Homework 1

CSCI 5481, Computational Techniques for Genomics
University of Minnesota
Instructor: Dan Knights

Instructions

- Please turn this assignment in on the course Canvas page.
- If there are multiple files to turn in, all text and code should be placed into a single folder with a name like *lastname_homework1*. The folder should then be compressed and submitted as a single archive (.zip or .tgz)
- You are encouraged to discuss this project with others, but you need to write your own code.
- Please write the names of anyone with whom you discussed this assignment at the top of your code.

Background

The purpose of this exercise is to get you familiar with downloading and processing genomic data, and with thinking about differences between coding sequencing and non-coding sequences and differences between nucleotide (DNA) and amino acid (protein) sequences.

Tasks

1. Download the whole-genome and separate-gene DNA sequences of SARS-CoV-2, the virus that causes COVID-19, from the Homework01 directory in the Files section of the course Canvas page.

2. (20 points) Write a program that counts how many times each 3-character *codon* (substring of 3 characters) appears in the whole-genome file, starting with characters 1-3, then characters 4-6, and so on till the end of the genome. If there are extra characters at the end because it is not perfectly divisible by 3, just ignore the last one or two. Your program should run like this:

   ```
   count_codons input.fna output.csv
   ```

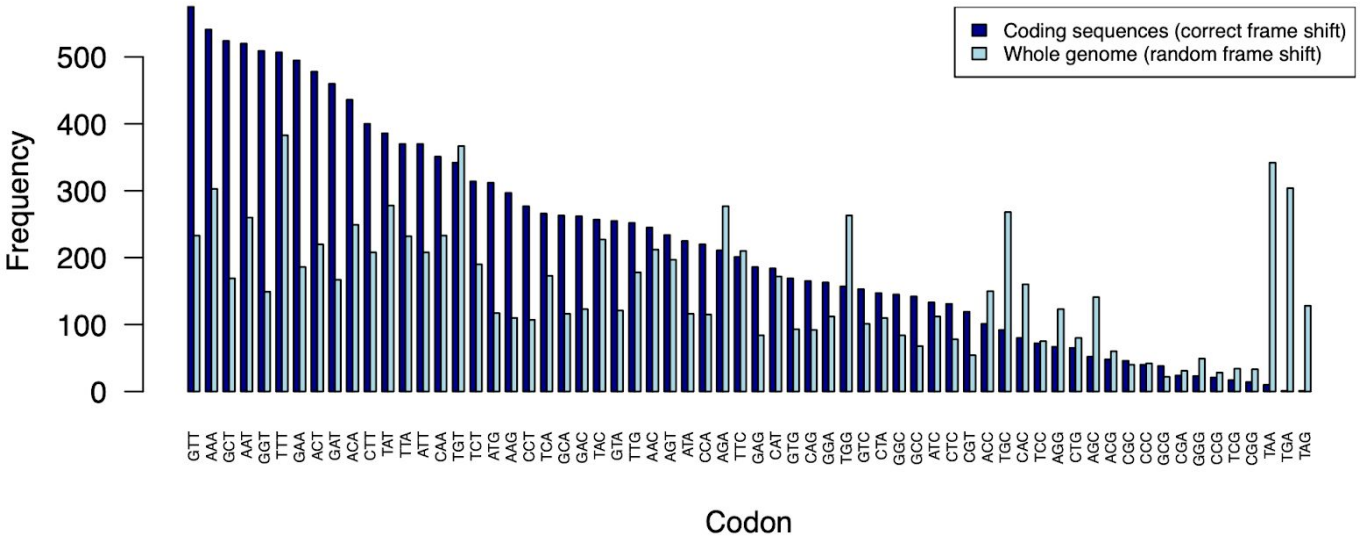
   Your program should output a comma-separated (CSV) file with the codon string in column 1 and the total count in column 2, like this:

   ```
   TTT,383
   TGT,367
   ...
   ```

   Include this code in your submission.
3. (20 points) Create a small fake genome file where you know the expected answer, and test your program for correctness. Include this test genome file and the expected answer (in a separate text file) in your submission.

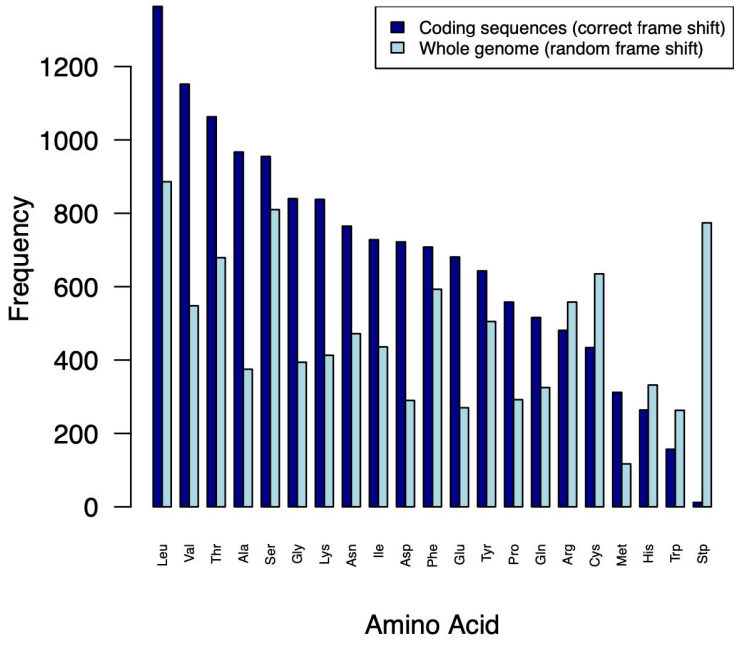
4. (20) Run the program on both input DNA files: the whole-genome file, and the file with the genome split into separate genes. Include the output CSV files with your submission.

5. (20) Make a barplot comparing side-by-side the counts of each codon in the two different files, sorted by count in the separate-gene file. You can use any program for visualization such as R, Python, or Excel. Your plot should look approximately like this:



You do not need to turn in your code for this step, only the figure.

6. (10 points) Convert the codon counts from your two CSV files to amino acid counts using the genetic code. You can use this table or an external package. Then make a similar barplot comparing amino acid counts between the two files. Your plot should look approximately like this:



Turn in the figure for this step.

7. (10 points) Where is the largest discrepancy in amino acid counts between the coding sequences (correct frame shift) and the whole genome sequence (random frame shift), and why?

Bonus

1. (3 points) Download an additional SARS-CoV-2 virus from NCBI and design a simple computational approach method to list all mutations between the two viruses that occur inside the known coding sequencing/genes. For each mutation, list:
    a. the nucleotide in the reference genome
    b. the different nucleotide in the other genome
    c. the amino acid for that nucleotide's codon in the reference genome
    d. the amino acid for that nucleotide's codon in the other genome.

    How many mutations were there? How many of them changed the amino acid being produced?

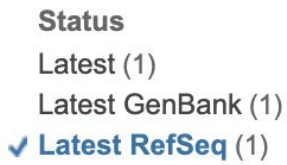
Deliverables

1. Please turn in, via moodle:
    a. Your well-commented code for step 2 above. Note in your code the names of any people with whom you discussed the assignment.
    b. The output CSV files in step 4 above.
    c. The output figures for steps 5 and 6 above.
    d. Your answer to question 7 above in txt/doc/pdf.

Appendix

For your reference, here is one way to find the raw genome files on the internet. This is provided only in case you are curious. You do not need to do these steps because the DNA files are already provided for you.

1. Google "NCBI" and go to the main NCBI webpage.
2. Select "Assembly" from the dropdown menu next to the search bar, and search for "SARS-CoV-2"
3. On the left, select only "Latest RefSeq" to find the latest reference version.



4. Click on the link to the latest RefSeq assembly of the genome. Note: this version is normally also the first result in the list if you don't filter the results.
5. Click on the link (normally on the right side) to "FTP directory for RefSeq assembly".
6. Download a file with a name like, "GCF_009858895.2_ASM985889v3_genomic.fna.gz" for the whole-genome sequence and "GCF_009858895.2_ASM985889v3_cds_from_genomic.fna.gz" for the separate-gene sequences.
7. Unzip both files.

8. Note: FASTA-formatted files from NCBI usually have line wraps on the DNA sequences after every 80 characters, which makes the files annoying to parse. You can remove the extra line wraps with:

```
awk '/^>/ {printf("\n%s\n",$0);next; } { printf("%s",$0);}  END
{printf("\n");}' < input.fna | sed '/^$/d' > output.fna
```