Ubiquitous Genomics

Assignment #1 | Apr 29, 2022

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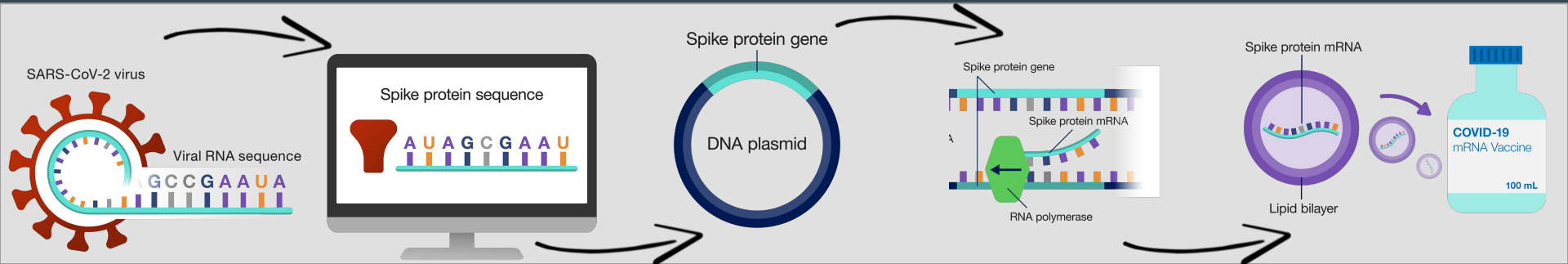
Agenda

- The Task
- Our Process
- Assignment Tasks:
  - Analyzing Pfizer and Moderna Vaccines
  - Comparison to the Wuhan Strain
  - BA.2 Protein Extraction
  - Building the mRNA Vaccine
- Key Takeaways
- References

THE TASK

The Task

1. Our goal was to develop a new vaccine for BA.2
2. How mRNA vaccines work:
   The spike protein is essential for the virus to attach to the host cell, thereby making it an effective antigen.
3. Isolate the spike protein from the sequence of BA.2
4. Use Pfizer's reference to determine the mRNA sequence, 5'UTR and 3'UTR, codon optimizations and the fatty lipid bilayer that protects it on the move.

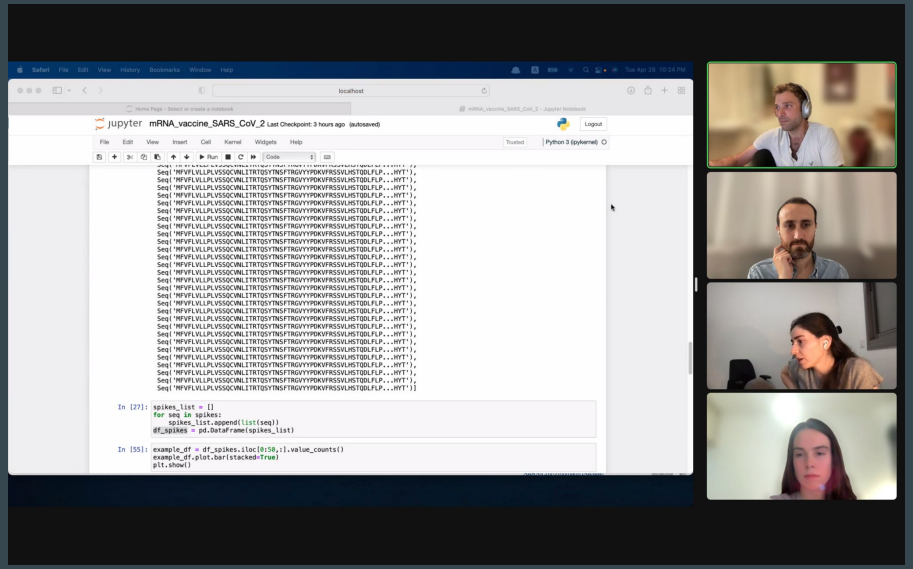


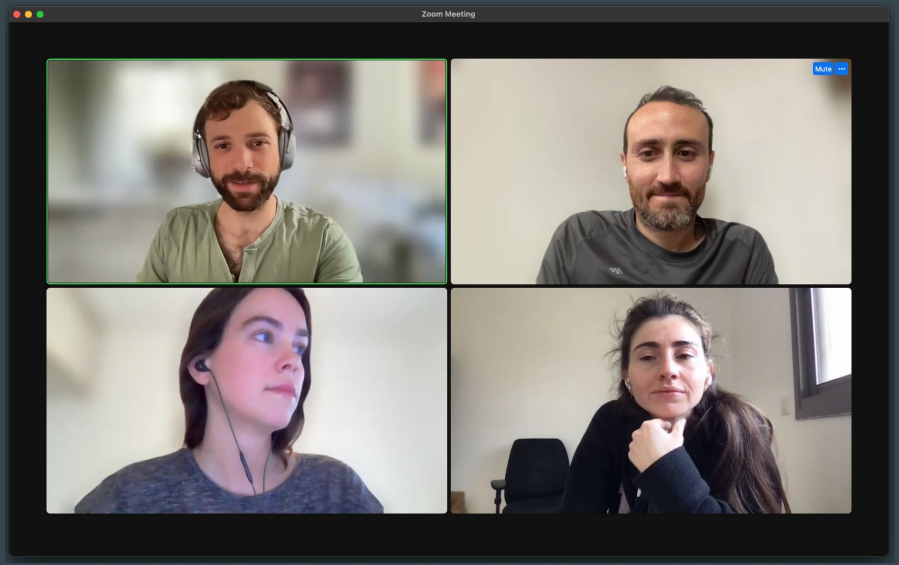
OUR PROCESS

Our Process

1. Started with reading the assignment
2. Got a bit scared :)
3. Went through the lectures, researched and gained confidence
4. Collected the relevant data
5. Got comfortable with BioPython
6. Data exploration
7. Researched more into GC-content, Spike lengths and additional terms
8. Wrapped the new vaccine 💉

And Of Course :)





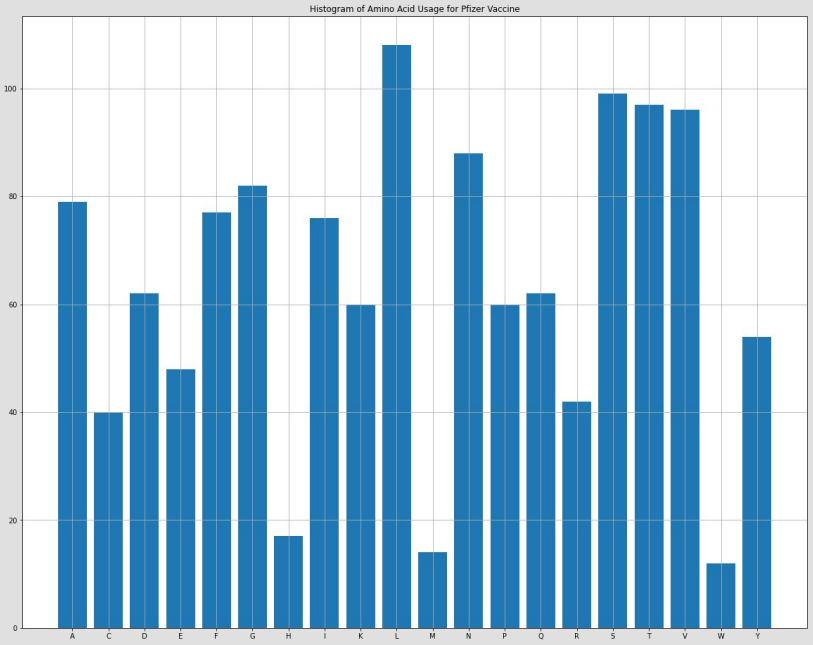
ASSIGNMENT TASKS

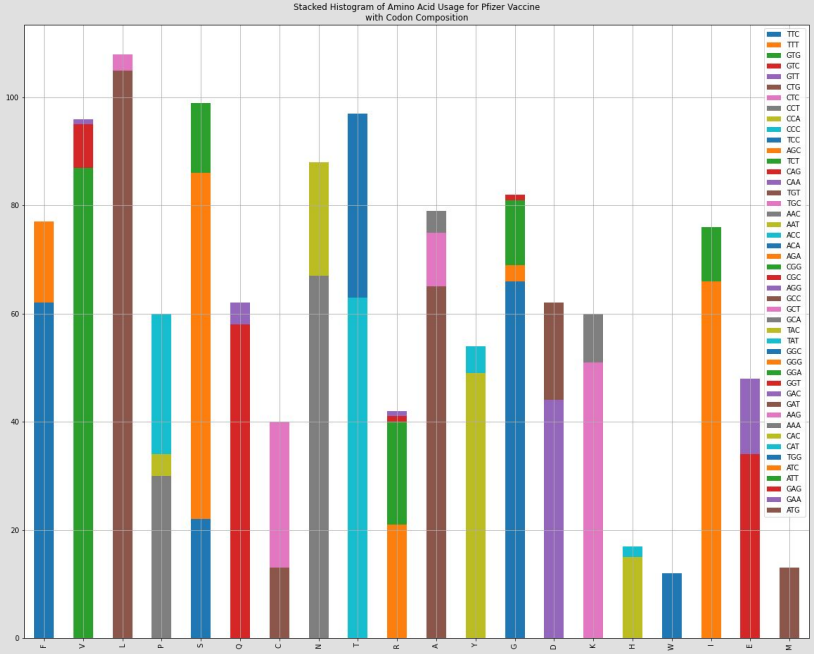
Part 1

Analyzing Pfizer and Moderna Vaccines

	Pfizer	Moderna
Initiation Codon	54	57
Termination Codon	3873 UGA	3876 UGA
Translated Length	1273	1273
Proteins	Identical protein level	

Pfizer Vaccine Distributions





Part 2

Comparison to the Wuhan Strain

Genome Length	29,903
S Gene Start	21,562
S Gene End	25,383

	Wuhan	Pfizer
GC-content	38%	57%
Protein Differences	985: K 986: V	985: P 986: P
Change Motivations	1. Higher G-C count converts more efficiently to proteins! 2. Proline substitution leads to a more rigid spike	

Wuhan Protein Sequence

Wuhan's protein's sequence is:

```
MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFSNVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQS
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Wuhan AUGUUUGUUUUU...
Pfizer AUGUUCGUGUUC...

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Part 3

BA.2 Protein Extraction

The Path to the Spike:

- First we tried to find the BA.2 spike by aligning the entire BA.2 seq against the Wuhan spike seq.
- Then we decided to search on the translated seq instead of RNA/DNA.
- We searched for proteins that match the Wuhan protein (and spike protein in general) length.
- We used BioPython align to search the protein with the best align score for each record.
- We searched for the most common spike.

Part 3

BA.2 Protein Extraction

Final Method:

1. Translate mRNA sequence.
2. Align each protein sequence with the Wuhan spike.
3. Choose protein sequence with highest alignment score.
4. Repeat on multiple BA.2 sequences.
5. Choose the most common sequence.

Alignment scores calculated using BioPython
`pairwise2.align.globalxx`

Part 3

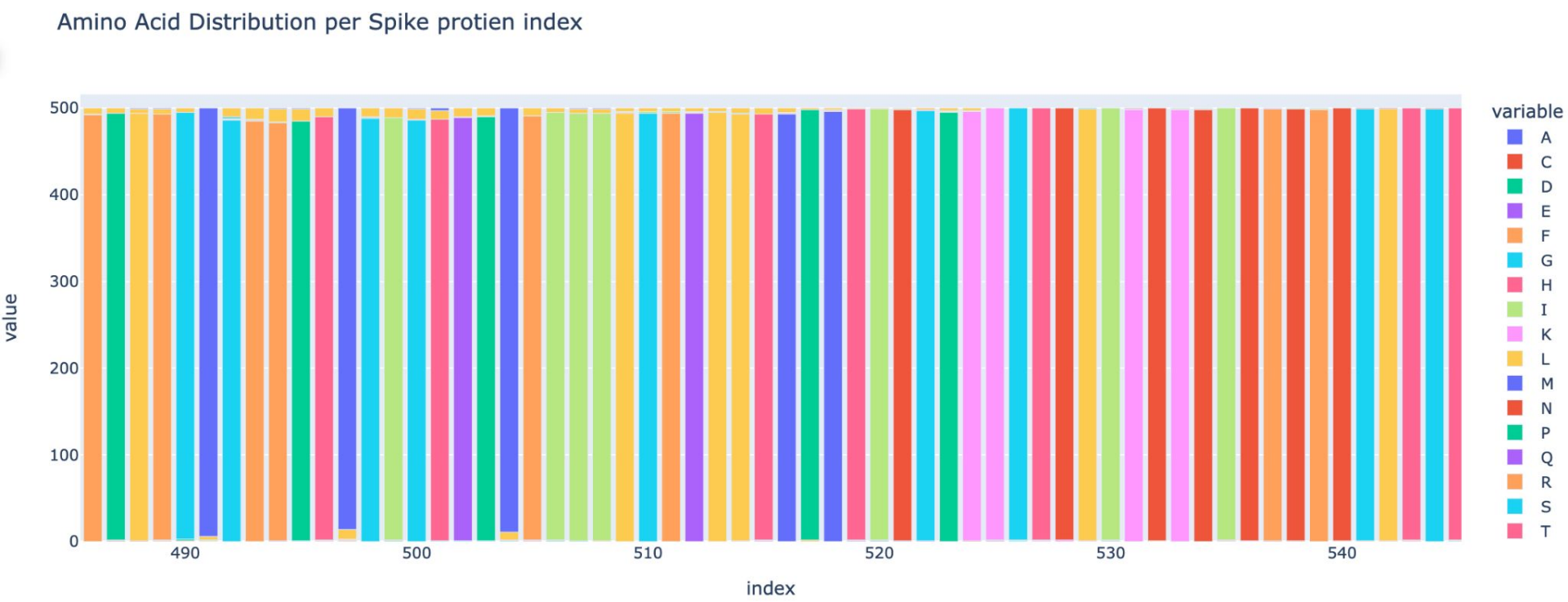
BA.2 Protein Extraction

Observations:

- We eventually decided to use the alignment score as it's a better measurement than length.
- We discovered that just by filtering proteins with the proper length we found the spike.
- We discovered shifts in the location of the spike protein between different BA.2 records.
- We also saw different variations of the spike protein between different records.

Alignment scores calculated using BioPython
`pairwise2.align.globalxx`

Comparison of BA.2 S Gene Amino-Acids



Part 4

Building the mRNA Vaccine

Method:

1. Use start-codon index in BA.2 S gene protein to extract S gene mRNA sequence
2. Use Pfizer lookup table to determine BA.2 codon mapping
3. Switch KV->PP based on index
4. Add 5’UTR and 3’UTR from Pfizer vaccine

UBI GROUP BA.2 VACCINE

GAGAAUAAACUAGUAUUCUUCUGGUCCCCACAGACUCAGAGAGAACCCGCCACCAUGUUUGUCUUCCUGGUGCUGCUGCCUCUGGUCUCCAGCCAGUGCGUCAAUCUGAUCACCCGGACACAAUCCUACACCAAUUCCUU
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KEY TAKEAWAYS

Key Takeaways

1. Pfizer's lookup table is partially understandable (e.g GC-content maximization), but there is still a multiple-options dilemma
2. Solution based on large sample and choosing most common protein sequence
3. Small changes can be make a huge difference and be very impactful (PP, GC)
4. The fact that extremely valuable sequence databases (commercial vaccines included!) are open-source and available is mind-blowing and powerful

REFERENCES

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THANK YOU 🙏