Force fields
Exercise 2 - Phi-Psi angles

We shall here investigate the dihedral angles of peptide bonds in polypeptides and proteins, and how force fields are parameterized to maintain these values.

$$\boldsymbol{\varphi} : C_{i-1}-N_i-C\alpha_i-C_i \qquad\qquad \boldsymbol{\psi} : N_i-C\alpha_i-C_i-N_{i+1}$$

1. Retrieve the following proteins structures from the Protein Data Bank and save them in a directory, then open them in Maestro. Alternatively, you can get the Project » Get PDB command from the toolbar.

- Human aquaporin, PDB ID 3GD8
- human hemoglobin (mutant), PDB ID 3QJB
- green fluorescent protein, PDB ID 2GX0
- Formaldehyde Ferredoxin Oxidoreductase, 1B25
- Retinol binding protein, 1HBQ
- Yeast Triosephosphate isomerase, 1YPI

Observe all the structures and see if you can find a representative of each type of secondary structure element (alpha helices, parallel and anti-parallel beta-sheets, … see yesterday's lecture for a list).
Which ones can you find? Which ones can't you find?
Using Tools » Measurements » Dihedral, measure one pair of (ϕ,φ) angles in each of the different representatives secondary structure elements you can find and report them on the Ramachandran plot included at the end of this document. Label them with the PDB ID, SSE, and the number of the amino acid to which they belong.

2. ϕ and φ maps of Ala, Gly and Pro

Build a capped Alanine, a capped Glycine and a capped Proline using the Builder and the Fragments window. Build also a dipeptide Ala-Gly. Make sure the four molecules are imported in the Project Table and have meaningful names so that you can easily find them again (e.g. *capped_ala*, *capped_gly*, *capped_pro*).

(Place the alanine as you did for the single alanine, and tick the 'Grow' box to bind the glycine to it. You only need to click on 'GLY' in the amino acids table to bind the two residues)

We shall calculate torsional maps, but while we did scan one torsion at a time in the previous exercise (cys C-S), we will here scan a couple of dihedrals (phi,psi) for the capped alanine and glycine.

Applications » Macromodel » Coordinate scan
Potential: Amber94, use default values for other options
Mini: set the maximum number of iterations to zero.

Scan: define the phi and psi angles, they should vary from -180° to 180°, using increments of 10° or less.

Once the scan is finished, you will be able to look at the different structures and plot the results using the 2D Plot tool (Tools » Plot coordinate scan). Open the .grd file generated by the scan calculation. You can also export the torsion values and energies to a .csv file to view with Excel or the Open Office suite if you wish.

What are the most energetically favorable values for the (phi, psi) angles in each case? Can you relate these values to what you know about (phi, psi) angles of amino acids in alpha-helices? Are alanines and glycines alpha-helices makers or breakers?

Proline has a constrained backbone and the value of its phi angle is restricted to ca. -60 degrees. Scan the values of psi and plot them, report the most favorable (phi,psi) values on the Ramachandran map.

Can you relate your results to what you know about the consequence of having a proline in an alpha-helix? In a beta-sheet?

3. Plot the (phi,psi) map of a Serine in a capped tripeptide ASA (sequence CH_3CO-Ala-Ser-Ala-NCH_3) and report the most energetically favorable (phi, psi) values on the Ramachandran map.

Ramachandran Plot - values from PDB structures
Report two points per PDB structure, label them with the pdb code, the
residue number and the secondary structure element you find them into.
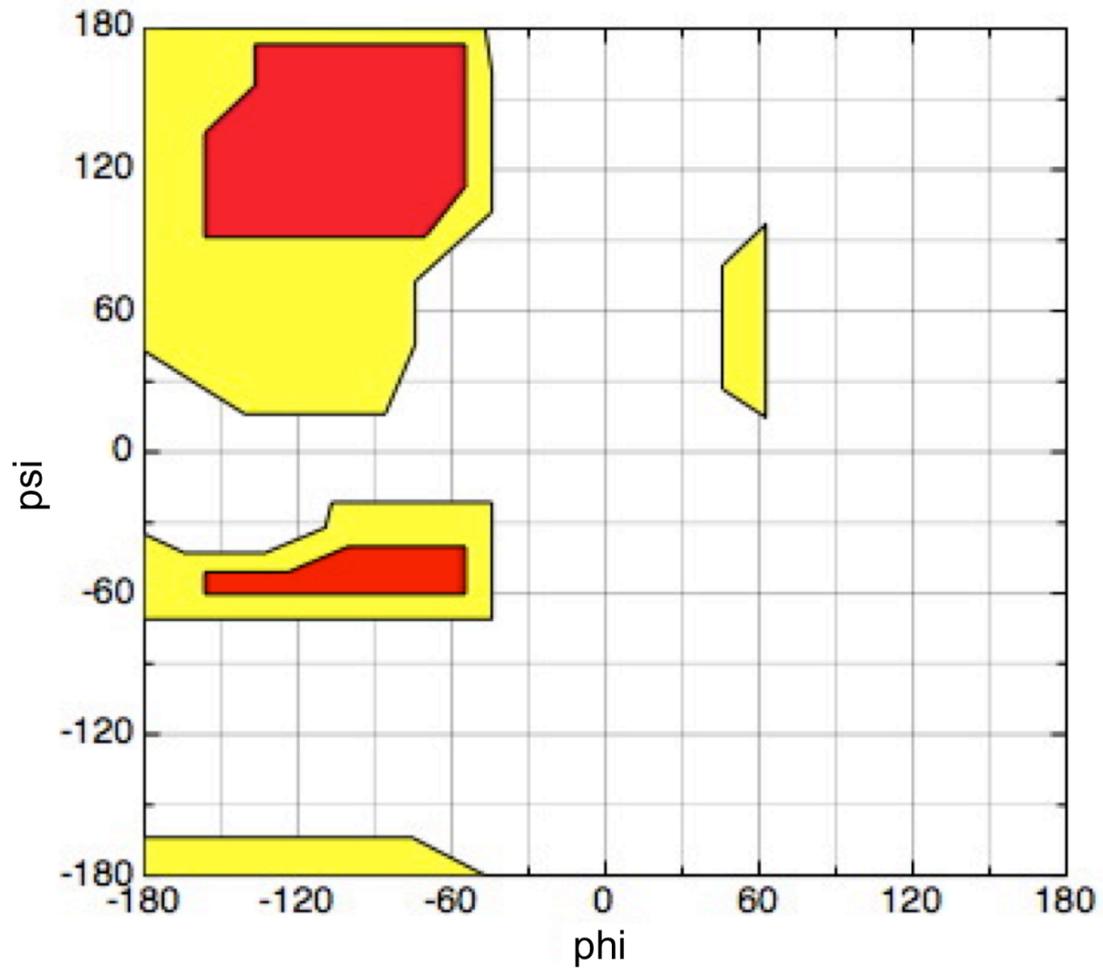
Ramachandran Plot - values dihedral scans

Report optimum (phi,psi) pairs found for the capped alanine, glycine, proline and for the alanine in the ala-gly dipeptide.