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Updating The SynthDNASim tool to create diverse DNA data sets

Introduction

In genomic research of rare diseases like Huntington's Disease (HD), it is common to have a lack of genomic data to start and perform research with. One of the reasons for this is the privacy issues surrounding the obtainment and use of genomic data. Thus, a possible solution to this is the development of a tool that can create diverse synthetic DNA data sets so the created synthetic DNA data set can be used for genomic research and make the research a lot more reproducible and faster. [1]
However, the synthetic DNA data set needs to be diverse enough to represent different populations. A single disease can have many different genetic characteristics because of differences in and between populations. Thus, factors of genetic evolution and ancestry need to be taken into account while creating a diverse DNA data set. [2]

The goal of this project is to create a diverse DNA data set including genetic evolution and ancestry factors. With HD as a use case, the data set will contain disease variants from European, African, and Middle Eastern populations. Here, we show the workflow of the diversified synthetic DNA simulator (SynthDNASim). This new tool updates the Synthetic DNA Simulator (see 'Materials and Methods' below) to help researchers create synthetic DNA representative of population diversity. The next steps are to validate the synthetic DNA data set and apply the FAIR principles to make it Findable Accessible Interoperable and Reusable for the community using semantic technologies.

Huntington's disease (HD)

HD is a rare disease that is hereditary and causes degeneration of nerve cells in the brain. Because of this, HD has an impact on the functional abilities of an individual, resulting in movement, cognitive, and mental disorders. HD is caused by an extended CAG repeat within the Huntingtin gene (HTT gene). [3] There are many different variants of HD within different populations, these variants are known as haplotypes. A haplotype is a combination of single nucleotide polymorphisms (SNP's, variants) in a gene that is found on the same chromosome. [4]

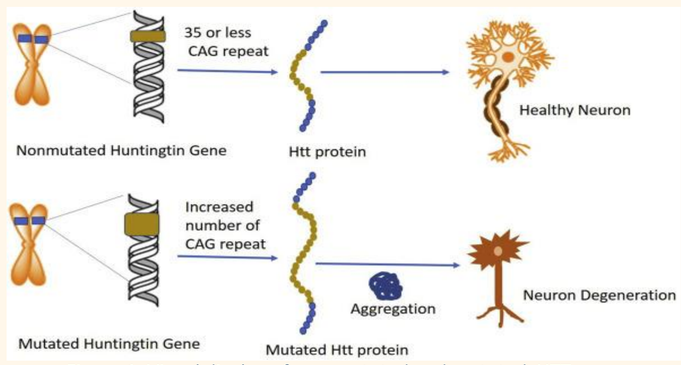
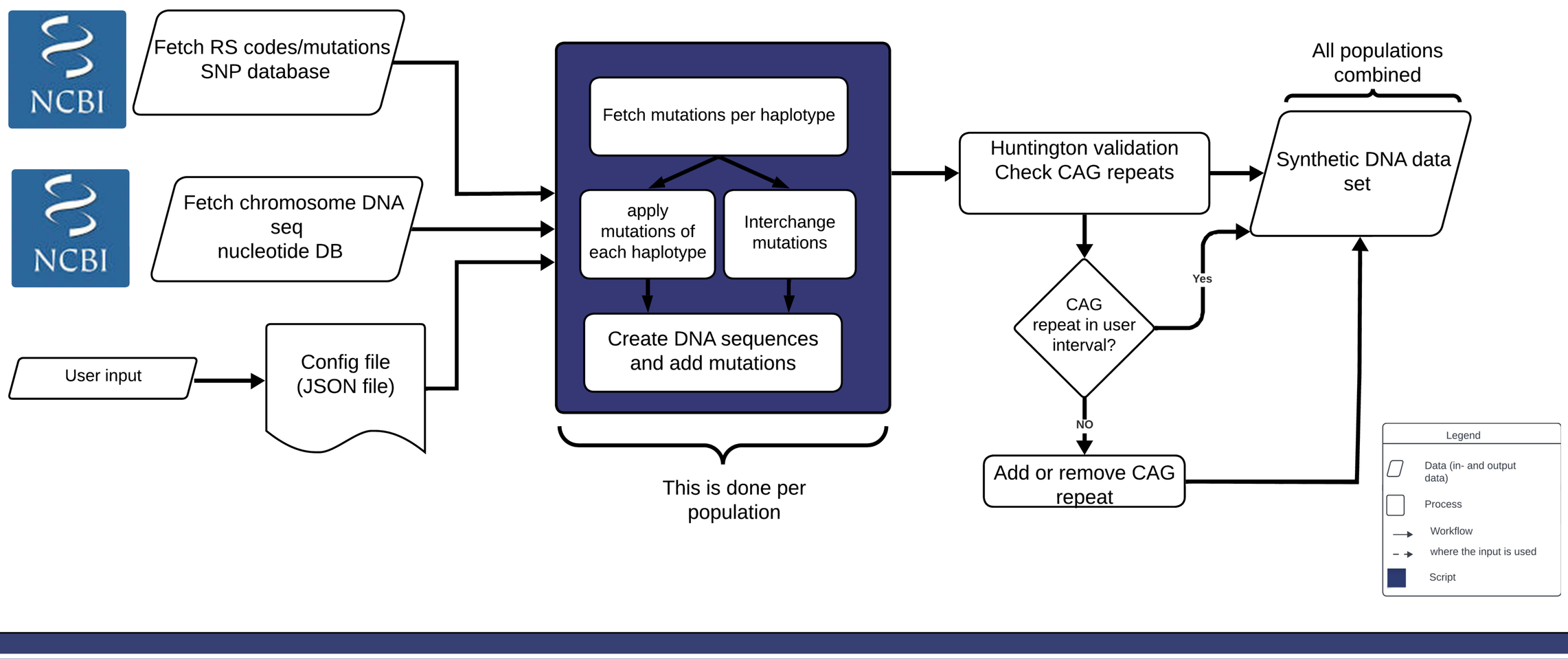


Figure 1. Visual display of non-mutated and mutated HTT gene. This figure also displays the protein and the effect of the protein on neurons (source: https://pubmed.ncbi.nlm.nih.gov/33659724/).

Creating diverse DNA sequences



Materials and Methods:

- Python scripts
- Original Synthetic DNA Simulator (scan QR code)
- NCBI SNP database and nucleotide database
- The FAIR principles will be a guiding factor within this project
- Each sequence has its metadata including haplotype, genetic variants, CAG repeats, gene, chromosome, etc. ic variants, CAG repeats, gene, chromosome, etc.

Future work:

The remaining work of this project:

- Validation of the generated synthetic DNA
- Use semantic methods and tools to make the project more FAIR. Create metadata using Data Catalog Vocabulary (DCAT) and share the tool and metadata using WorkflowHub and Common Workflow Language (CWL). [5-7]

For future research:

- Determine a standard protocol to validate the created synthetic DNA data set.
- Add synthetic clinical data.

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