

Programming Assignment

For this assignment, submit two programming files, one for each problem. You must also submit two figures, one of the Ramachandran plot of valine and one showing the observed and calculated χ_1 side chain dihedral angle distribution.

Problem 1

Ramachandran plots allow us to investigate the sterically allowed and disallowed backbone dihedral angle combinations ϕ and ψ in proteins. Using the file *Val_residues.txt* provided, produce a Ramachandran plot for valine residues. The file *Val_residues.txt* contains 1000 valine dipeptides taken from a database of high-resolution protein crystal structures. The data for a representative valine dipeptide is shown in Table 1. The C_α , carboxyl carbon, and oxygen atoms on the prior amino acid are labelled pCa, pC, and pO. The N, C_α and H atoms on the subsequent amino acid are labeled: nN, nCa and nH. Using this file, calculate ϕ and ψ for each residue and produce a Ramachandran plot similar to that shown in Figure 1.

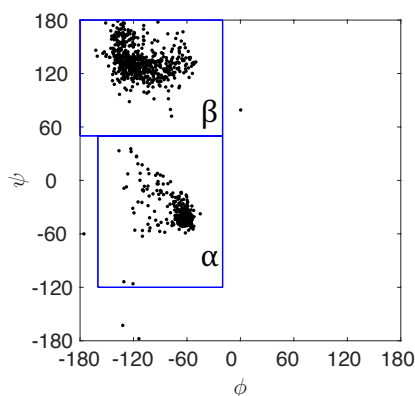


Figure 1: Ramachandran plot for 1000 valine residues from high-resolution protein crystal structures. The Ramachandran limits for α -helices and β -sheets are shown in blue.

Problem 2

The hard sphere model assumes that atoms in proteins interact only via steric repulsion. The file *Val_rotated.txt* contains the coordinates of one Val dipeptide as it is rotated around its side chain dihedral angle, χ_1 . The dihedral angle is specified in column 1. Using this data, calculate the repulsive Lennard-Jones energy (which approximates the hard-sphere potential in the low-temperature limit) for each side chain conformation using Equation 1 below:

$$U_{RLJ}(r_{ij}) = \frac{\epsilon}{72} \left[1 - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right]^2 \Theta(\sigma_{ij} - r_{ij}), \quad (1)$$

where r_{ij} is the center-to-center separation between atoms i and j , $\Theta(\sigma_{ij} - r_{ij})$ is the Heaviside step function, ϵ is the energy scale of the repulsive interactions, $\sigma_{ij} = (\sigma_i + \sigma_j)/2$, and $\sigma_i/2$ is the radius of atom i .

In this equation, assume $\epsilon = 1$. The Heaviside step function sets $U = 0$ when the atoms are not overlapping ($r_{ij} > \sigma_{ij}$), otherwise it is equal to 1. The atomic radii, in Å, are listed in *Val_radii.txt*. The total energy $U_{RLJ}(\chi_1)$ should be calculated between all non-bonded pairs involving side chain atoms. For example, the energy should be calculated between Cg1 and N but not between Cg1 and Ca.

The total energy $U_{RLJ}(\chi_1)$ can be converted into a probability distribution using $P(\chi_1) = A e^{-\frac{U_{RLJ}(\chi_1)}{k_B T}}$, where $k_B T / \epsilon = 0.01$ and A is a normalization constant so that $\int_0^{2\pi} P(\chi_1) d\chi_1 = 1$.

Plot the predicted probability distribution and compare it to the distribution observed in high-resolution protein crystal structures. You should generate the observed distribution from the file discussed in Problem 1. The observed distribution should be similar to that shown in Figure 2.

Table 1: Atom labels and coordinates for the first Val dipeptide in Val_residues.txt

residue	atom	x	y	z
1	pCa	44.099000	24.134000	26.241000
1	pC	45.053000	22.984000	25.974000
1	pO	45.393000	22.682000	24.836000
1	N	45.456000	22.276000	26.994000
1	Ca	46.324000	21.157000	26.691000
1	C	45.841000	19.833000	27.304000
1	O	45.468000	19.773000	28.470000
1	Cb	47.733000	21.483000	27.158000
1	Cg1	48.632000	20.266000	27.059000
1	Cg2	48.276000	22.605000	26.292000
1	H	45.260000	22.406000	27.821000
1	Ha	46.310000	21.025000	25.730000
1	Hb	47.710000	21.757000	28.088000
1	Hg11	49.524000	20.497000	27.362000
1	Hg12	48.277000	19.555000	27.615000
1	Hg13	48.671000	19.966000	26.137000
1	Hg21	49.176000	22.827000	26.576000
1	Hg22	48.291000	22.320000	25.365000
1	Hg23	47.708000	23.386000	26.380000
1	nN	45.873000	18.745000	26.512000
1	nCa	45.441000	17.413000	26.991000
1	nH	46.141000	18.756000	25.695000

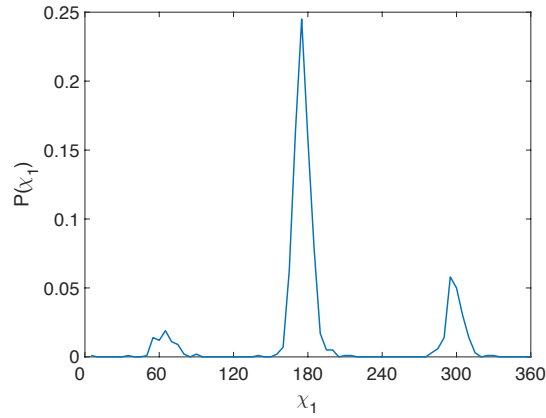


Figure 2: The side chain dihedral angle distribution $P(\chi_1)$ for Val observed in high-resolution protein crystal structures.

Non-Programming Assignment

Problem 1

Derive the expressions for the x-, y-, and z-components of the force \vec{F}_j on atom $j=i+1$ from the previous atom i and successive atom $k=i+2$ using the bond angle potential,

$$V_{ba} = \frac{k_\theta}{2} (\theta_{ijk} - \theta_0)^2, \text{ where } k_\theta \text{ is the constant bond stiffness, } \theta_{ijk} = \cos^{-1} \left(\frac{\vec{r}_{ij} \cdot \vec{r}_{kj}}{r_{ij} r_{kj}} \right) \text{ is the bond}$$

angle between bonded atoms $i, j,$ and $k, \vec{r}_{ij} = \vec{r}_i - \vec{r}_j,$ and θ_0 is the preferred bond angle. Note

$$\text{that } \vec{F}_j = \frac{-dV_{ba}}{dx_j} \hat{x} + \frac{-dV_{ba}}{dy_j} \hat{y} + \frac{-dV_{ba}}{dz_j} \hat{z}.$$