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A phylogenetic study of COVID-19 data from Aragon and Catalonia over a year: learning Bioinformatics during a world pandemic

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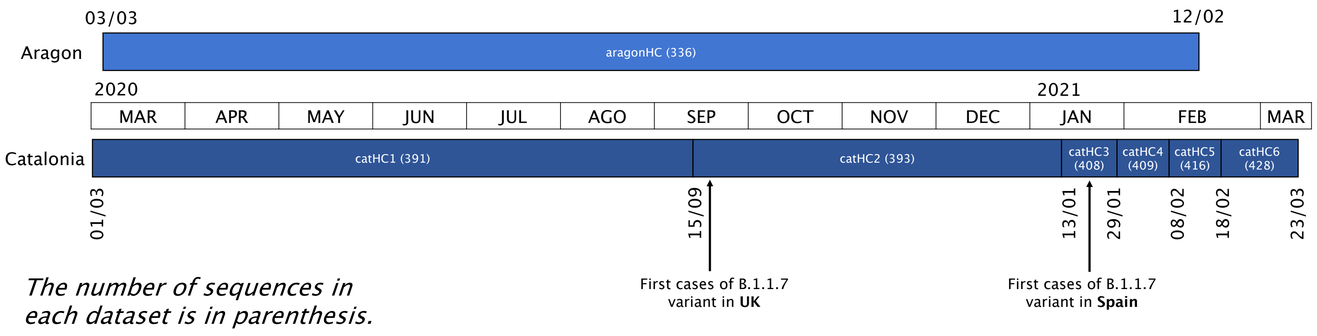
Motivation

- Teaching undergraduate Bioinformatics through a cooperative project in the context of a pandemic (Spring Semester 2021).
- Analyze the variability of SARS-CoV-2 virus in the Aragon area and compare it with Catalonia.
- Track the UK-variant of the virus (B.1.1.7), which was becoming predominant at the time.

Data



The number of sequences in each dataset is in parenthesis.

- The data used consisted of all the high coverage nucleotide sequences available at GISAID coming from Aragon and Catalonia submitted up to March 23rd, 2021.
- Data was split chronologically into 7 datasets of approximately 400 sequences each.
- The sequence of the B.1.1.7 variant was included in each dataset.
- Each student had the task of analyzing one of the datasets.

Methodology

The analysis of each dataset was divided into three tasks:

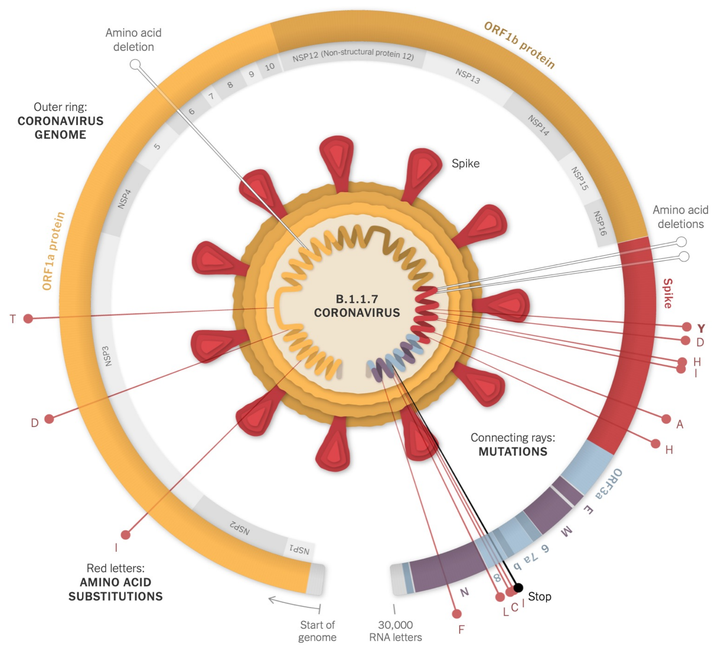
1. **Multialignment:** This task was performed using Clustal Omega and MAFFT. SARS-CoV-2 reference sequence NC_0455512.2 was used for guiding the multialignment. For instance,

```
$ mafft --auto --addfragments gisaid_seqs.fasta RefSeqWuhan.fasta \
   > alignment.fasta
```

2. **Conservation index calculation:** It was computed for each column i of the alignment using an entropy method, paying special attention to the ORF1a, Spike, ORF3a and N genes:

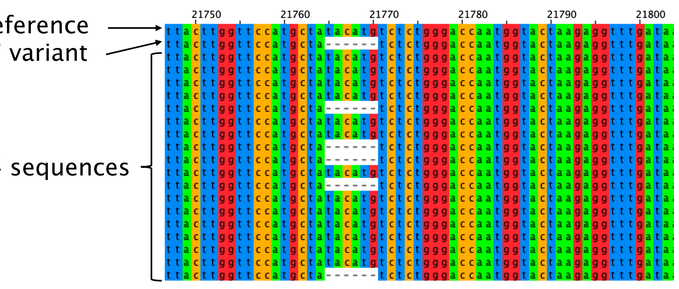
$$C(i) = -\sum_{v\in\{A,G,C,T\}} f_v(i)\ln\big(f_v(i)\big)$$

3. **Phylogeny reconstruction:** From the best multialignment, a phylogeny tree was reconstructed with maximum likelihood methods from FastTree and RAxML. Different evolution models, in particular Jukes-Cantor and Generalized Time-Reversible (GTR), were tested, and the best scoring phylogeny was selected for each dataset.

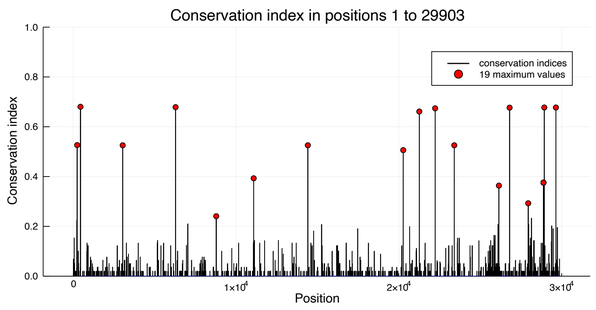


Source: The New York Times

Results



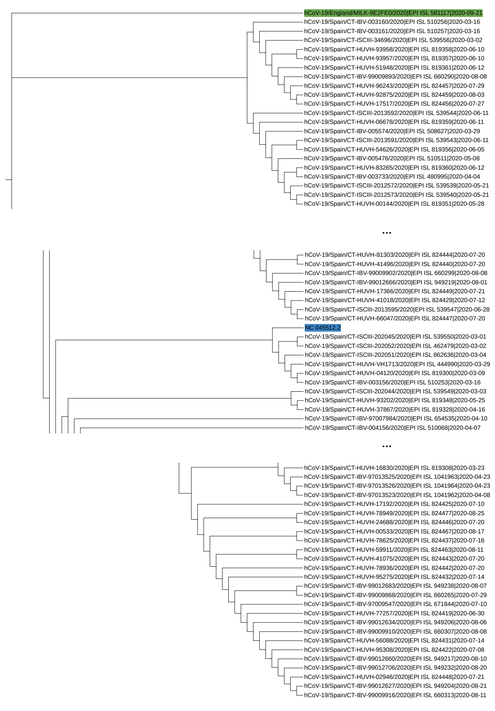
Fragment of a **multialignment** with catHC4 dataset.



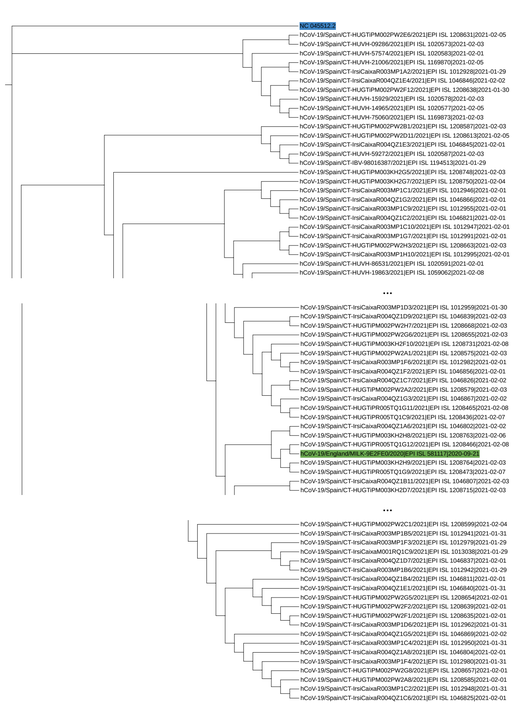
Conservation indices from aragonHC multialignment.

Reconstructed **phylogenies** from different multialignments.

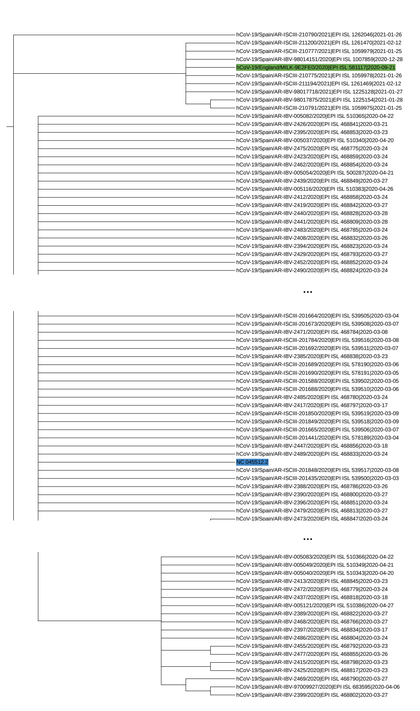
*SARS-CoV-2 reference sequence is marked in **blue**, and the B.1.1.7 variant in **green**.*



catHC1 (before first cases of B.1.1.7)



catHC4 (after first cases of B.1.1.7)



aragonHC

Conclusions

- SARS-CoV-2 virus can be used to teach the main genomic bioinformatics tools to Computer Science students.
- FastTree and RAxML are both able to obtain meaningful phylogenies for datasets of size 400 and sequence size 30k bp for the test case considered.
- The results obtained from the phylogenies and conservation index analysis are consistent with the national and European periodical reports. The lack of detailed local reports prevents further comparisons.

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References

1. ECDC. Threat Assessment Brief: Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom. *European Centre for Disease Prevention and Control*.
2. ESCUELA DE INGENIERÍA Y ARQUITECTURA DE ZARAGOZA. *Directrices y recomendaciones para la impartición de la docencia en el segundo semestre del curso 2020-2021*. 11 January 2021.
3. ESPAÑA, CENTRO DE COORDINACIÓN DE ALERTAS Y EMERGENCIAS SANITARIAS. *Actualización nº 386. Enfermedad por el coronavirus (COVID-19)*. 31 May 2021.
4. EUROPEAN COMMISSION. *European Commission. Communication from the Commission to the European Parliament, the European Council and the Council, A united front to beat COVID-19*.
5. INE. Edad Media de la Población por comunidad autónoma, según sexo. *Instituto Nacional de Estadística*.
6. INE. Población por comunidades y ciudades autónomas y sexo. *Instituto Nacional de Estadística*.
7. LIU, Kevin, LINDER, C. Randal and WARNOW, Tandy. RAxML and FastTree: Comparing Two Methods for Large-Scale Maximum Likelihood Phylogeny Estimation. WU, Rongling (ed.), *PLoS ONE*. 21 November 2011. Vol. 6, no. 11, pp. e27731.
8. PAIS, Fabiano Sviatopolk-Mirsky, RUY, Patrícia de Cássia, OLIVEIRA, Guilherme and COIMBRA, Roney Santos. Assessing the efficiency of multiple sequence alignment programs. *Algorithms for Molecular Biology*. December 2014. Vol. 9, no. 1, pp. 4.

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Scan the code to download the paper, supplementary material, and GISAID acknowledgements →