcV (Overmars et al., 2013), a linear-genomic context visualization tool tailored to provide a simple and quick visual access to the publicly available genomic data from NCBI (Pruitt et al., 2012). The tool incorporated the capabilities of the earlier MGV (Kerkhoven et al., 2004), and extended the visualization with data export options to advance the gene-specific analysis of microbial genomes. We now present CiVi, which has been developed using the same philosophy, to extend the circular viewing options provided by the original MGcV. The extensions include the possibility to display annotation data like COG category, PFAM domain or subcellular location directly on the genome map and to reveal the position of selected annotations through a keyword search option. CiVi also enables the
2 Usage and implementation

GVi enables users to create custom circular microbial genome maps in a simple step-wise fashion, adding data ring by ring. The interface consists of a panel on the right in which the map is displayed and four panels on the left related to the different menus, labeled: (i) ‘Genome and data selection’; (ii) ‘On display’; (iii) ‘Data import’; and (iv) ‘Elements and genomic context’. For every ring the user can subsequently set (panel i): the organism and genome of interest, the type of information, the coloring and the radius of the ring. The types of information that can be included directly are: the location of the genes on the +strand and -strand, COG categories (NCBI RefSeq), GC%, GC-skew and AT-skew (calculated; Overmars et al., 2013), PFAM domains, and subcellular location predictions (PSORTdb; Nancy et al., 2011). A keyword matching option allows highlighting genes whose gene product, gene name, COG code or PFAM ID match a query. In addition, the coordinates and a title or background coloring can be added, and gene-associated quantitative data can be represented by either (bar graph like-) spikes or by a red-to-green gradient. The categorical data have been linked to fixed colors. Map additions are tracked in the ‘On display’-panel, in which added rings can also be removed. Users can upload three types of data in the ‘Data import’-menu: quantitative data (e.g. expression ratios), the predicted position of sequence elements (e.g. regulatory elements) and/or custom color schemes to designate any genomic region in the genome map. Different genomes can be included in a single circular map, but as synteny is not determined this feature should only be used with very closely related genomes.

2.1 Analysis and visualization of sequence elements

An integrated view of genome-wide experimental data and the predicted location of particular regulatory elements can be very allusive in the analysis of transcriptional networks (as illustrated in Fig. 1 and supplementary file S1). The position of any particular genomic element with respect to the location and orientation of the surrounding genes can hint at the biological role of that element. GVi generates plots in the ‘Elements and genomic context’-panel for each uploaded set of sequence elements, in which both the distance to the neighboring genes and the orientation with respect to the genes is summarised (Fig. 1B). Similarly, the biological role of a particular element may be derived from the functional characteristics of the gene context. The user can download the positions and the annotation data for the gene context for subsequent analysis using the ‘Generate context table’-link.

2.2 Implementation

GVi is a web-application developed using a combination of python, javascript, MySQL and SVG. GVi was implemented as a single page application; the front-end makes server side calls through Jquery and AJAX and receives a response from the server. The maps can be downloaded in SVG, PNG or PDF format, where conversions are done using ‘Batik Rasterizer’. The maps in SVG-format can be enhanced usability, interactivity (via mouse-over) and speed.

3 Conclusion

GVi is a versatile and easy-to-use web-application to create custom circular genome maps. It provides a visual integration of publicly available genomic data and additional provided data, the latter including e.g. gene expression data and genomic elements. The functional analysis of latter elements is aided by the characterization of their genomic context, a feature that is unique to GVi.
Funding
This work was supported by the BioRange programme of the Netherlands Bioinformatics Centre (NBIC), which is supported by the Netherlands Genomics Initiative (NGI).

Conflict of Interest: none declared.

References