Analysis of a protein-protein interface

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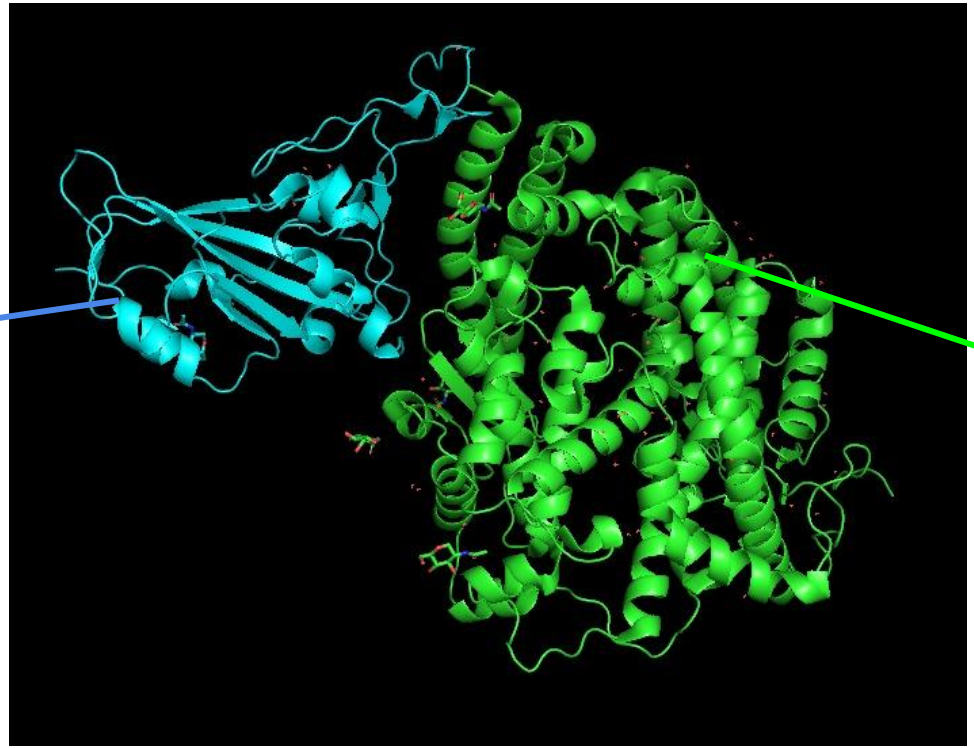
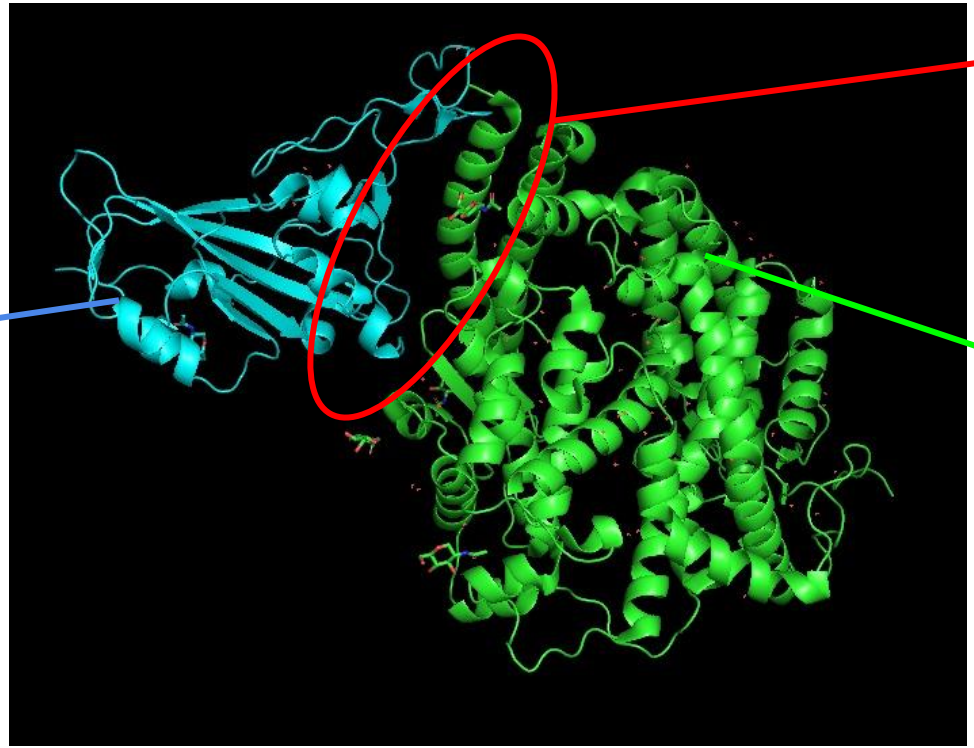
Spike RBD-ACE2

Objective: To evaluate the relative contribution of interface residues to the interaction energy in the protein-protein complex between the Receptor Binding Domain (RBD) of SARS-Cov-2 Spike Protein and its receptor Angiotensin Converting Enzyme (ACE2).

Angiotensin Converting Enzyme (ACE2)



Receptor Binding Domain (RBD)


Interface residues
Angiotensin Converting Enzyme (ACE2)
Receptor Binding Domain (RBD)

Strategy: We will evaluate the contribution of individual amino acid residues through the following steps:

1. **Determine amino acid residues** that form the interface between the complex components.

2. **Determine the contribution to the stability of the complex** by mimicking a traditional Ala-scanning experiment, i.e. replacing each residue in turn by Ala and evaluating the changes in the complex interaction energy.

3. Use the system to **evaluate SARS-Cov-2 spike variants on ACE2 binding**

1. **Determine amino acid residues** that form the interface between the complex components.

The interface between is defined by a **list of residues on both chains that have at least one atom below a given distance**.

a. Using pymol inspect visually the structure and choose a suitable distance in the way that all contact residues are included. Add 1-2 Å to that distance so the adjacent residues are also considered. → **Determine the distance**

b. Prepare a python script (standalone or in a Jupyter notebook) to define the list of interface residues on each chain → **List of the interface residues**

c. Prepare a python script or notebook to evaluate the **Interaction energy** among chains

2. **Determine the contribution to the stability of the complex** by mimicking a traditional Ala-scanning experiment

a. Determine the effect of replacing each interface residue by Ala in the overall interaction energy, and make a plot of the results obtained, **highlighting those residues that are more relevant for the stability of the interface**.

b. Prepare images with pymol of the interface highlighting the relevant residues and interactions.

3. Use the system to **evaluate SARS-Cov-2 spike variants on ACE2 binding**

a. Find the most relevant sequence variants for RBD (alfa, beta, and delta SARS-Cov-2 strains) and analyze the effect of the actual mutations on the energy.

Script Rules

a. Prepare reusable scripts (use meaningful command lines)
b. Document the code
c. One single script or several forming a pipeline (preferred)
d. Outputs properly formatted
e. Prepare reusable functions

Report

a. Complete report of the operations done
b. Critical comparison of energies, types of interaction between the two cases.
c. Scripts/Notebooks (ideally on github)
d. Images of the interface, highlighting relevant residues / interactions