

SSBI
ASSIGNMENT 02

Task 1 - Torsion Angles

a)

A	B	C	D
3)	2)	1)	4)

b)

Amino acid	χ_1	χ_2	χ_3	χ_4	χ_5
MET	N-CA-CB-CG	CA-CB-CG-SD	CB-CG-SD-CE	-	-
ALA	-	-	-	-	-
PRO	N-CA-CB-CG	CA-CB-CG-CD	CB-CG-CD-N	CG-CD-N-CA	CD-N-CA-CB
TYR	N-CA-CB-CG	CA-CB-CG-CD	-	-	-
LYS	N-CA-CB-CG	CA-CB-CG-CD	CB-CG-CD-CE	CG-CD-CE-NZ	-
ARG	N-CA-CB-CG	CA-CB-CG-CD	CB-CG-CD-NE	CG-CD-NE-CZ	CD-NE-CZ-NH ₁

c) most preferred -68° -176° -66° -68° 65° 54° -171° -159° least preferred [2]

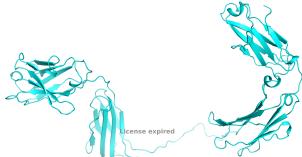
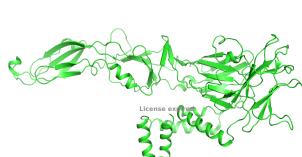
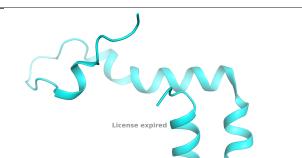
Task 2 - Protein Data Bank I

1. How many amino acids does each primary structure contain?

The monoclonal antibody 231[1] (PDB: 1IGT) consists of two heavy chains, each of which is 444 amino acids long and two light chains à 214 amino acids (1,316 amino acids in total). The structure with PDB-id: 5IRE consists of three E proteins (504 Amino acids) and three M proteins (75 amino acids) of the Zika virus[3] (1,737 amino acids in total).

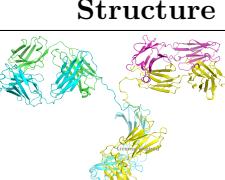
2. What is the prevailing secondary structure of each protein?

Both proteins contain loops, β -sheets and α -helices. While in the antibody, β -sheets are clearly dominant, in the Zika virus β -sheets and α -helices are equally important. In the Mab231, there are also a few linker regions.

Chain	secondary structures	Structure
Mab231 light chain	mostly β -sheets	
Mab231 heavy chain	mostly β -sheets	
Zika virus E protein	β -sheets and α -helices	
Zika virus M protein	only α -helices	

3. How many chains do the proteins consist of?

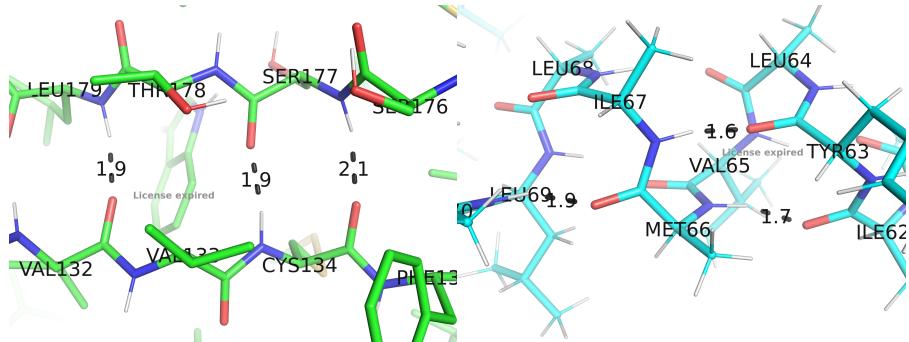
The monoclonal antibody consists of four chains (two heavy and two light chains). The Zika virus proteins are represented in a complex of three E proteins and 3 M proteins.

ID (name)	Chain	Length	Structure
1IGT (Mab231)	LC1 (A)	1.316	
	LC2 (C)	214	
	HC1 (B)	444	
	LC2 (D)	444	
5IRE (Zika virus)	A (E protein)	1.737	
	C (E protein)	504	
	E (E protein)	504	
	B (M protein)	75	
	D (M protein)	75	
	F (M protein)	75	

4. What is the role of the quaternary structure for the 5IRE protein entry?

The quaternary structure represented in the entry "5IRE" consists of a complex of six proteins. In a fully assembled Zika virus 180 of the envelope (E) proteins together with the membrane (M) protein make up the icosahedral shell of the virus [3].

5. For both proteins, find three hydrogen bonds and three disulfide bonds.



Structure	Residues	Bond Length	Bond Type
β -sheet of LC1 of 1IGT (chain A)	Leu179 - Val132 Cys134 - Ser177 Ser177 - Cys134	1.9 Å 1.9 Å 2.1 Å	hydrogen bonds
Disulfide bonds between HC1 (chain b) and HC2 (chain d) of 1IGT	chB Cys242 - chD Cys242 chB Cys240 - chD Cys240 chB Cys237 - chD Cys237	2.0 Å 2.0 Å 2.0 Å	disulfide bonds
α -helix of the M protein of 5IRE (chain B)	Ile67 - Tyr63 Met66 - Ile32 Ile70 - Met66	1.6 Å 1.7 Å 1.9 Å	hydrogen bonds
Disulfide bonds within the E protein of 5IRE (chain a, c, e)	chA Cys105 - chA Cys74 chA Cys116 - chA Cys92 chC Cys105 - chC Cys74	2.0 Å 2.0 Å 2.0 Å	disulfide bonds

6. How many disulfide bonds do you find in each protein? Which residues form these bonds?

The structure "1IGT" contains 17 disulfide bonds, the structure "5IRE" contains 6 disulfide bonds.

ID	Chain	Residue	ID	Chain	Residue
1IGT	A	CYS 23	1IGT	A	CYS 88
1IGT	A	CYS 134	1IGT	A	CYS 194
1IGT	A	CYS 214	1IGT	B	CYS 128
1IGT	B	CYS 22	1IGT	B	CYS 92
1IGT	B	CYS 142	1IGT	B	CYS 208
1IGT	B	CYS 237	1IGT	D	CYS 237
1IGT	B	CYS 240	1IGT	D	CYS 240
1IGT	B	CYS 242	1IGT	D	CYS 242
1IGT	B	CYS 274	1IGT	B	CYS 340
1IGT	B	CYS 390	1IGT	B	CYS 456
1IGT	C	CYS 23	1IGT	C	CYS 88
1IGT	C	CYS 134	1IGT	C	CYS 194
1IGT	C	CYS 214	1IGT	D	CYS 128
1IGT	D	CYS 22	1IGT	D	CYS 92
1IGT	D	CYS 142	1IGT	D	CYS 208
1IGT	D	CYS 274	1IGT	D	CYS 340
1IGT	D	CYS 390	1IGT	D	CYS 456
5IRE	A	CYS 74	5IRE	A	CYS 105
5IRE	A	CYS 92	5IRE	A	CYS 116
5IRE	C	CYS 74	5IRE	C	CYS 105
5IRE	C	CYS 92	5IRE	C	CYS 116
5IRE	E	CYS 74	5IRE	E	CYS 105
5IRE	E	CYS 92	5IRE	E	CYS 116

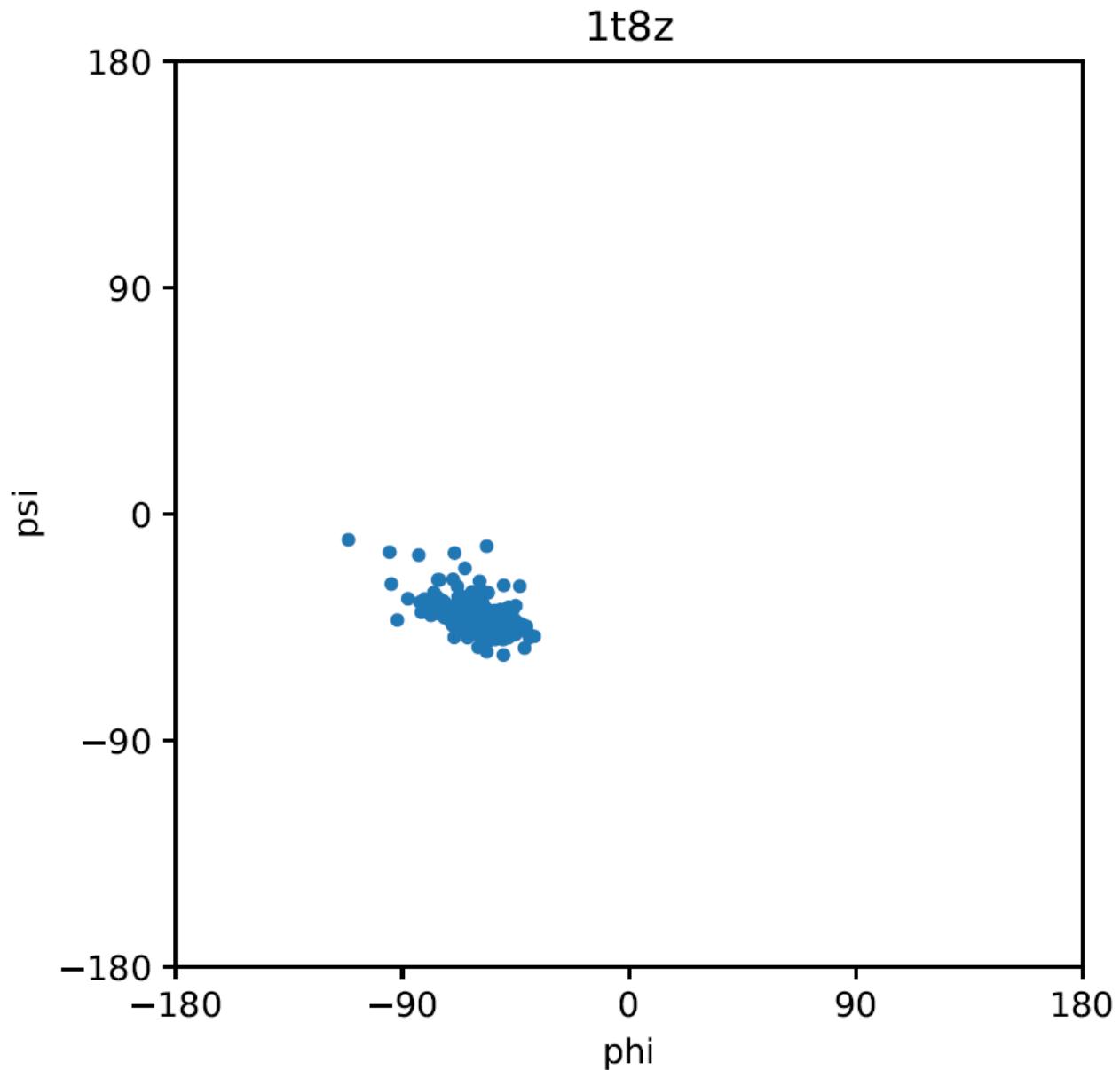
What is the relationship of the disulfide bond type to structure stability?

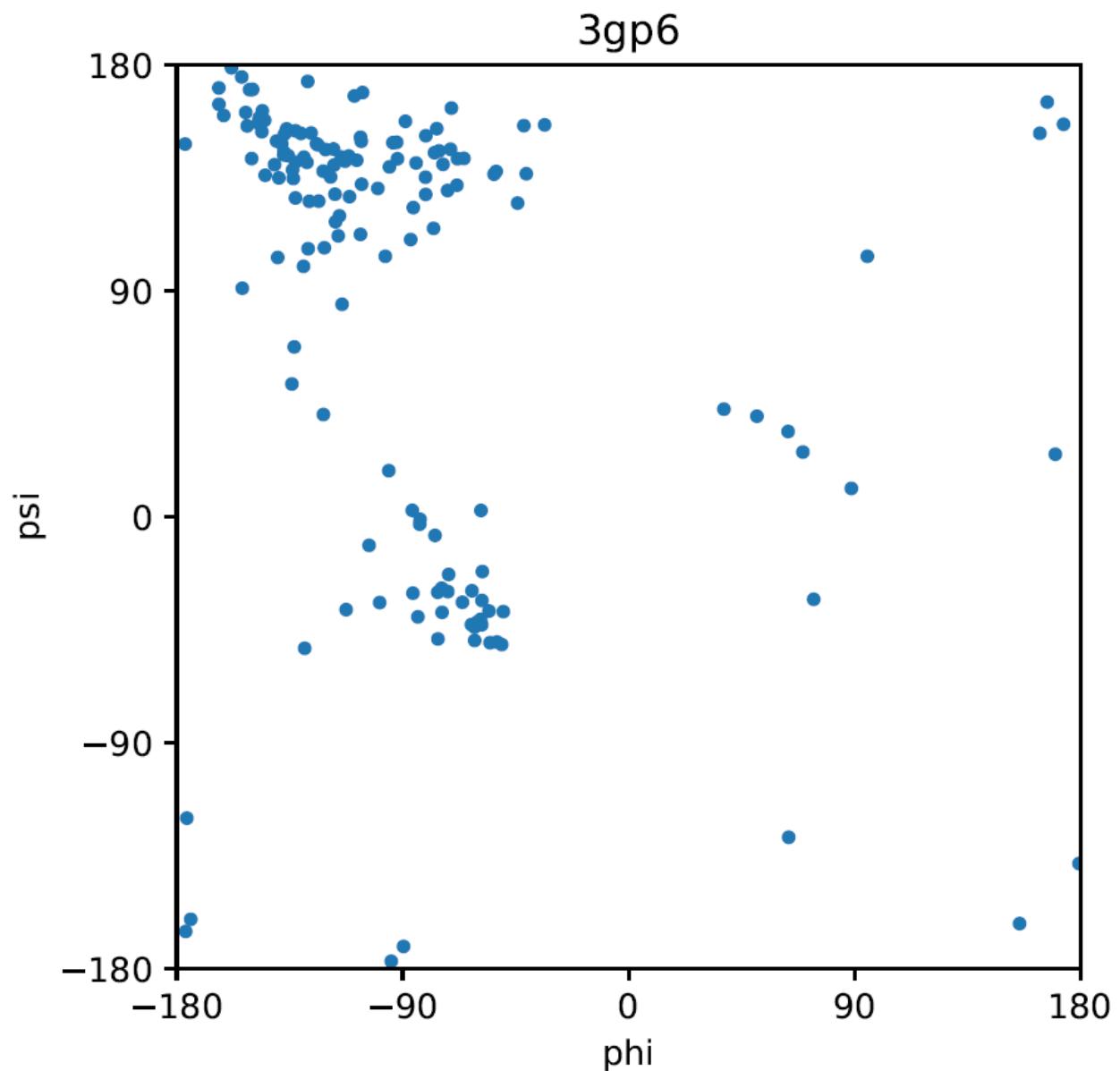
Disulfide bonds are covalent bonds and thus much stronger than most other protein-protein interactions (Hydrophobic interaction, ionic interaction, hydrogen bonds). They are often important links in between different chains of a protein, as we see for example with the three disulfide bonds, connecting the two heavy chains of the monoclonal antibody Mab231.

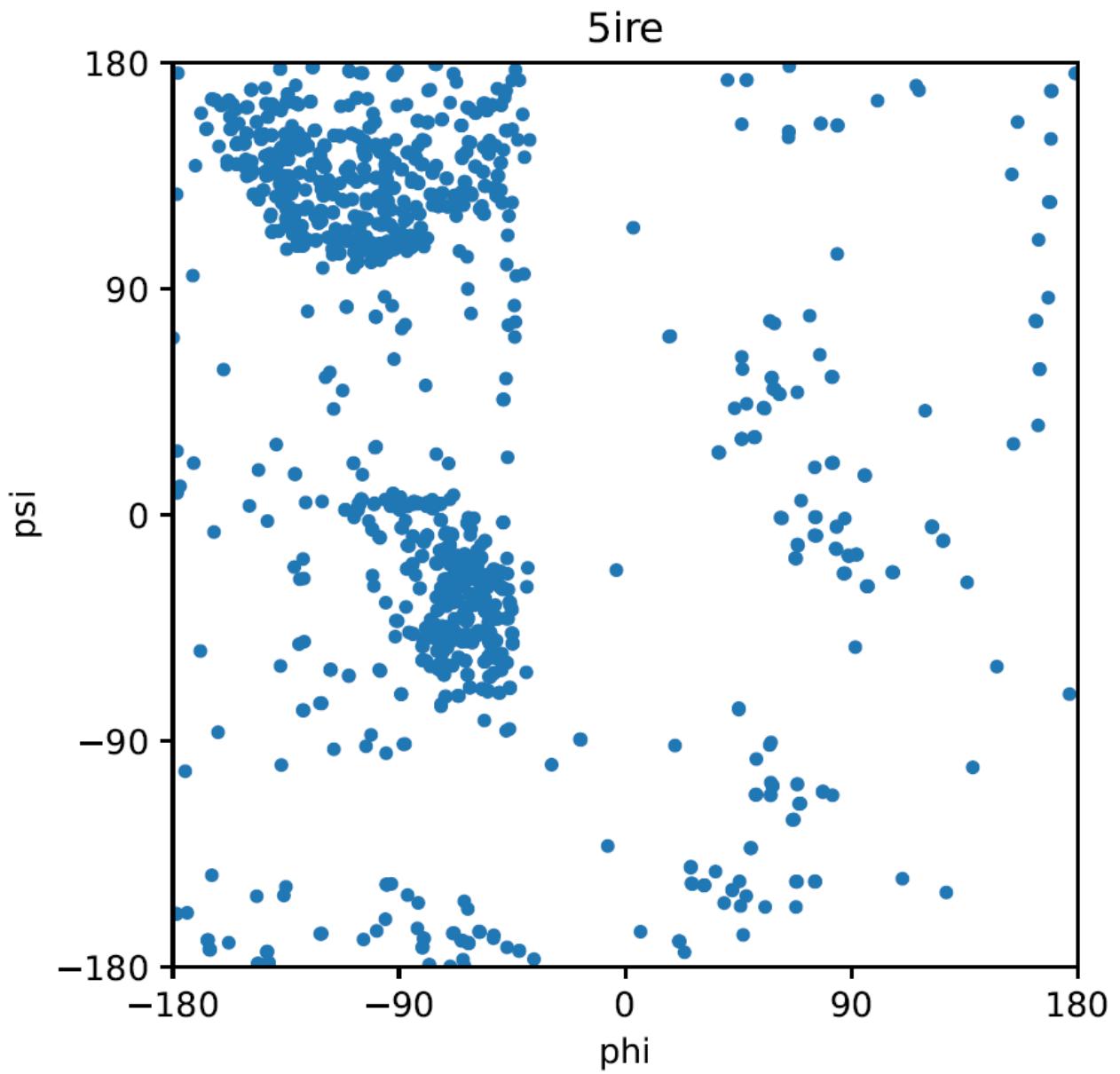
Task 3 - Ramachandran Maps

To plot Ramachandran maps from multiple PDB files to a PDF document, the python script *kubach-ramachandran.py* has been set up. It uses the packages argparse (command line interaction), Biopython (PDB parsing), numpy (vector calculations), matplotlib (plot maps to PDF). Those packages are required to run the program. An exemplary run and documentation on how to use the script can be found in the *README.md* file.

With the structures 1T8Z, 3GP6 and 5IRE, the following plots have been produced:







The structure 1T8Z of a Tryptophan-Zipper consists mainly of alpha helices, which is why in the Ramachandran plot all angles are concentrated in a small area around $\phi = 50^\circ$ and $\psi = 50^\circ$. The structure 3GP6 represents a β -barrel. The dots in the Ramachandran plot are more scattered and while mostly in the β -sheet region on the upper left, there are still spots in the α -helix region. The Zika virus complex 5IRE has a mix of β -sheets and α -helices (see also Task 2), which correlates with the Ramachandran plot.

Task 4 - Unusual Structure Motifs

1. **What properties make the left-handed conformation feasible, compared to other amino acids?**

The left-handed conformation is more energetically favorable than π - and 3_{10} -helices. They are too densely / loosely packed.

2. **What would you expect to happen if a glycine residue in a long polyglycine helix was exchanged to a different proteinogenic amino acid?**

The helix will be interrupt at this point due to sterical hindrance.

3. Would D-alanine prefer left- or right-handed helices?

D-alanine will prefer left-handed helices. The side chain of D-alanine located on the opposite side of L-alanine, which makes a left-handed turn sterically more favorable.

References

- [1] L J Harris, S B Larson, K W Hasel, and A McPherson. Refined structure of an intact IgG2a monoclonal antibody. *Biochemistry*, 36:1581–97, 2 1997.
- [2] Hannelore Schrauber, Frank Eisenhaber, and Patrick Argos. Rotamers: To be or not to be?: An analysis of amino acid side-chain conformations in globular proteins. *Journal of Molecular Biology*, 230(2):592–612, 1993.
- [3] Devika Sirohi, Zhenguo Chen, Lei Sun, Thomas Klose, Theodore C. Pierson, Michael G. Rossmann, and Richard J. Kuhn. The 3.8 Å resolution cryo-em structure of zika virus. *Science*, 352:467–470, 4 2016.