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Applications Note

Subject Section

VRPG: an interactive web viewer for reference pangenome graphs

Zepu Miao[1], Jia-Xing Yue[1,*]

[1]State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Sun Yat-sen University Cancer Center, Guangzhou, China.

*To whom correspondence should be addressed.

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Abstract

Summary: With the increasing availability of high-quality reference genome assemblies, pangenome graph is emerging as a new paradigm in genomics research for identifying, encoding, and interpreting the genetic variation landscape at the population and species levels. While impressive progresses have been made in recent years in building pangenome graph, there is a general need for novel bioinformatic tools that enable researchers to better navigate and explore such pangenome graph towards novel biological insights. Here with VRPG, we present a web-based interactive viewer of reference pangenome graph and demonstrated its use with yeast and human reference pangenome graphs.

Availability and implementation: VRPG is written in Python and HTML. It is free for use under the MIT license, available at https://github.com/codeatcg/VRPG .
Demonstration: https://www.evomicslab.org/app/vrpg/

Contact: yuejiaxing@gmail.com
Supplementary information: Supplementary data are available at *Bioinformatics* online.

1 Introduction

Long-read-based DNA sequencing has become the go-to-choice for most genome sequencing projects nowadays, empowering the production of chromosome-level telomere-to-telomere (T2T) genome assemblies for diverse organisms (including human) (Yue *et al.*, 2017; Jiao and Schneeberger, 2020; Nurk *et al.*, 2022). With such T2T reference assembly panel continuously expanding at both population and species levels, researchers began to use pangenome graph to better represent the population- and species-wide genomic variation landscapes in a sequence-resolved manner (Eizenga *et al.*, 2020). Compared with the conventional single linear reference genome, pangenome graph offers more sensitive and accurate read mapping and variant discovery, especially in the presence of sequence polymorphisms and structural variants (Paten *et al.*, 2017). Therefore, a population- or species-wide representative pangenome graph is expected to shed novel insights into the interpretation of the genotype-to-phenotype association and the discovery of missing heritability.

While a number of tools have been developed to build pangenome graph based on genome alignments, Minigraph (Li *et al.*, 2020) and seqwish (Garrison and Guarracino, 2022) are among the most popular ones. For the pangenome graph built by Minigraph, a reference pangenome graph can be derived using the reference Graphical Fragment Assembly (rGFA) format. Compared with the standard GFA format, rGFA also records the origin of each graph constitutive segment from the input linear genomes and therefore allows for traversing the pangenome graph along a stable coordinate system. This unique feature makes the reference pangenome graph a natural and intuitive extension to the conventional linear reference genomes.

Visualization is an important part of data exploration, especially for complex data structure such as pangenome graphs. An intuitive visualization of pangenome graph can greatly assist researchers to explore and understand the global and local genomic variation in their graph representation. Although originally developed for visualizing de Bruijn assembly graph, Bandage quickly became a popular choice for interactively displaying pangenome graph with a focus on large-scale topology (Wick *et al.*, 2015). GFAviz is an equivalent alternative to Bandage, also allowing users

to interactively navigate and zoom over genome graphs (Gonnella *et al.*, 2019). Sequence Tube Maps is another genome graph viewer that borrows inspiration from London's iconic Tube Map and focuses on depicting the fine-scale sequence details (Beyer *et al.*, 2019). MoMI-G provides an integrated visualization solution by presenting genome graph in two flavors: Circos plot and SequenceTubeMaps plot (Yokoyama *et al.*, 2019).

Here we present VRPG, a web-based interactive viewer for reference pangenome graph. VRPG takes advantage of the stable coordinate information encoded in the rGFA format and renders visualization with a customized version of the force-directed graph implemented in D3.js (https://github.com/d3/d3-force). Users can freely extract, move, zoom in or out, and save images on the displayed graph for interactive data exploration in real time.

2 Implementation and feature highlights

VRPG was implemented in Python and HTML, and runs on the Linux, macOS, and windows operating systems. VRPG is easy to deploy and highly efficient in visualizing complex reference genome graphs derived from tens or hundreds of genome assemblies on the fly. In the graph rendered by VRPG, genomic segments from the pre-defined reference assembly are shown along the center line of the rendered graph in purple, while segments from non-reference assemblies are shown around the center line in other colors (Figure 1). For each such reference or non-reference segment, we pre-calculated its mapping depth in each input assembly based on the assembly-to-graph alignment. In VRPG, users can easily obtain the source assembly, genomic coordinates, and mapping depth of each segment by a simple click on the corresponding segment. VRPG also provides a "Highlight" feature to enable users to highlight the path of the query assembly in the pangenome graph based on a pre-calculated assembly-to-graph alignment.

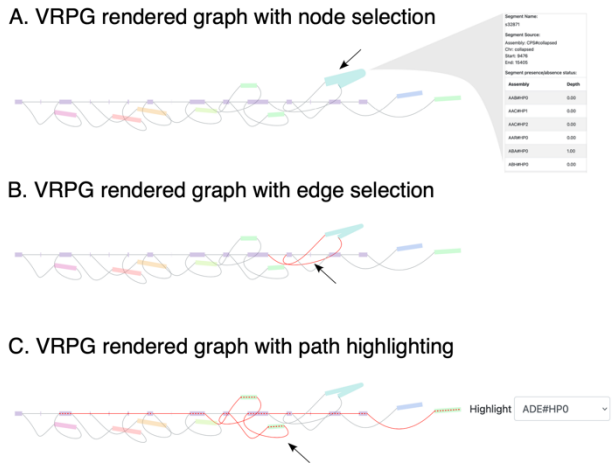

Fig. 1. The reference pangenome graph visualization with VRPG. A) VRPG visualization with the node s32871 selected. B) VRPG visualization with the two edges surround the node s32871 selected. C) VRPG visualization with the assembly-to-graph mapping path of the assembly ADE#HP0 highlighted.

3 Application demonstration

To demonstrate the application of VRPG in real world examples, we set up a demonstration website (https://www.evomicslab.org/app/vrpg/) to visualize reference pangenome graphs derived from 143 yeast and 90 human genome assemblies respectively. The human reference pangenome graph is a public dataset, whereas the yeast reference pangenome graph is built based on the *Saccharomyces cerevisiae* reference assembly panel (ScRAP) that we recently constructed (O'Donnell *et al.*, 2022). Both graphs were constructed by Minigraph (Li *et al.*, 2020) via a standard reference pangenome graph building protocol (Supplementary Note).

4 Conclusions

We developed VRPG, a web-based interactive viewer for reference pangenome graph. We expect VRPG become a useful visualization tool to help researchers to explore and interpret pangenome graph in an interactive and intuitive way.

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Conflict of Interest: none declared.

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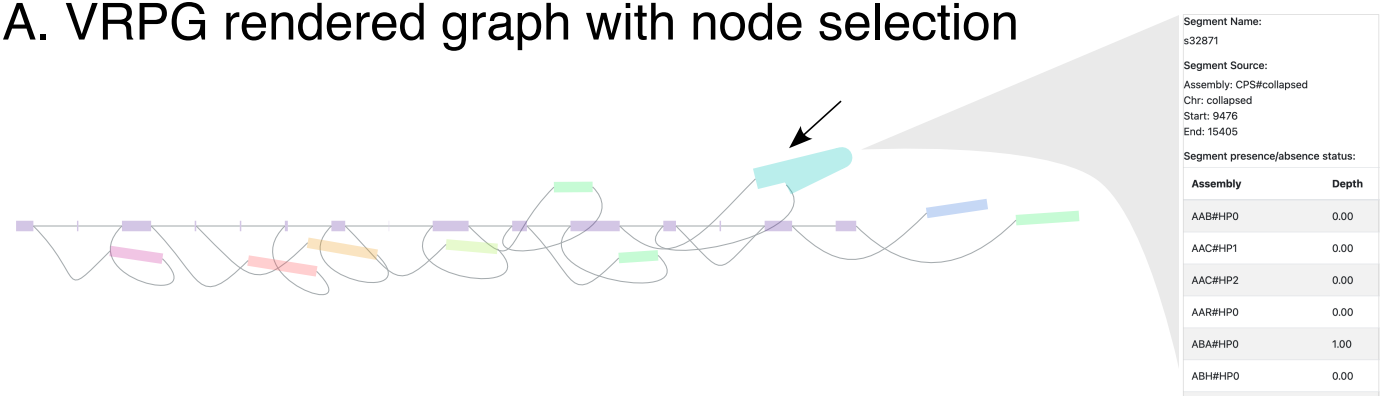
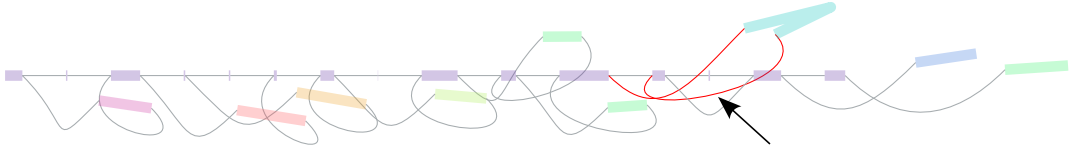
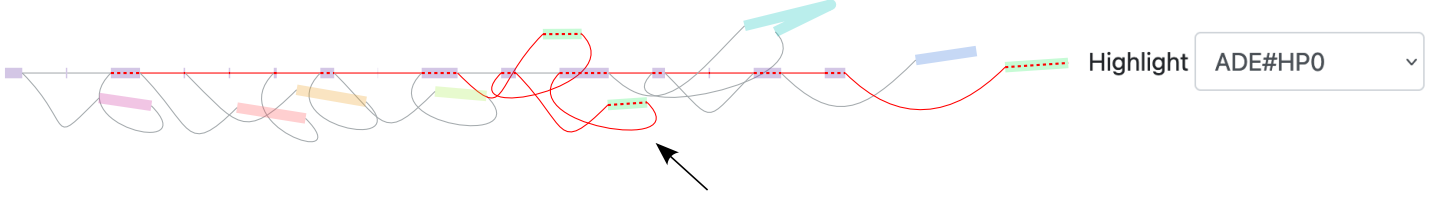
A. VRPG rendered graph with node selection



B. VRPG rendered graph with edge selection



C. VRPG rendered graph with path highlighting