BS52013 Coursework 1

As directed, I first used ColabFold with default settings to build five structural models from the sequence of PDB entry 8URN, without the C-terminal 6-His tag.

Selecting the best model:

Model 1 was ranked as the best structural model, so it is the model I will use for the purposes of this assignment.

AlphaFold estimates the quality of each model using two predicted model accuracy scores: pLDDT (predicted Local Distance Difference Test) and pTM (predicted Template Modelling score).

In this instance, model 1 had the highest pLDDT score by 0.1, and whilst it does not have the highest pTM score, the difference between the pTM of this model and the next ranking model, the difference is just 0.009. Therefore, model 1 still ranks the highest of all models, so was selected as the best model.

Included in the submitted files is the PDB file of this model.

An image of the structurally aligned proteins exported from PyMOL:

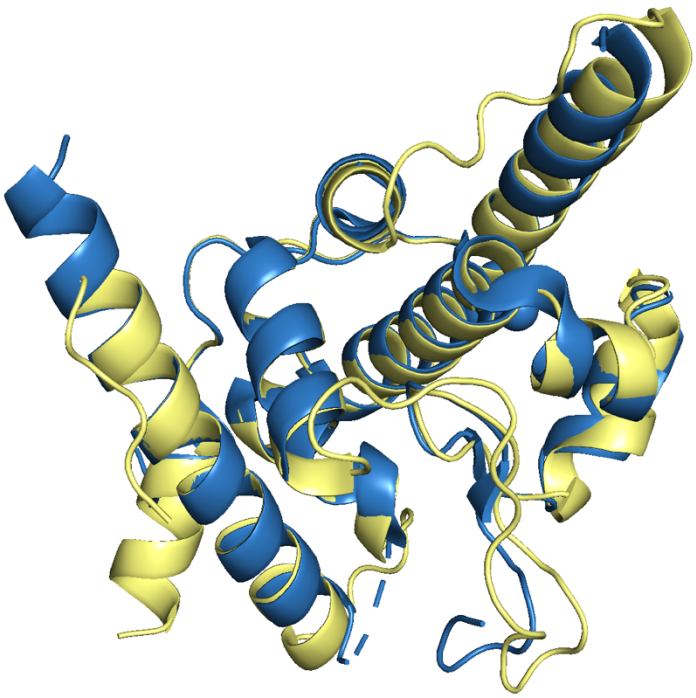

Figure 1: *Model 1structurally aligned to PDB structure 8URN using PyMOL. The model is coloured yellow, and the PDB structure is coloured blue.*

The RMSD between the model and the PDB structure is **0.438.**

Can you identify a disulfide bond between Cys residues (and where)?

There is one disulphide bond in the model structure – between CYS 51 and CYS 120, as shown in figure 2.

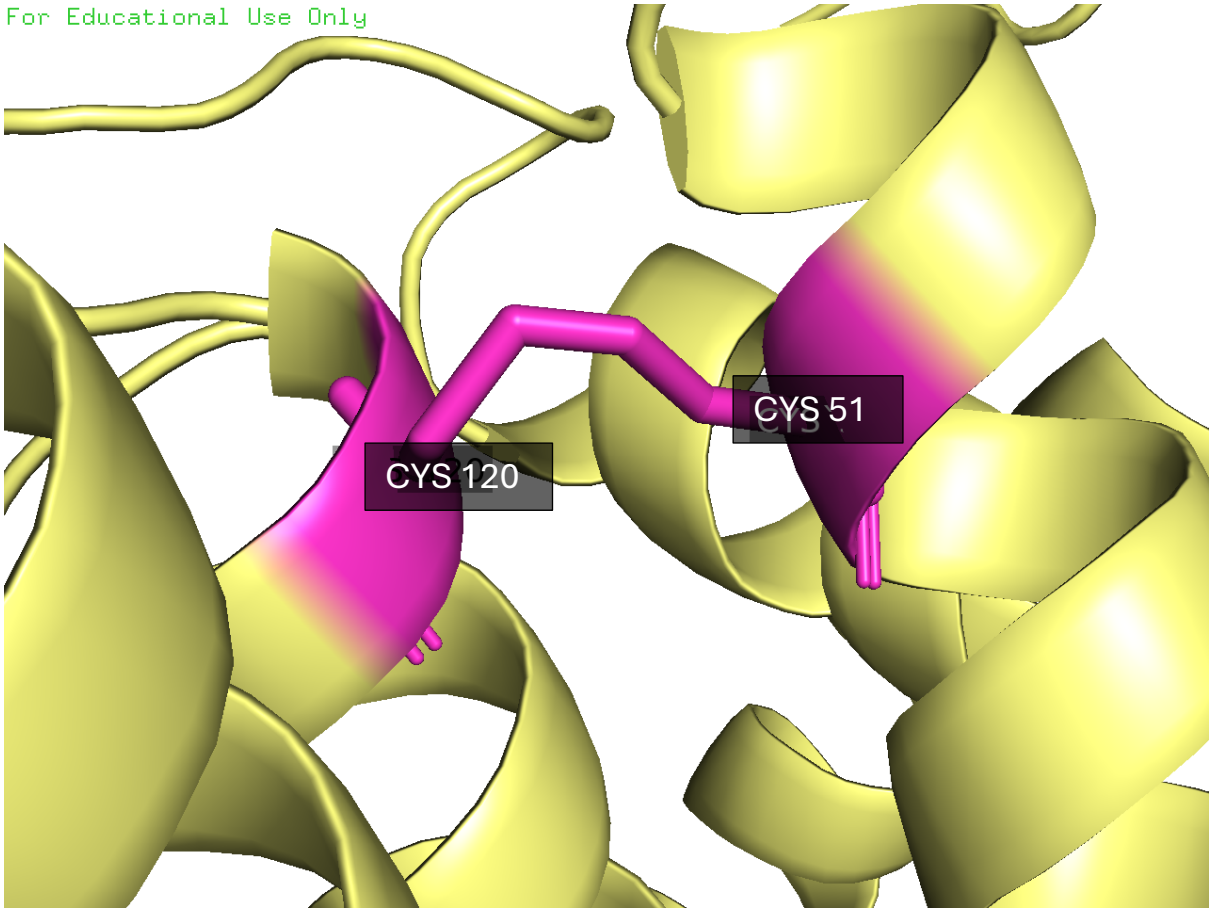

Figure 2: *A close up look of the disulphide bond in the model structure.*

Explain which parts of the model are more and less reliable and explain; also comment on the match.

Overall, the model is a very good match to the PDB structure, but as expected, the loops are much less accurate in the model.

Additionally, the modelling of both the N- and C-termini of the model is not reliable, and is a poor match to the PDB structure. At the C- terminus, the model has a loop where the PDB structure has a longer helix. Moreover, at the N-terminus, on the PDB entry, positions 1-5 are unmodelled. On the AlphaFold model, these positions are modelled as simply being an extension of the helix, which seem reasonable.

A PyMOL image of the electrostatic surface potential of the modelled protein as produced by APBS:

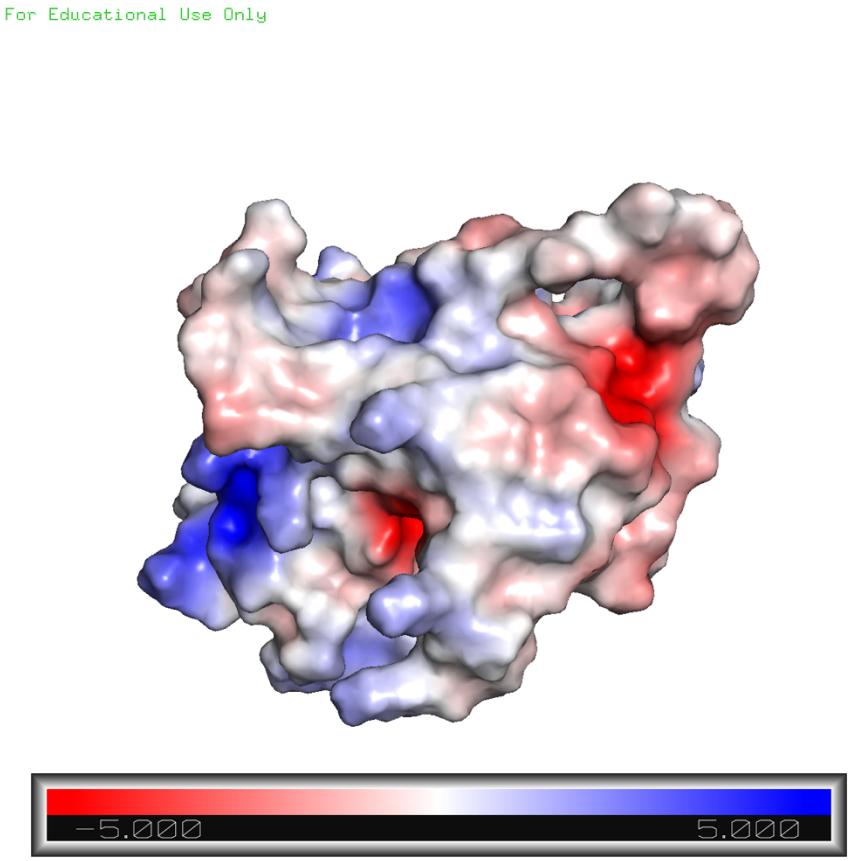

Figure 2: *Image generated using the PyMOL APBS electrostatics plugin, showing the negative and positive electrostatic potential on the surface of model 1.*