Course Project: Structural Analysis of the Hemoglobin Complex

Proteomes Interactomes and Biological Networks

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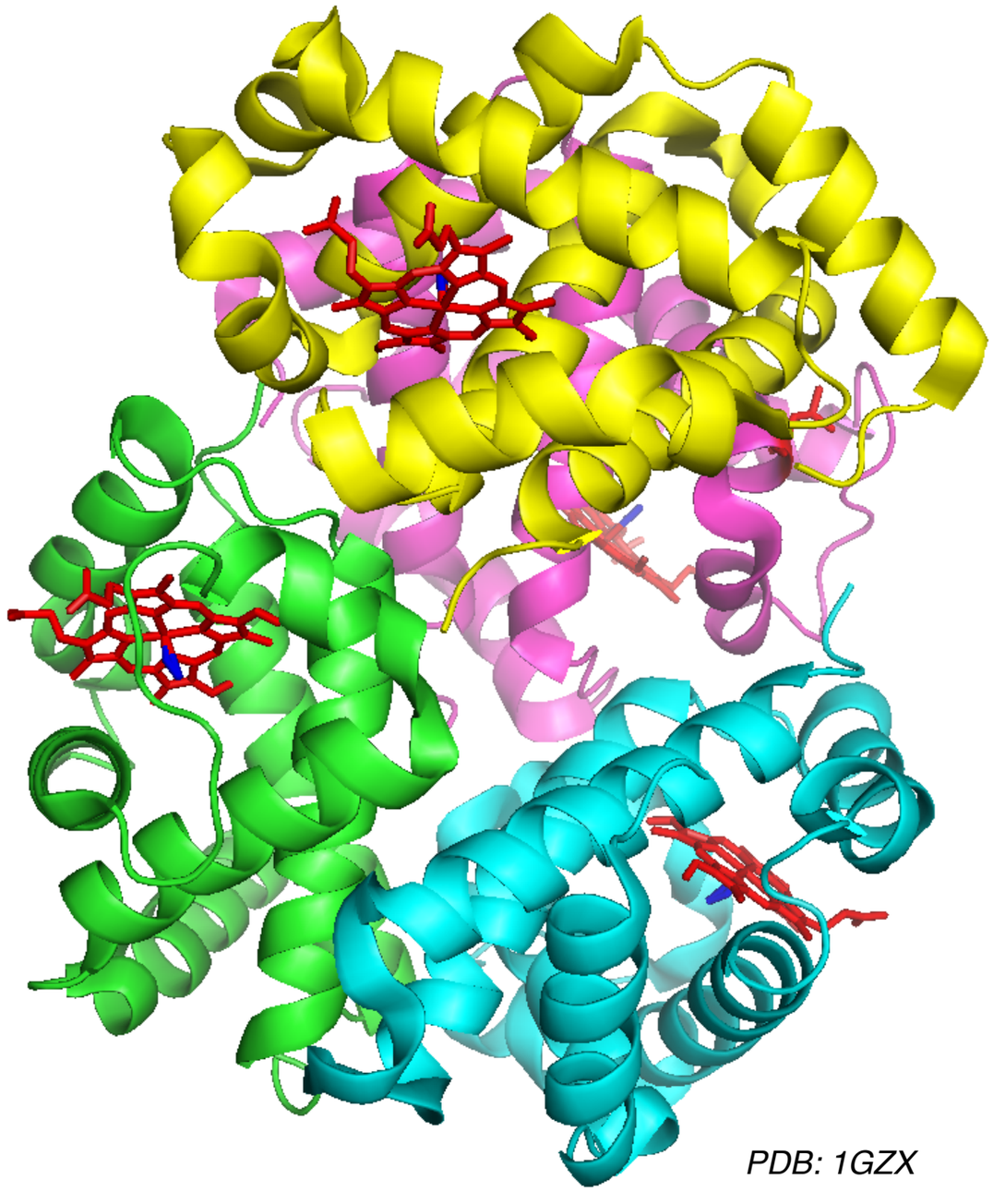
Hemoglobin

Hemoglobin is an oxygen-transport protein. It is a tetramer composed by two subunits designated α and β, with stoichiometry α2β2.

The four subunits of hemoglobin sit roughly at the corners of a tetrahedron, facing each other across a cavity at the center of the molecule. Each of the subunits contains a heme prosthetic group.

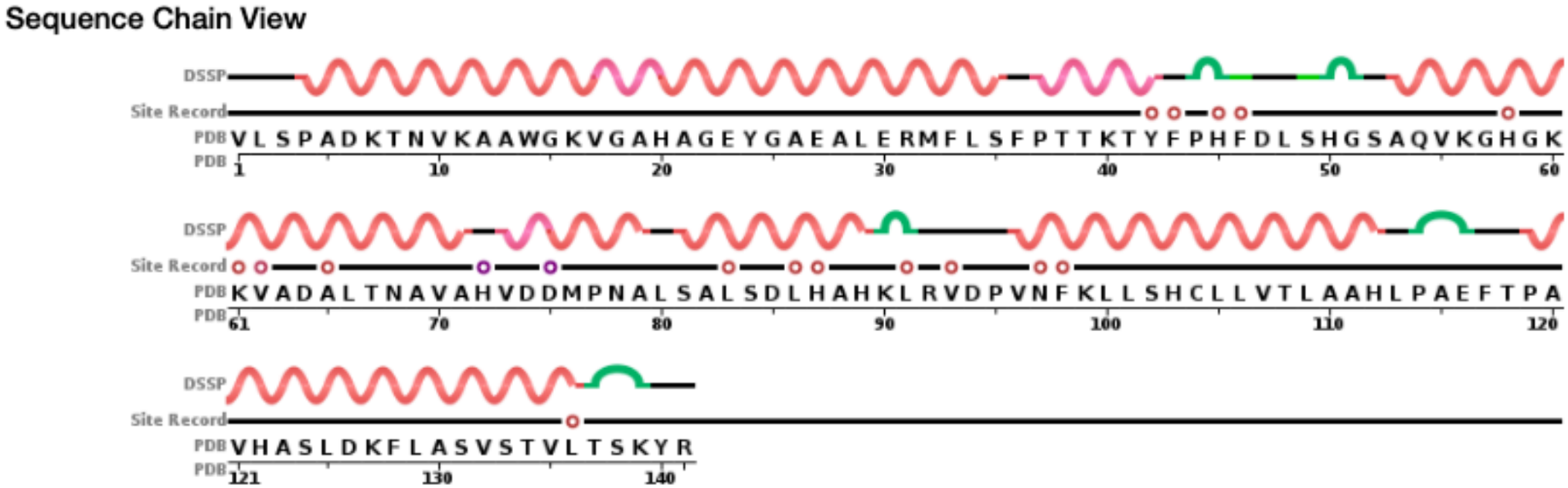
Each individual heme molecule contains one Fe2+ atom. The heme group binds oxygen while still attached to the hemoglobin monomer.



PDB: 1GZX

Subunit Alpha

All-alpha chain A and C of the PDB structure 1GZX composed by 141 residues



Site Record Legend

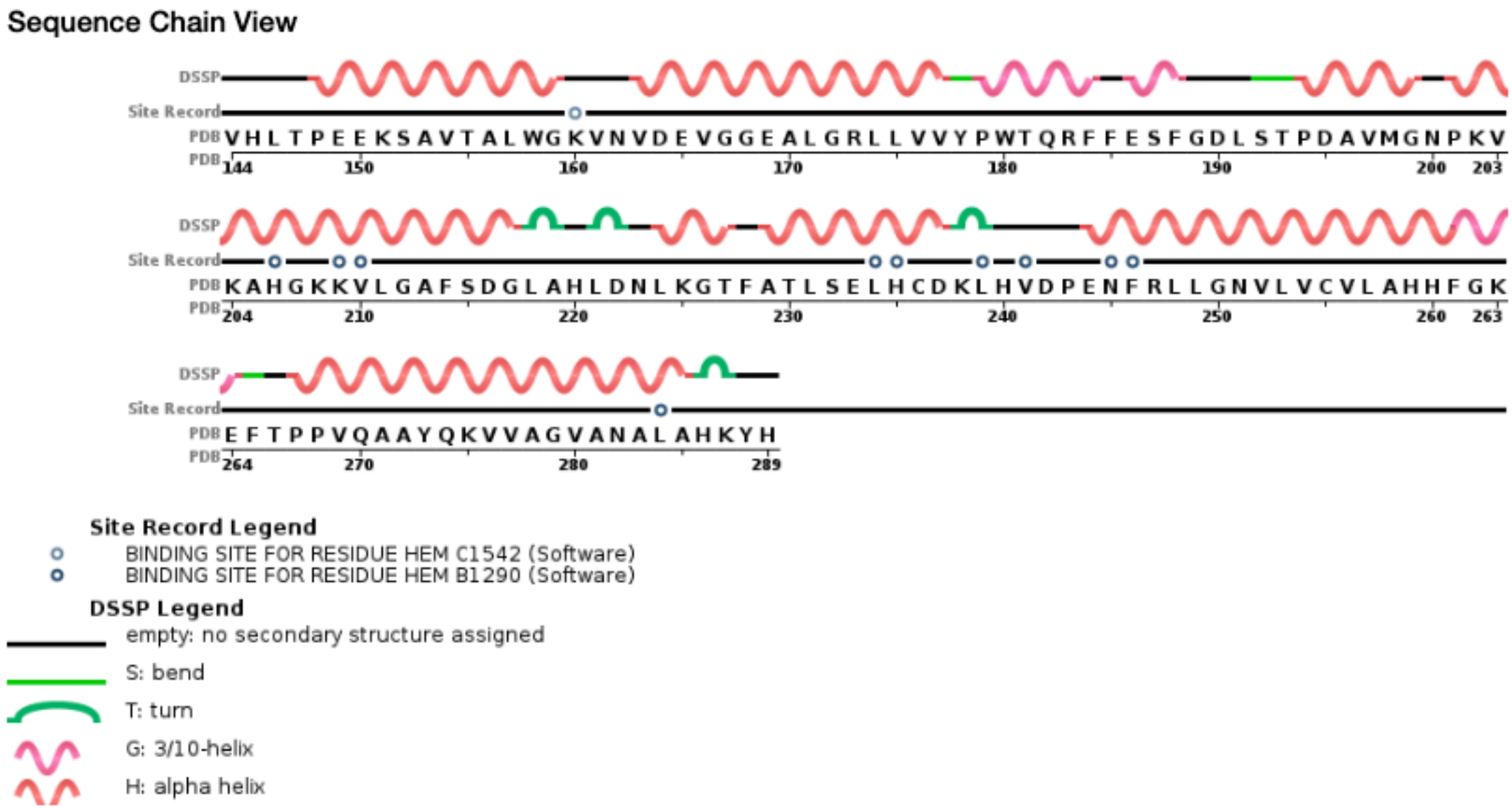
- BINDING SITE FOR RESIDUE HEM B1290 (Software)
- BINDING SITE FOR RESIDUE HEM A1142 (Software)
- BINDING SITE FOR RESIDUE OXY A1143 (Software)

DSSP Legend

- empty: no secondary structure assigned
- S: bend
- T: turn
- G: 3/10-helix
- H: alpha helix

Subunit Beta

All-alpha chain B and D of the PDB structure 1GZX composed by 146 residues



Sequence Comparison

The alignment of the two sequences shows that they share ~44% of the residues

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The best scores are:                                      n-w bits E(1)
HBB_HUMAN 147 bp                                ( 147)  373 65.3 1.4e-161

>>HBB_HUMAN 147 bp                                        (147 aa)
 n-w opt: 373  Z-score: 320.6  bits: 65.3 E(1): 1.4e-161
global/local score: 373; 43.6% identity (74.5% similar) in 149 aa overlap (1-142:1-147)

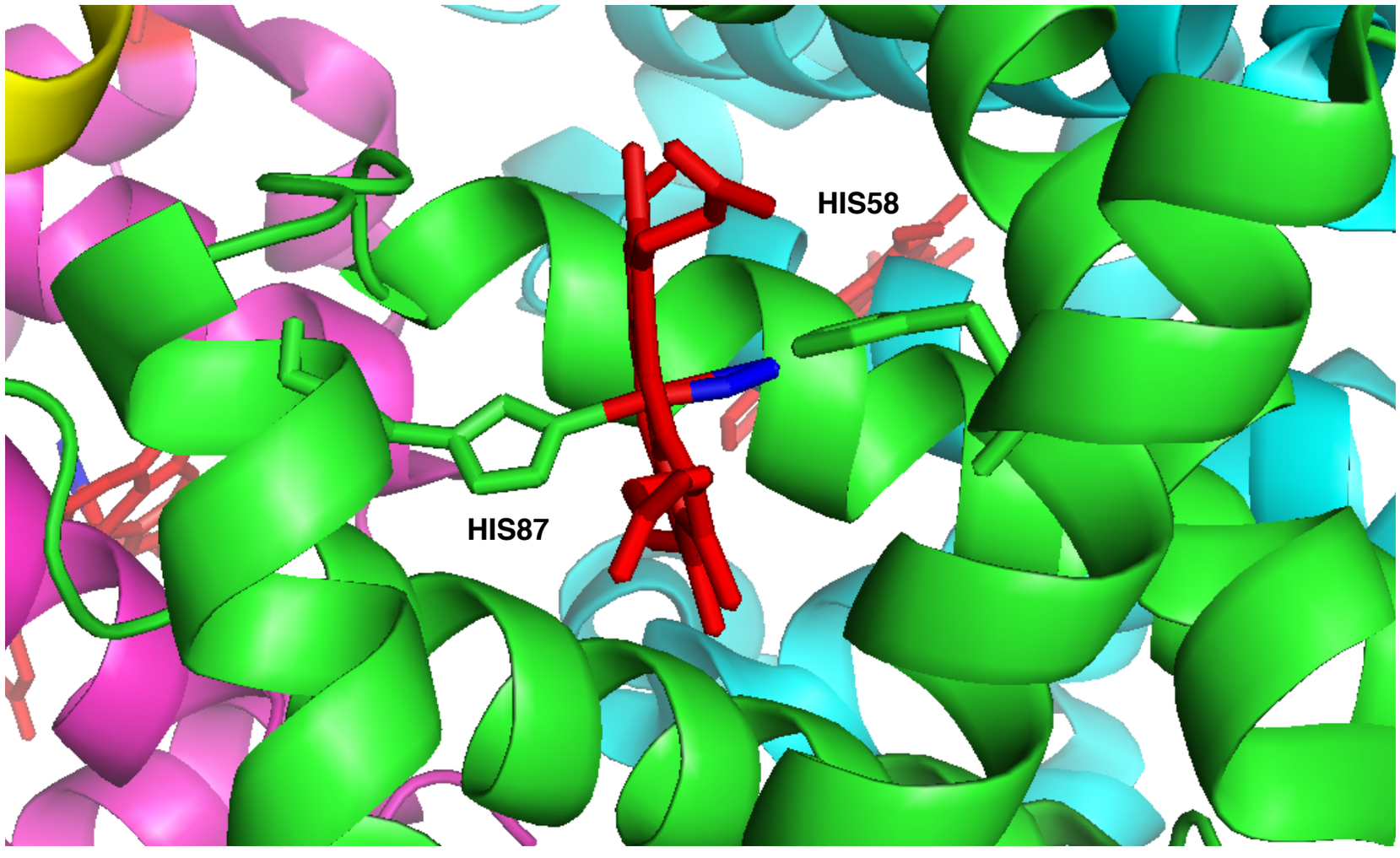
                10        20        30        40        50
HBA_HU MV-LSPADKTNVKAAWGKVGAHAGEYGAEALERMFLSFPTTKTYFPHF-DLS-----HGS
       :: :.: .:. : : ::::  .. : :.::: :... .: :. .:  : :::      :.
HBB_HU MVHLTPEEKSAVTALWGKV--NVDEVGGEALGRLLVVYPWTQRFFESFGDLSTPDAVMGN
               10          20        30        40        50

            60        70        80        90       100       110
HBA_HU AQVKGHGKKVADALTNAVAHVDDMPNALSALSDLHAHKLRVDPVNFKLLSHCLLVTLAAH
        .::.::::  :.....::.:.. .....::.::  ::.::: ::.::.. :. .:: :
HBB_HU PKVKAHGKKVLGAFSDGLAHLDNLKGTFATLSELHCDKLHVDPENFRLLGNVLVCVLAHH
       60        70        80        90       100       110

           120       130       140
HBA_HU LPAEFTPAVHASLDKFLASVSTVLTSKYR
       .  :::: :.:. .: .:.:...:. ::.
HBB_HU FGKEFTPPVQAAYQKVVAGVANALAHKYH
      120       130       140
```

Heme and Oxygen

Anchoring of the heme is facilitated by a histidine nitrogen that binds to the iron.
A second histidine is near the bound oxygen.



PDB: 1GZX

Problem 1

Given the PDB structure 1GZX for each one of the monomers:

- Considering a minimum atom distance of 3.5 Å, identify the residues in proximity of the heme and oxygen group.
- Using the same procedure identify the possible interacting residues among the monomers.
- Generate the dssp file of the whole structure and all substructure and calculate the surface of interaction between all the monomers.
- Evaluating the differences in relative solvent accessibility, identify the interacting residues among all the monomers.
- Compare the results obtained for each monomer.

Suggestions

- Modify the program for parsing a PDB file including the file ‘HETATM’ that includes the coordinate of the Heme and Oxy groups

- The distance between two group of atoms is minimum distance between all possible pairs combinations

- The functions used to calculate the distance between prostetic groups and monomers can be modified to calculate the distance between monomers.