Replicating Ford et al.'s investigation on the immune consequences and antibody binding affinity of SARS-CoV-2 variant XBB.1.5 using an *in silico* approach

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Introduction

- We replicated Ford *et al*. (2023; doi: 10.3389/fviro.2023.1172027)
- Our general objective was predicting changes in neutralizing antibody activity for SARS-CoV-2 XBB.1.5 using *in silico* protein modeling
- Our specific goals were to corroborate Ford *et al*. while optimizing the predictions of protein structures and protein docking in the context of an automatizable computational workflow

Methods

- The flowchart (top right corner) summarizes the methodology, which is based on Ford. et al. (2023)
- We compared different parameters in AlphaFold2 (AlphaFold Colab and ColabFold) to predict target viral proteins whenever needed
- We used HADDOCK to estimated the binding activity between the Spike protein's RBD of four SARS-CoV-2 variants (XBB.1.5, BM.1.1.1, B.1.1.52, and BJ.1) and ten neutralizing antibodies (LY-CoV555, LY-CoV1404, P5C3, COVOX-150, AZD1061, AZD8895, C110, EY6A, 58G6, and CV38-142)
- Protein structures and protein-to-protein interactions were manipulated and observed in PyMOL and ChimeraX

Conclusion

- We can use ColabFold's parameters for faster and equally accurate predictions
- ChimeraX is a more user-friendly option to PyMOL
- HADDOCK scores have to be multiplied by -1 to report scores in the same standard as other programs where the most negative values are read as the strongest binding affinities
- Ford *et al*. results are reproducible even using slightly different methodologies–this further validates this approach for large scale drug screening

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Artificial Intelligence can **predict** how new SARS-CoV-2 variants **escape** current treatments

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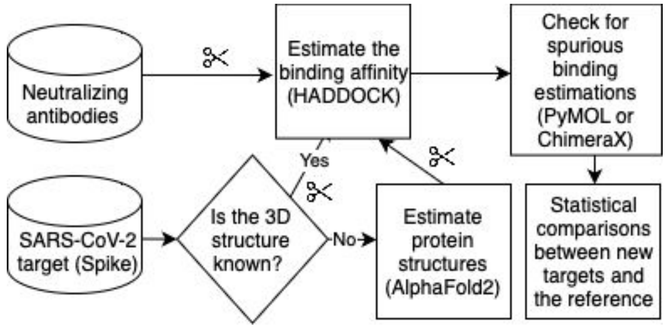
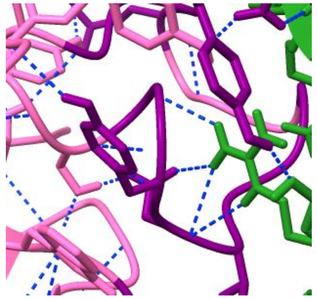
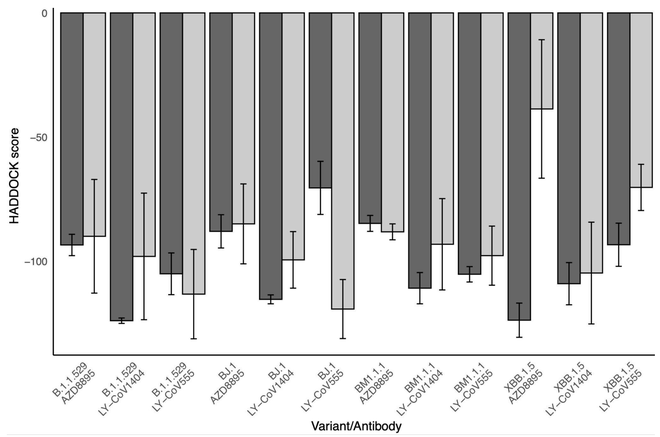


The flowchart above summarizes our methodology. The scissors symbol indicate editing or formatting of structural files in ChimeraX.



The image above is a visualization of HADDOCK predictions produced in ChimeraX. The image shows SARS-CoV-2 variant XBB.1.5(green) strongly interacting with the neutralizing antibody AZD1061(pink). The active sites on AZD1061 are shown in dark purple and weak H-bonds, where the binding affinity is not as strong, are shown in dotted blue lines.



The plot above summarized our results and shows that we (light gray) were able to replicate Ford *et al*.'s (dark grey) HADDOCK scores (Y-axis) for each pair of variant and antibody (X-axis).

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