Visualization for genomics: the Microbial Genome Viewer

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ABSTRACT
Summary: A Web-based visualization tool, the Microbial Genome Viewer, is presented that allows the user to combine complex genomic data in a highly interactive way. This Web tool enables the interactive generation of chromosome wheels and linear genome maps from genome annotation data stored in a MySQL database. The generated images are in scalable vector graphics (SVG) format, which is suitable for creating high-quality scalable images and dynamic Web representations. Gene-related data such as transcriptome and time-course microarray experiments can be superimposed on the maps for visual inspection.

Availability: The Microbial Genome Viewer 1.0 is freely available at http://www.cmbi.kun.nl/MGV
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INTRODUCTION
The ongoing data explosion in the field of genomics, transcriptomics and metabolomics has created the need for data-handling tools that are able to reveal complex relations and patterns. In the field of genomics, much effort has been paid to structuring and standardization of data. The need for worldwide standards for data exchange is clearly represented by the numerous projects defining protocols for information storage in XML. Besides the growing need for structuring the data explosion, visualization of these data is an essential step in the flow of knowledge. As yet, not many free software tools are available for interactive visualization of circular or linear genome maps. Programs like GenomePlot (Gibson and Smith, 2003) and GenoMap (Sato and Ehira, 2003) are used for creating chromosome wheels and linear maps of genomic data stored in tab-delimited or GenBank/EMBL format, respectively. Both are standalone programs; the latter can also plot microarray expression or other types of quantitative data. Disadvantages of both programs are the lack of interactivity with the pictures and the requirement of specific input formats.

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A non-interactive structural DNA analysis and visualization is provided for all sequenced genomes by GenomeAtlas (Pedersen et al., 2000) through a dedicated Web-interface. Additionally, commercial software exists like GenoStar and DNASTAR, which include genome visualization and analysis.

IMPLEMENTATION
Here, we present the Microbial Genome Viewer (MGV), a Web-based tool for interactive visualization of annotation and transcriptome data on chromosome wheels and linear genome maps. Genome annotation data are retrieved from a local MySQL database enabling rapid visualization. Data include all the relevant information on the complete genomes from the GenBank/EMBL/DDBJ databases. Several supplementary annotation methods have been automated in order to enrich this database. Terminator structures were added with TransTerm (Ermolaeva et al., 2000) and all organisms were scanned for COG (Tatusov et al., 2001) and Pfam domains (Bateman et al., 2002) using a Paracel GeneMatcher2 machine.

Scalable vector graphics (SVG) was chosen as the format for visualization. SVG is a language for describing two-dimensional images in XML and has been recommended by the W3C consortium (http://www.w3c.org/SVG). The possibility of adding animation, interaction and the supplementation of scripting languages makes SVG highly suitable for the visualization of complex data generated by the genomics community. Other advantages are the small file size and scalability for obtaining high-resolution images for posters and publications. SVG plugins for a wide range of platforms are available (http://www.adobe.com/SVG).

Genes can be colored according to different annotation methods. The classification of COG domains in functional categories enables functional coloring of the genome maps (Tatusov et al., 2001). Numerical data like GC%, GC-skew, AT-skew and data from microarray experiments can be visualized with a color gradient. Microarray data are accepted in multiple formats. Additionally, manual selection and
Fig. 1. Chromosome wheel from Lactobacillus plantarum WCFS1 (Kleerebezem et al., 2003) including COG-domain coloring of genes, GC% (red), GC-skew (blue) and AT-skew (green). (B) Linear genome map of replication origin from Escherichia coli K-12. Genes are colored according to COG functional categories. (C) Transcriptome experiment (glucose repression) from Bacillus subtilis 168 (Yoshida et al., 2001). Red, downregulation; green, upregulation; yellow, intermediate regulation; black, rRNA genes.
coloring can be made based on open reading frame numbers, keywords or customized functional categories. Gene annotation data and external databases like the NCBI are cross-linked with the genome maps by mouse-over functions.

Examples of pictures generated with the MGV are shown in Figure 1; more examples can be found at http://www.cmbi.kun.nl/MGV/examples

**FUTURE**

Subsequent versions of the Microbial Genome Viewer will enable the combinatorial visualization of the genome maps with metabolic pathways and gene regulatory networks. Different levels of visualization will ultimately be connected by transcriptome and metabolome data.

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