BioE 131 Final Project Report

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My project focuses on the Flavivirus family, specifically all four serotypes of the dengue virus (DENV-1 through DENV-4). Dengue virus is a global public health threat, causing an estimated 390 million infections annually, with severe forms such as dengue hemorrhagic fever leading to significant morbidity and mortality. Unlike other Flaviviruses, dengue's unique pathogenesis involves antibody-dependent enhancement (ADE) as well as multiple-subtype infection (antibodies and infection from one subtype assist in the infection by another), complicating vaccine development.

Each serotype's distinct genome and protein structures thus necessitate a holistic approach to understanding their biology. By providing annotated genome data and visualizing the 3D structures of encoded proteins, this database aims to facilitate structural biology research that supports vaccine and therapeutic development.

The inclusion of Protein3D visualization from JBrowse2's available plugins directly addresses a critical need: understanding the molecular interactions of viral proteins within and across all serotypes. This integration bridges genome annotation with protein structural data, enabling researchers to explore functional insights crucial for designing vaccines that account for all four serotypes and their potential interactions.

The database includes the complete genome sequences of DENV-1 through DENV-4, sourced from GenBank FTP download URLs. Each genome is annotated with gene structures (e.g., capsid, envelope, and non-structural proteins), regulatory elements important for viral

replication and translation, and some data associated with pathogenicity and drug resistance. The Protein3D plugin provides interactive visualizations of 3D protein structures for key viral proteins.

I also provided some guidance to other students on Ed facing technical challenges during their JBrowse2 setup. For example, I addressed an error caused by insufficient permissions during directory creation:

```
Error: EACCES: permission denied, mkdir '/jbrowse2'
    at async mkdir (node:internal/fs/promises:857:10)
    at async AddAssembly.run (/usr/local/lib/node_modules/@jbrowse/cli/lib/commands/add-assembly.js:204:13)
    at async AddAssembly._run (/usr/local/lib/node_modules/@jbrowse/cli/node_modules/@oclif/core/lib/command.js:301:22)
    at async Config.runCommand (/usr/local/lib/node_modules/@jbrowse/cli/node_modules/@oclif/core/lib/config/config.js:424:25)
    at async Object.run (/usr/local/lib/node_modules/@jbrowse/cli/node_modules/@oclif/core/lib/main.js:95:16) {
  errno: -13,
  code: 'EACCES',
  syscall: 'mkdir',
  path: '/jbrowse2'
```

I fixed this by realizing that the exported filepath variable (APACHE_ROOT in my implementation) was not updating in the current terminal session. I recommended sourcing the shell script exporting the variable to ensure proper setup in subsequent commands (calling source script.sh instead of ./script.sh).

Sources

https://pmc.ncbi.nlm.nih.gov/articles/PMC6509522/

https://pdb101.rcsb.org/motm/103