Course Project: Structural Analysis of the Hemoglobin Complex

Proteomes Interactomes and Biological Networks

December 2 and 3, 2019
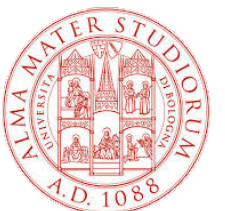
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Biomolecules Folding and Disease

# 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.
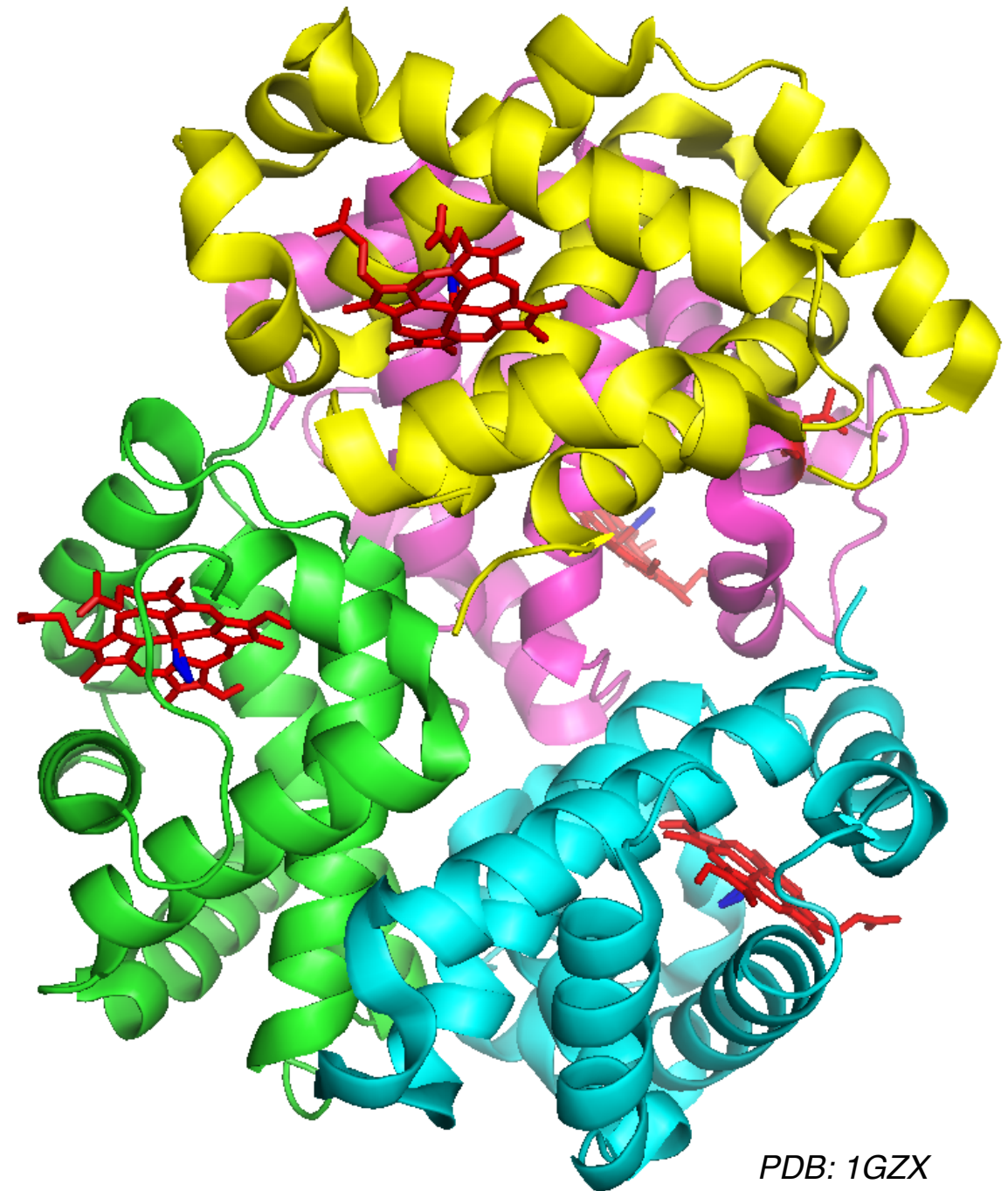
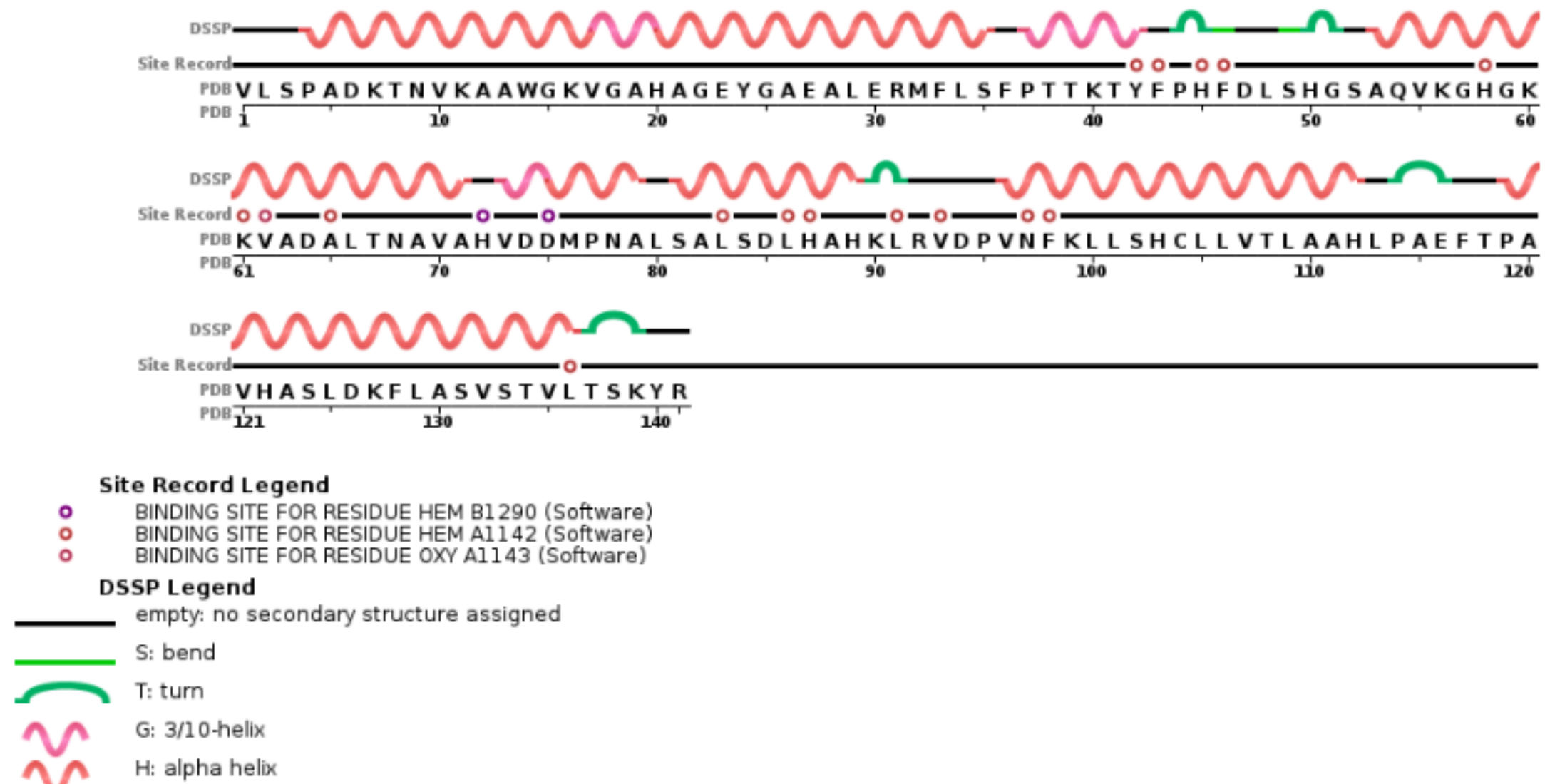*PDB: 1GZX*

Subunit Alpha

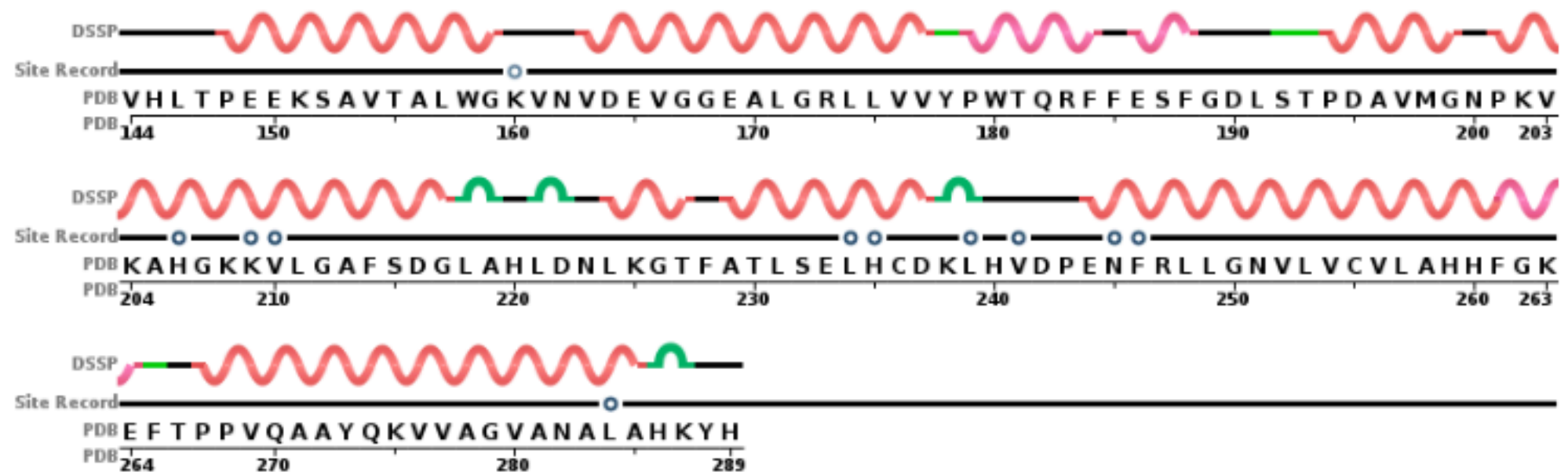All-alpha chain A and C of the PDB structure 1GZX composed by 141 residues

Sequence Chain View

DSSP	
Site Record	
PDB	V L S P A D K T N V K A A W G K V G A H A G E Y G A E A L E R M F L S F P T T K T Y F P H F D L S H G S A Q V K G H G K
PDB	1 10 20 30 40 50 60

DSSP	
Site Record	
PDB	K V A D A L T N A V A H V D D M P N A L S A L S D L H A H K L R V D P V N F K L L S H C L L V T L A A H L P A E F T P A
PDB	61 70 80 90 100 110 120

DSSP	
Site Record	
PDB	V H A S L D K F L A S V S T V L T S K Y R
PDB	121 130 140

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 Chain View

DSSP

Site Record

PDB V H L T P E E K S A V T A L W G K V N V D E V G G E A L G R L L V V Y P W T Q R F F E S F G D L S T P D A V M G N P K V

PDB 144 150 160 170 180 190 200 203

DSSP

Site Record

PDB K A H G K K V L G A F S D G L A H L D N L K G T F A T L S E L H C D K L H V D P E N F R L L G N V L V C V L A H H F G K

PDB 204 210 220 230 240 250 260 263

DSSP

Site Record

PDB E F T P P V Q A A Y Q K V V A G V A N A L A H K Y H

PDB 264 270 280 289

Site Record Legend

- ○ BINDING SITE FOR RESIDUE HEM C1542 (Software)
- ○ BINDING SITE FOR RESIDUE HEM B1290 (Software)

DSSP Legend

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

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
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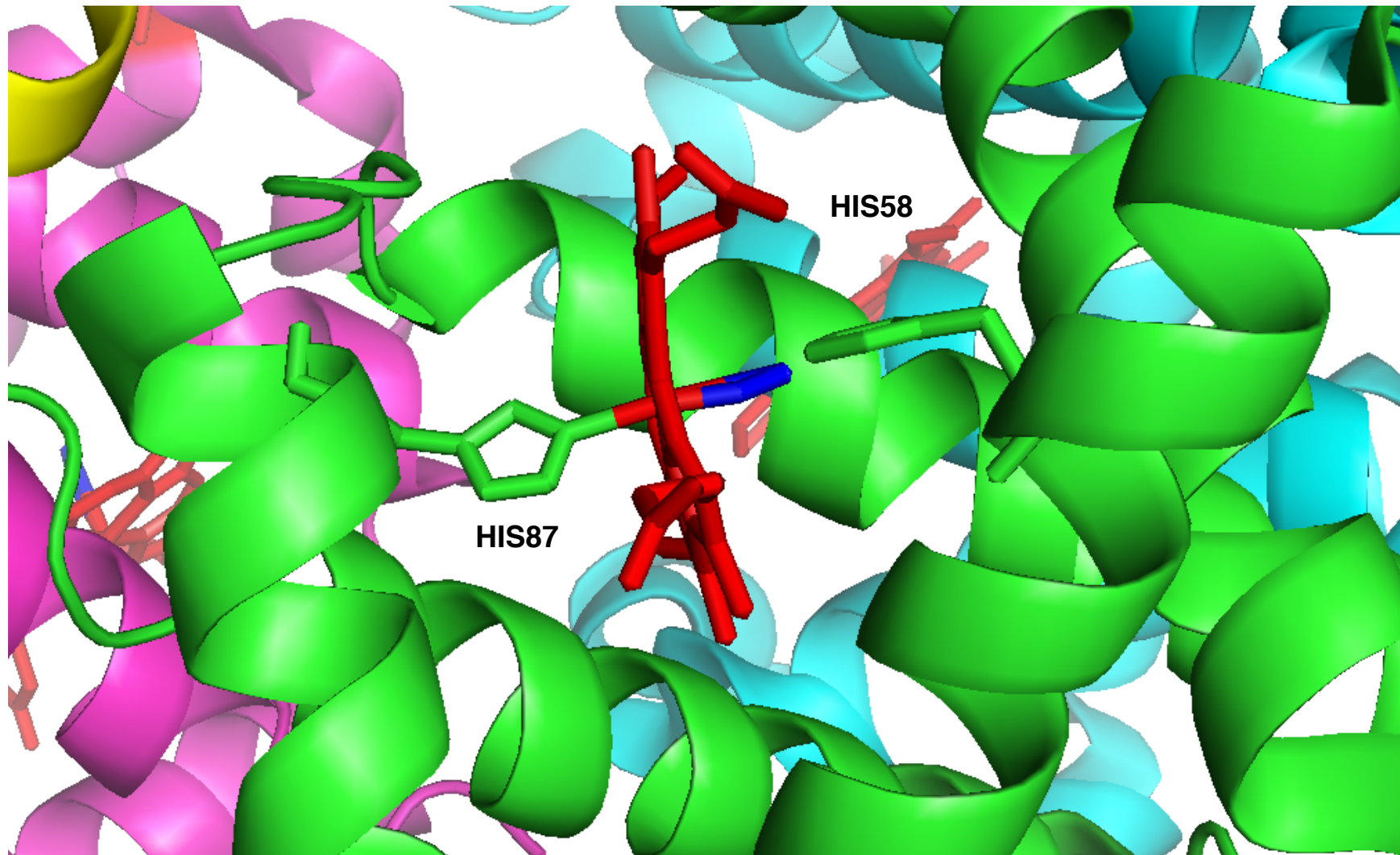
Heme and Oxygen

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

HIS58

HIS87

PDB: 1GZX

Problem 1

Given the PDB structure 1GZX for each monomer:

- 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.

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 monomer

Problem 2

Given the PDB structure 1GZX:

- Generate the dssp file of the whole structure and the substructures 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:

- Generate the dssp of the single monomers and the four structures excluding one monomer.

- The comparison of the different dssp allows to calculate the surface of interaction that each monomer has with the remaining ones.