Assessing SARS-CoV-2 evolution through the analysis of emerging mutations

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1 Highlights

- **A novel method for detecting patterns of SARS-CoV-2 cooccurring mutations.**
- **Detection of evolutionary paths of SARS-CoV-2 virus.**

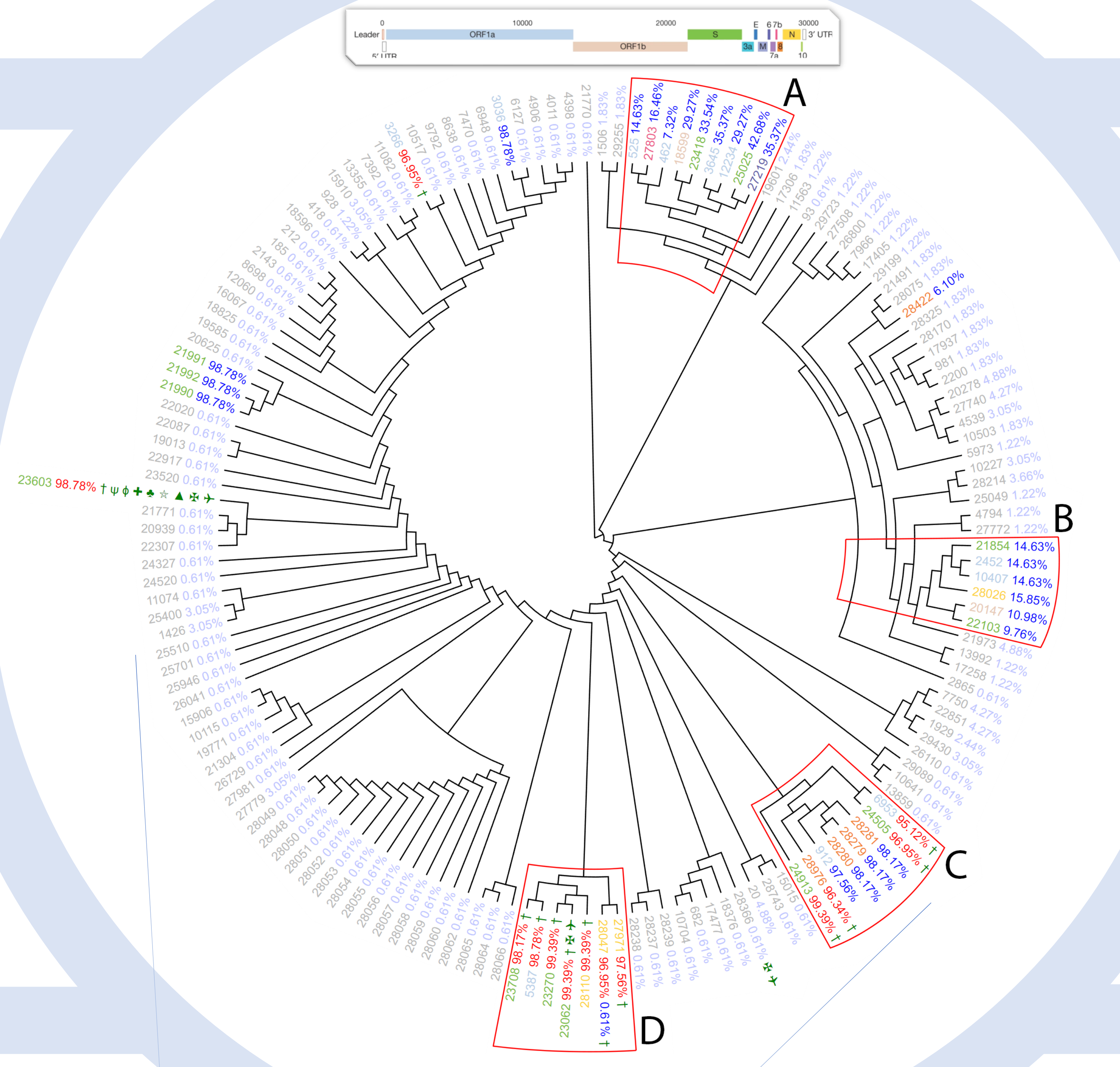
2 Background – Rationale

- Inferring a reliable phylogeny on SARS-CoV-2 is an **inherently complex** task [1].
- Existing classification methods of SARS-CoV-2 populations depend on phylogenetic inference.
- Many novel sub-typing methods fail to determine the phylogenetic relationships among different sub-types [3].

Aim Of The Study 3

- **Can we detect new patterns of co-occurring mutations beyond the strain-specific / strain-defining ones, in SARS-CoV-2 data, through the application of ML methods?**
- **Can we use those patterns in order to groups SARS-CoV-2 populations revealing potentially evolutionary paths?**

*Epidemiologically unrelated individuals could be infected with nearly identical viral genomes. **"Who infected whom"** is tremendously difficult to be determined [2].*

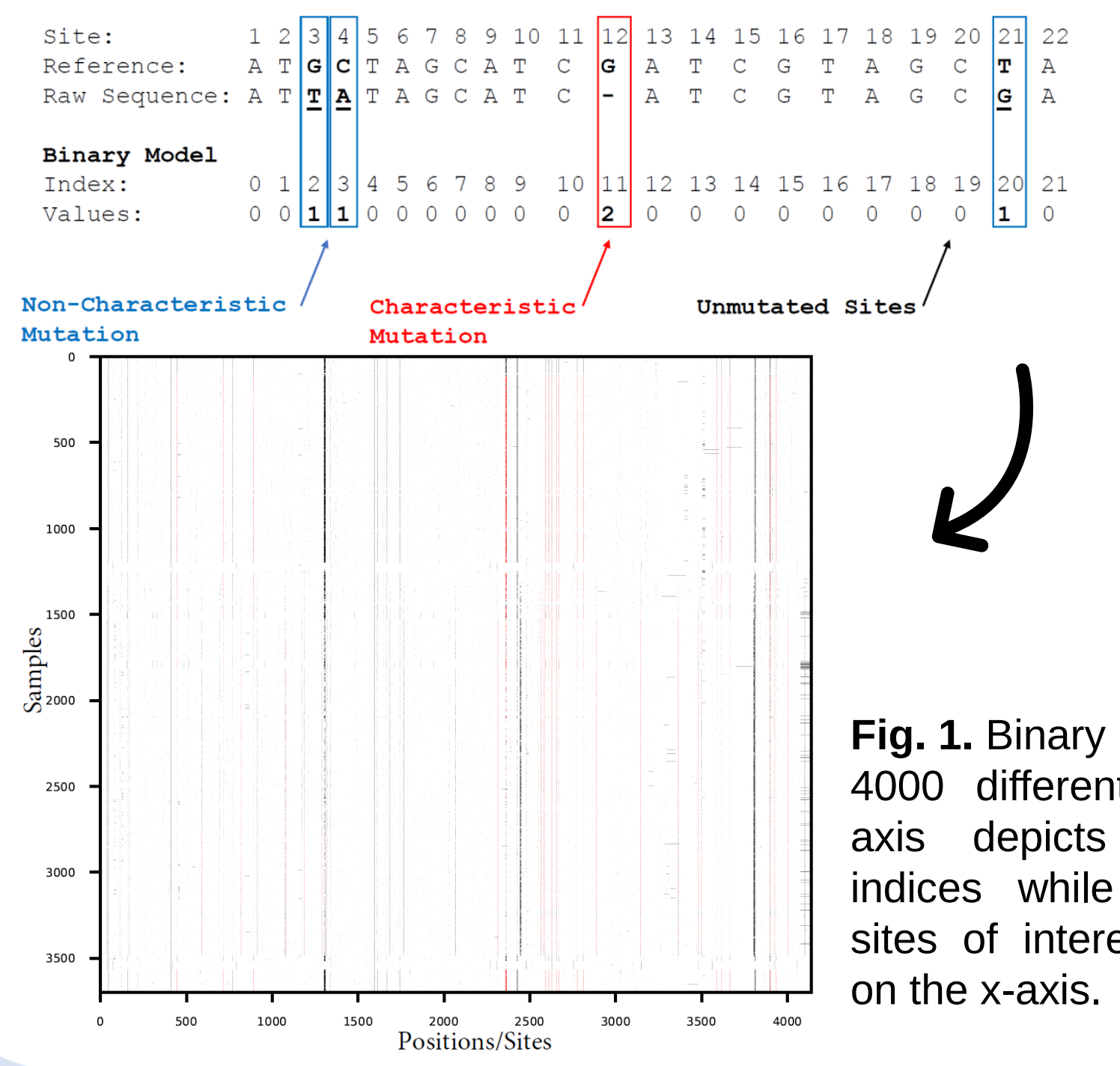


4 Materials

5411 samples and metadata

ENA accession number: PRJEB44141

- Modeling of raw sequences:



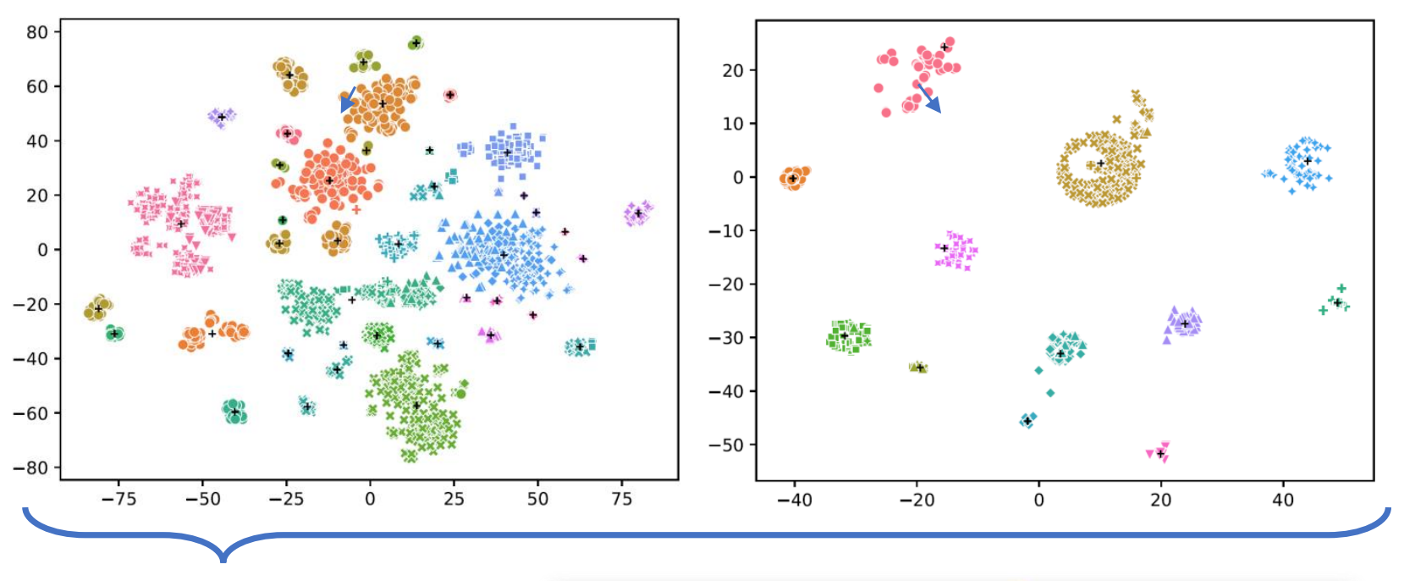
```
Site:          1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
Reference:     A T G C T A G C A T  C  G  A  T  C  G  T  A  G  C  T  A
Raw Sequence:  A T T A T A G C A T  C  -  A  T  C  G  T  A  G  C  G  A

Binary Model
Index:         0 1 2 3 4 5 6 7 8 9  10 11 12 13 14 15 16 17 18 19 20 21
Values:        0 0 1 1 0 0 0 0 0 0  0  2  0  0  0  0  0  0  0  0  1  0
```

Fig. 1. Binary model Along ~ 4000 different samples. y-axis depicts the sample indices while the mutated sites of interest are shown on the x-axis.

Methods 5

Fig. 2 & 3. Samples clustering on TSNE 2D space based on Non-characteristic & Pango characteristic mutations.



Co-occurring mutations between different clusters of samples of the same lineage were identified.

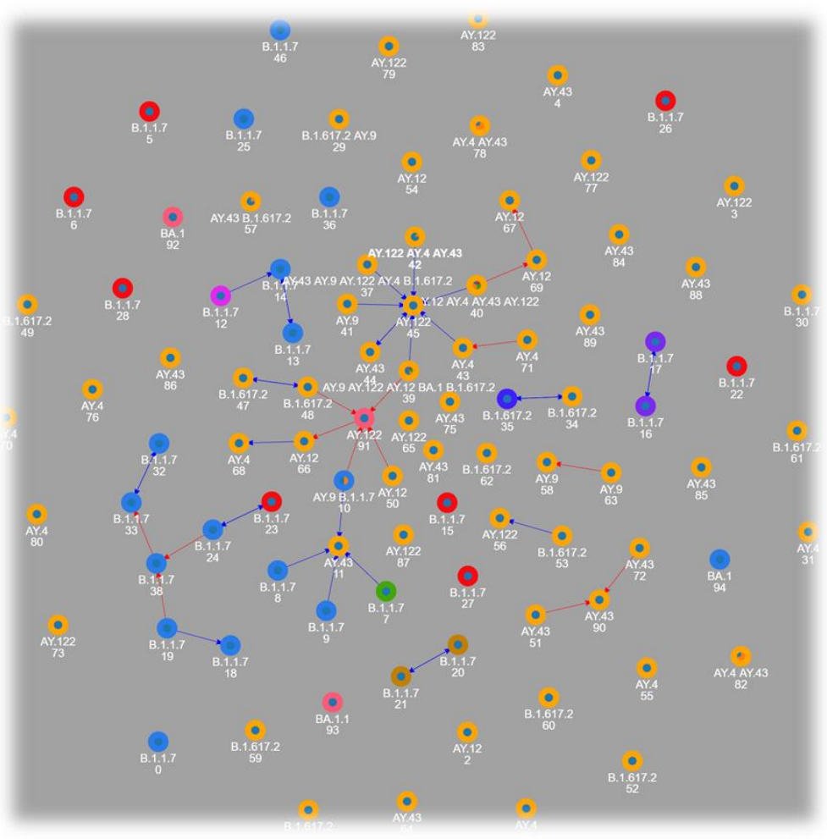


Fig. 4. Directed network. Each node is a cluster, and each arrow implies the existence of at least one co-occurring mutation between two clusters of **Fig. 2.**

6 Results

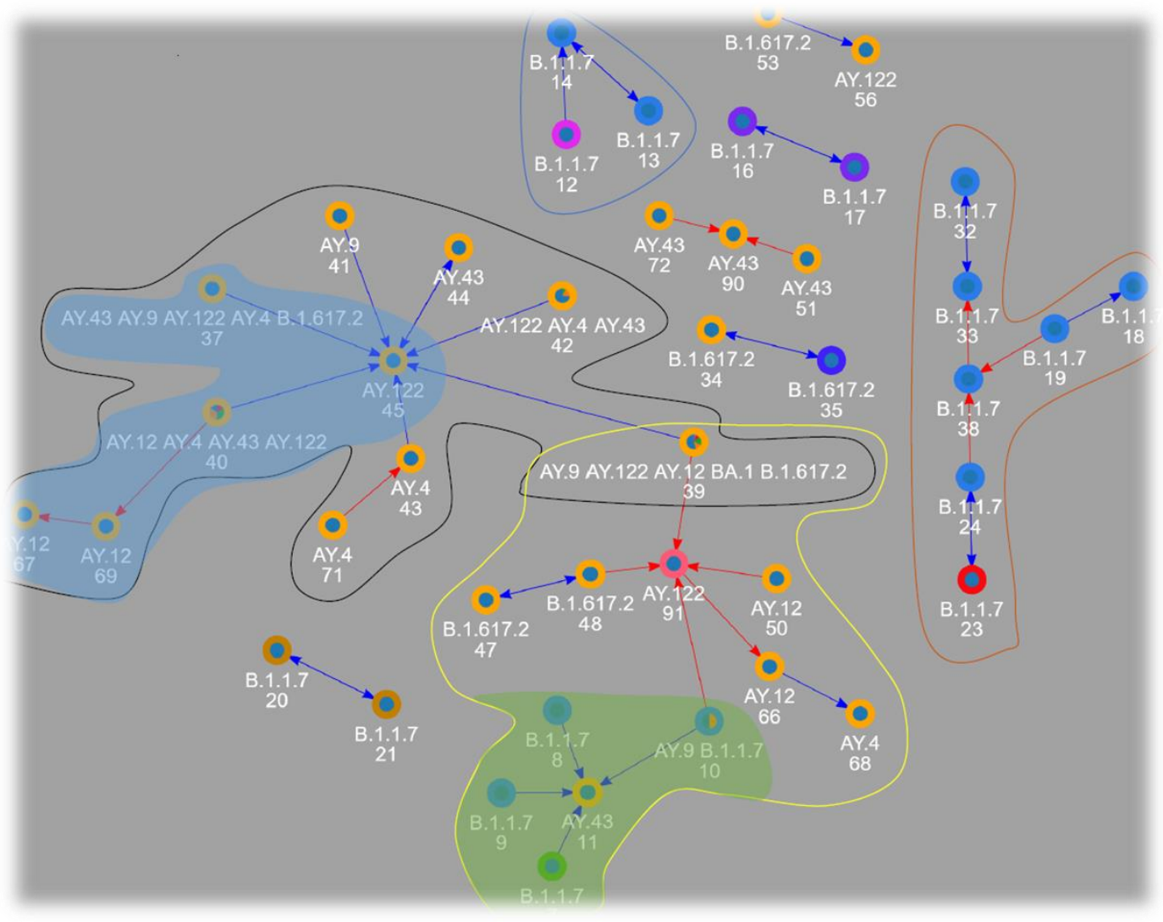
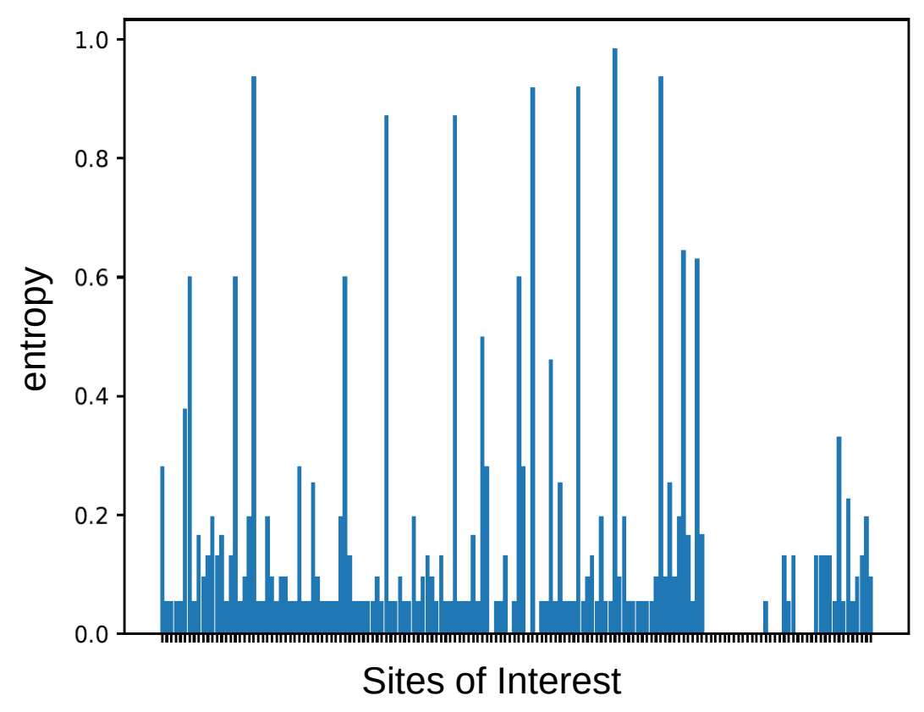
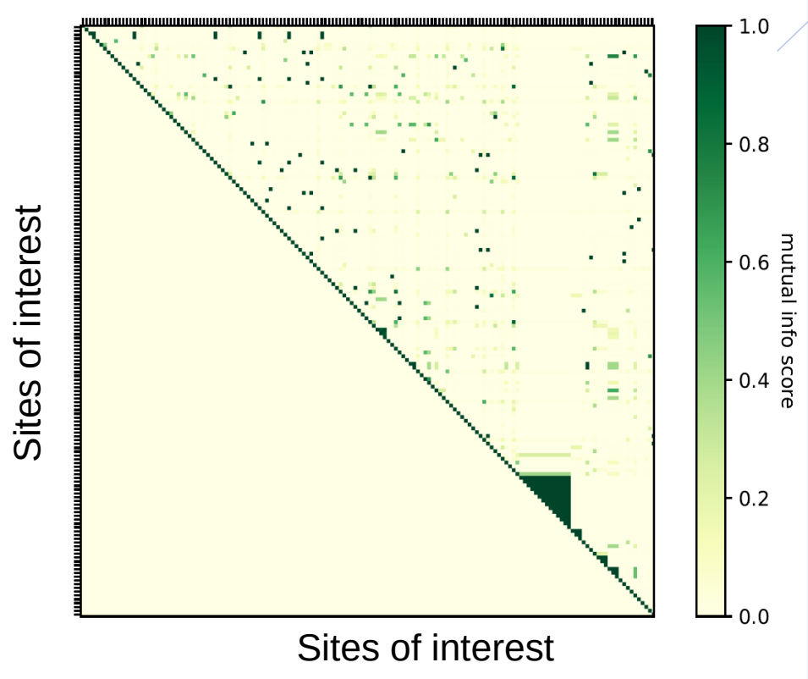


Fig. 5. Paths of interest based on **Fig. 4.**





Nodes : 32 33 38 24 23 19 18

Validation:

For each path:

- MSA of the reported samples was obtained.
- Mutual info between all pairs of sites was calculated.
- Hierarchical clustering.

According to the central dendrogram:

- Group, close to the root of the tree with medium to high rates of non-characteristic mutated sites.
- Sites of non-characteristic mutations appear to be mutated at lower percentages than those in A.
- High prevalence of non-characteristic and characteristic mutations that belong to B.1.1.7 lineage, at very high rates.
- Presence of the B.1.1.7 - characteristic mutation (23062) at very high rates that belongs to the BA.1 and BA.1.1 and it is strongly correlated to other B.1.1.7-characteristic mutations.

Conclusions 7

- We present **a computational method for detecting patterns of co-occurring mutations potentially revealing the evolution of SARS-CoV-2**.
- Evolutionary pressure could lead to new B.1.1.7 sub-lineages, forcing those mutations to prevail.
- **Circulation of non-characteristic mutations closely related to characteristic mutations** could potentially reveal useful patterns.
- Could help us identify potentially important mutations in future lineages.
- Correlation is not causation though, and thus further research is needed to be done on drivers of evolution and the emergence of new mutations.

References 8

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GenOptics

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Source code

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