Task 12:
Principal Component Analysis on a Torus
Classical Complex Systems WiSe 2023/24

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(Matriculation Number: 5582876)

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Contents

1 Introduction

Proteins are fundamentally composed of monomeric units called amino acids. Each of these amino acids possesses a standard *backbone* structure that facilitates the linkage of one amino acid to another in the sequence. These linkages are referred to as *peptide bonds*.

Backbone dihedral angles, (ϕ and ψ), play a key role in the structural configuration of proteins (where the word *di-hedral* accounts for the fact that the angles are measured between two faces/planes). ϕ is defined as the angle in the chain C'-N-C$^{\alpha}$-C' (where C' denotes the carbon atom in the carboxyl group, N is Nitrogen and C$^{\alpha}$ denotes the alpha carbon). Similarly, ψ is the angle in the chain C'-N-C$^{\alpha}$-C' [1]. The definitions of ϕ and ψ is depicted in the figure 1 [2].

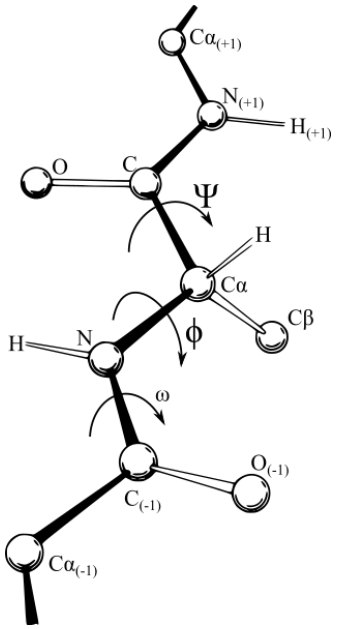


Figure 1: Depiction of dihedral angles [2]

The molecule that is analyzed in this project is

alanine dipeptide (Ac-Ala-NHCH$_3$), a peptide consisting of two alanine molecules linked by a peptide bond (see figure 2).

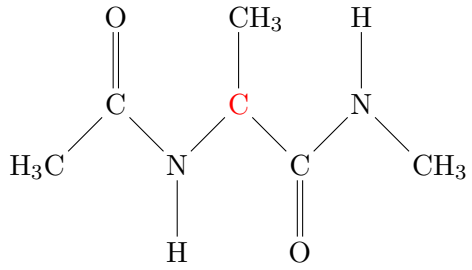


Figure 2: Line diagram of alanine dipeptide. The alpha Carbon (marked in red) is connected to two peptide bonds.

1.1 Principal Component Analysis

Principal Component Analysis (PCA) is a powerful technique for reducing the complexity of a high-dimensional system[3]. It involves expressing the system in a coordinate space defined by *principal components*. The original data projected along these components are linear combinations of the original variables, organized so that the projection along the first principal component (PC1) accounts for the maximum variance within the system. Each subsequent principal component captures progressively less variance than its predecessor. Hence this method is commonly used to reduce the dimensionality of a high-dimensional system like that in macromolecules.

1.2 Dihedral Principal Component Analysis (dPCA)

While PCA works well for linear data, the periodic nature of the dihedral angle data gives rise to artifacts in the calculation of PCA. The method can misinterpret the proximity of angles (for example $-180°$ and $179°$) and give misleading results. In the context of such periodic data, hence the calculation of mean, variance and covariance can also be affected (see equations 8,9), which are central to the PCA method.

A solution to this issue was proposed in the dihedral-PCA (dPCA) method [4]. The angles are transformed using sine and cosine functions, effectively linearizing the circular data.

$$\begin{pmatrix}\phi\\ \psi\end{pmatrix} = \begin{pmatrix}\sin(\phi)\\ \cos(\phi)\\ \sin(\psi)\\ \cos(\psi)\end{pmatrix} \tag{1}$$

The data gets remapped as follows:

$$[-\pi,\pi)\times[-\pi,\pi)\mapsto\mathbb{R}^4 \tag{2}$$

This sort of 'unwrapping' of the circular data circumvents the issues in the PCA mentioned above [5]. The detailed method is outlined in section 2.3.

1.3 Dihedral Principal Component Analysis on a Torus (dPCA+)

While the dPCA method is designed to address the problems arising from periodic data, it gives rise to complexities that make the results difficult to interpret. Since the dihedral angle space form a torus, a method preserving such a topology was introduced in [6](named dPCA+, with the '+' to indicate its superiority over dPCA). The basic idea here is to minimize the projection error caused by the periodicity of the dihedral angles. This is implemented by identifying a maximal gap in the sampling and shifting the data such that the maximal gap lays at the periodic boundary. Hence the data gets remapped as:

$$(\phi,\psi)^T\mapsto(\phi+\phi_{\text{offset}},\psi+\psi_{\text{offset}}) \tag{3}$$

This transformed data can then be analyzed by a standard PCA.

2 Methods

2.1 Task I: Basic Data Consideration

The data given in the ASCII file contains 2.5×10^6 points in the trajectory of alanine dipeptide. The trajectory is given as two columns containing the ϕ and ψ angles respectively:

$$\phi,\psi\in[-180°,180°[\tag{4}$$

In the task instructions, it is given that the points are separated by Δt =200 fs. Since the number of

data points, say N, is 2.5×10^6, the timescale of the entire trajectory can be calculated as

$$\begin{aligned} t_{\text{final}} &= N \times \Delta t \\ &= 2.5 \times 10^6 \times 200\,\text{fs} \\ &= 2.5 \times 10^6 \times 200 \times 10^{-15}\text{s} \\ &= 5 \times 10^{-7}\text{s} \\ &= 500\,\text{ns} \end{aligned} \tag{5}$$

After importing the data using the `read_csv` function in the `pandas` package and setting the above timescale, we can plot the time evolution of the dihedral angles as shown in figure **??**. Here one can see how the angles evolve on several timescales. We observe fast oscillatory motions on the picosecond scale **??**(A,B), as well as shifts between different conformational states at nanosecond scale (C,D,E and F).

The circular (and not linear) nature of the given data (equation 4) gives rise to some problems for analysis. At the stage of basic data visualization, one can already see that a quick viewing of the plot in figure **??** can be misinterpreted. For example, consider the jump from $\phi_1 \approx -100°$ to $\phi_2 \approx +140°$ in the panel E of the figure. For linear data, this jump would mean that the value changes by $\Delta\phi = 140 - (-100) = 240$ units. However, since these are angles, the actual jump[1] is only by 110° (see figure 4).

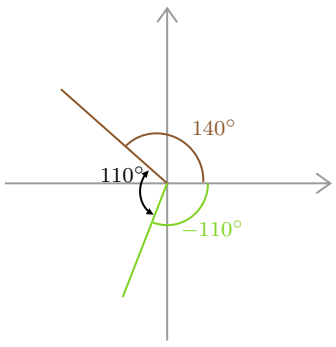


Figure 4: Example to show possible misinterpretation of circular data: If $\phi_1 = 140°$ and $\phi_2 = -110°$, it is easy to see geometrically that $\Delta\phi = 110°$.

A common way of visualizing dihedral angles is to make a Ramachandran plot[7], which is a two-dimensional heatmap of the dihedral angles. After converting the angles to radians, this plot is made here using the built-in `matplotlib` package `hist2d`, with 200 bins. The bins are chosen through trial to avoid noisy spikes arising from a higher bin count. A three-dimensional plot of the same is made in figure 6.

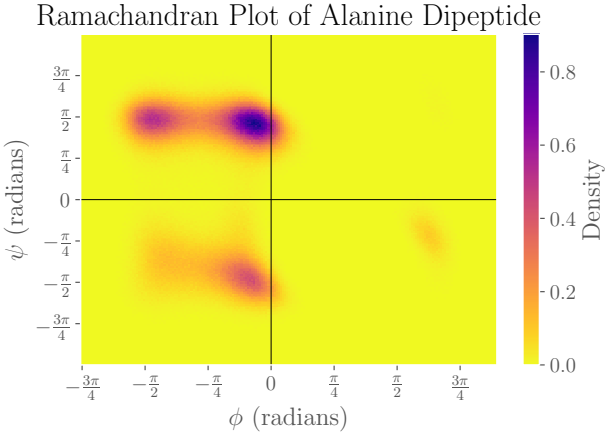


Figure 5: The Ramachandran plot of alanine dipeptide, a two-dimensional probability distribution as a function of ϕ and ψ.

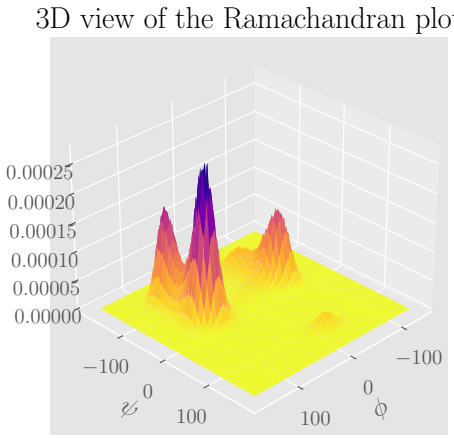


Figure 6: 3D-projection of the Ramachandran plot made in figure 5.

Transforming the distribution to logarithmic scale improves the visibility of the different states observed in the plot (see figure 7). Hence we determine the two-dimensional free energy $\Delta G(\phi, \psi)$ as

[1] A function called `angle_difference` is defined in the Jupyter notebook to calculate the actual difference between two angles.

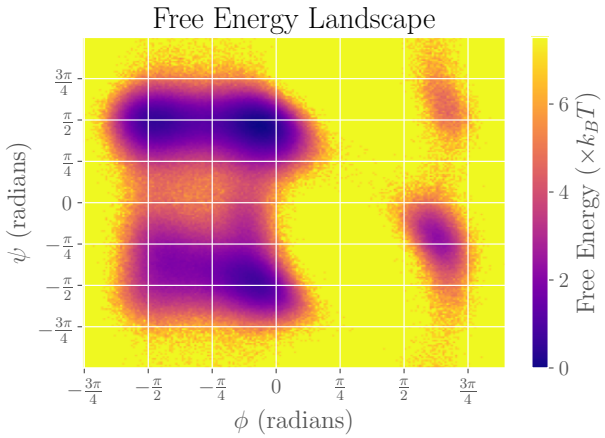


Figure 7: The plot of two-dimensional free energy given by equation 6. Setting the logarithmic scale enhances the visibility of the various regions around the minima, as compared to figure 5

follows:

$$\Delta G(\phi, \psi) = -\ln\left(\frac{P(\phi,\psi) + \rho_{\min}}{\rho_{\max}}\right), \qquad (6)$$

where $\rho_{\min}$ and $\rho_{\max}$ correspond to the minimum and maximum values in the distribution $P(\phi, \psi)$. The free energy is hence obtained in units of k_BT. The function `calculate_free_energy` is defined in the notebook to compute the two-dimensional free energy given the probability distribution as a function of two coordinates. This function is used in all four tasks to make the Ramachandran plot in log scale. A simple histogram of the dihedral angles (figure **??**) indicate multiple minima positions. The `bins='auto'` parameter of `hist2d` can be used to choose the bin count automatically, which gave about 350 bins for ϕ and 150 for ψ. The minima from the 1d distributions are roughly identified on the Ramachandran plot by annotating the plot with vertical and horizontal lines (corresponding to constant ϕ and ψ values respectively). The points of intersection rightly matches with the observed minima in the Ramachandran graph. The plot also shows that the landscape has a nature of continuity at the boundary (for example, look along the constant ϕ line near $\phi = \frac{3\pi}{4}$ in figure 9). This is another reason to consider a periodic treatment of dihedral angles.

The points of minima in the heatmap (figure 9) correspond to different stable conformational states of the dipeptide, since it spends more steps in the trajectory in these states. The distribution of the trajectory indicates that the most stable conformations are the two states in the second quadrant (ψ^+, ϕ^-), which correspond to the β sheet conformation of polypeptides [8]. The sharpest peak appears around the point $\phi = -10°$, $\psi = 85°$.

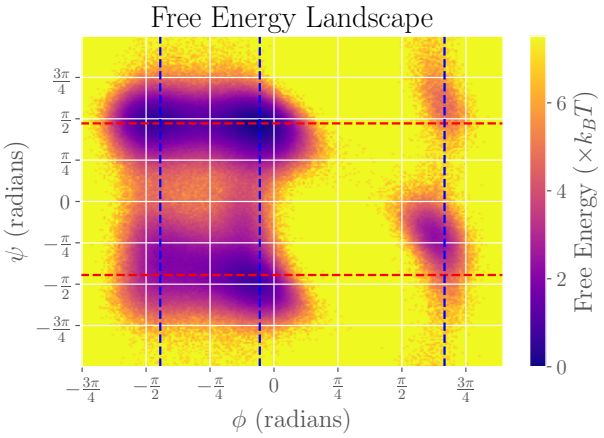


Figure 9: Free energy landscape annotated with rough estimates of minima obtained from figure **??**.

2.2 Task II: Principal Component Analysis (PCA)

The trajectory of the dipeptide molecule were imported as two arrays:

$$\phi = \begin{pmatrix} \phi_1 \\ \phi_2 \\ \vdots \\ \phi_N \end{pmatrix} \qquad \psi = \begin{pmatrix} \psi_1 \\ \psi_2 \\ \vdots \\ \psi_N \end{pmatrix} \qquad (7)$$

The first task in the project was to perform a regular PCA of the variables given. The covariance between the variables is defined as

$$\mathrm{Cov}(\phi, \psi) = \frac{1}{N}\sum_{i=1}^{N} (\phi - \langle\phi\rangle)(\psi - \langle\psi\rangle), \qquad (8)$$

and the variance of each variable

$$\mathrm{Var}(\xi) = \mathrm{Cov}(\xi, \xi) = \frac{1}{N}\sum_{i=1}^{N} (\xi - \langle\xi\rangle)^2 \qquad (9)$$

with $\xi \in \{\phi, \psi\}$. The covariance matrix is defined with these two quantities as elements:

$$C = \begin{pmatrix} \mathrm{Var}(\phi) & \mathrm{Cov}(\phi,\psi) \\ \mathrm{Cov}(\phi,\psi) & \mathrm{Var}(\psi) \end{pmatrix} \tag{10}$$

The covariance matrix was computed using the `numpy` method `cov(arr1,arr2)`, where `arr1` and `arr2` are the arrays whose covariance is studied. Diagonalizing the matrix, the eigenvalues (λ_1, λ_2) and eigenvectors $\vec{e}_1$, $\vec{e}_2$ were computed. The eigenvector corresponding to the higher eigenvalue of the two is the principal component 1 (PC 1), a unit vector. After centering the data by subtracting the mean value, the data points were projected along the principal components, by taking a dot-product.

$$(\vec{e}_0, \vec{e}_1)^T \cdot (\phi(t), \psi(t))^T = (V_1(t), V_2(t))^T \tag{11}$$

Finally, the free energy and the one-dimensional distributions of the data projected (labeled V_1 and V_2) were plotted (figures 15 and 16 respectively).

2.3 Task III: dPCA

To linearize the (periodic) data, the sine and cosine transformations of the dihedral angles were computed, thereby getting four arrays. The PCA (or more precisely, dPCA) was performed on the four new variables $\sin\phi, \cos\phi, \sin\psi$ and $\cos\psi$. The arrays of these four variables were stacked into a single variable `stacked_arr` (of order $4 \times N$) to compute the covariance matrix. The covariance matrix (equation 10) in this case was a 4×4 matrix, compared to the PCA, where we the matrix had order 2×2. The elements of this covariance matrix can be explicitly written down as in equation 12.

The four obtained eigenvectors were arranged in decreasing order, and the principal components were identified. Following the guidelines of the given task, the data was projected only to the first two principal components. A scree plot, the free energy and one-dimensional distributions were plotted for the resulting components.

2.4 Task IV: dPCA+

As given in the task description, the maximal gap in the histogram by minimizing the point density of a corridor. For a bin size of 150, the two-dimensional histogram of the free energy along both dihedral angles is plotted. This plot was chosen over the regular Ramachandran plot because the latter only showed points of high concentration, so the choice of a maximal gap would be too broad to choose from. The maximal gap was identified in three stages:

1. As a starting point, a visual estimate of a potential cut point for ϕ was made. A line at the estimated point was plotted in the 2D free energy plot (vertical line corresponding to constant ϕ value, and horizontal line corresponding to constant ψ).

2. This cut point was fine-tuned by following a kind of bisection method successively. For example, if one low point-density corridor was identified between ϕ-values $\pi/4$ and $\pi/2$, a constant ϕ line was made at their mean position, *i.e.,* at $\phi = 3\pi/8$. The initial guessed line was then shifted to this position to see if it could be further improved. After two iterations, a ϕ value of $11\pi/32$ was finalized to be the first guess (figure 13). The estimated positions were also visualized in the one-dimensional projections (Note that at this point, this value is still a *guess*).

3. To fine-tune the above choice, a function `find_best_maximal_gap` was defined to perform a search for the bins with the least number of counts in the neighbourhood of the guessed value. On inputting the histogram data, this function identifies the best bin to shift the data. The numpy function `searchsorted` is utilized for this purpose[2]. The values returned by this search function is finalized for further analysis.

The initial guess and optimized values (called ϕ_0 and ψ_0 from here onward) are shown in the free energy plot in figure 11. The angles are shifted by defining the function `shift_angles`. Hence the range of the data transforms as equation 13.

[2]The `searchsorted` function here takes a sorted array (`bin_edges` in this case) and a value (`guess_value`) and returns the index at which this value should be inserted to maintain the order of the array.

$$C_{\text{dPCA}} = \begin{pmatrix} \text{Var}(\sin(\phi)) & \text{Cov}(\sin(\phi), \cos(\phi)) & \text{Cov}(\sin(\phi), \sin(\psi)) & \text{Cov}(\sin(\phi), \cos(\psi)) \\ \text{Cov}(\cos(\phi), \sin(\phi)) & \text{Var}(\cos(\phi)) & \text{Cov}(\cos(\phi), \sin(\psi)) & \text{Cov}(\cos(\phi), \cos(\psi)) \\ \text{Cov}(\sin(\psi), \sin(\phi)) & \text{Cov}(\sin(\psi), \cos(\phi)) & \text{Var}(\sin(\psi)) & \text{Cov}(\sin(\psi), \cos(\psi)) \\ \text{Cov}(\cos(\psi), \sin(\phi)) & \text{Cov}(\cos(\psi), \cos(\phi)) & \text{Cov}(\cos(\psi), \sin(\psi)) & \text{Var}(\cos(\psi)) \end{pmatrix} \tag{12}$$

$$[-\pi, \pi) \times [-\pi, \pi) \mapsto [-\pi + \phi_{\text{offset}}, \pi + \phi_{\text{offset}}) \times [-\pi + \psi_{\text{offset}}, \pi + \psi_{\text{offset}}) \tag{13}$$

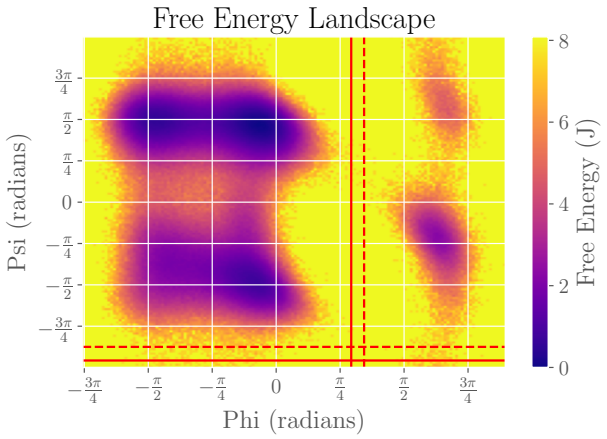


Figure 11: Identifying the maximal gap window. After an initial visual guess (dotted lines), the `find_best_maximal_gap` function optimizes this choice by a search (optimized position in continuous red line). The final cut points are $\phi_0 \approx 52.8°$ and $\psi_0 \approx -172.3°$.

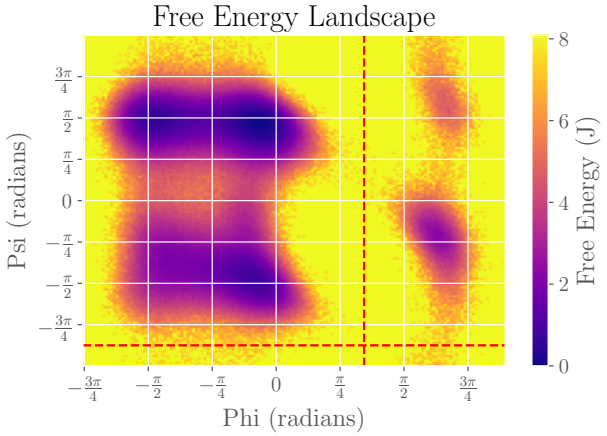


Figure 13: Initial (visual) guess for the maximal gap

Using the new shifted distributions of ϕ and ψ, a PCA is performed with these variables, and associated plots made, just as in the previous tasks.

3 Results

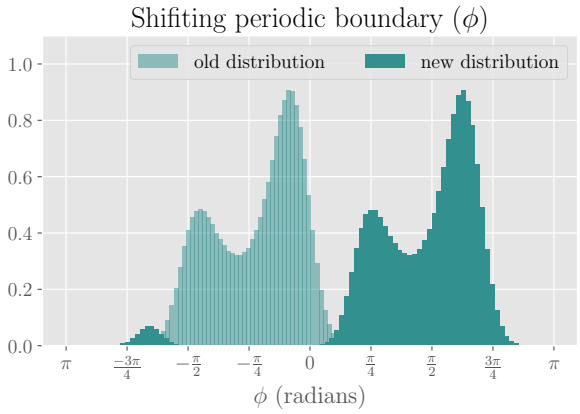
3.1 PCA

A scree-plot of the eigenvalues (figure 14) shows the percentage of total variance explained by each PC in the direct PCA analysis of the dihedral angles. It shows that the first PC explains about 80% of the total variance in the system. The two-dimensional free energy and one-dimensional distributions of V_1 and V_2 are also plotted (figures 15 and 16). The distribution along V_1 shows two peaks, suggesting that projecting onto V_1 captures two major conformations or states of the dipeptide. However, the broader and multi-peaked distribution along V_2 indicates additional dynamics that V_1 alone does not capture.

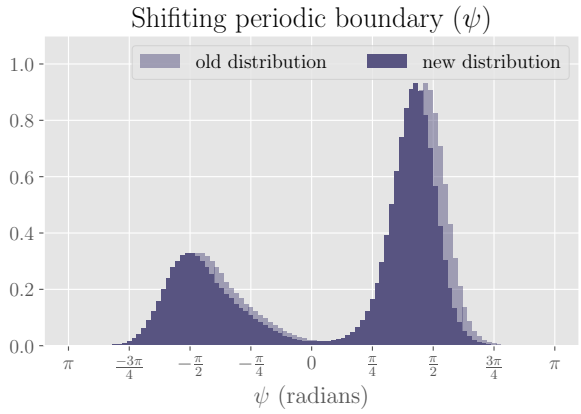
By projecting only onto the first principal component (V_1), we neglect possibly transitional states between the major conformations that are captured by V_2. These could represent less stable, but biologically significant, intermediate states of the dipeptide's motion or conformational changes that contribute to the overall flexibility and function of the molecule.

3.2 dPCA

The scree plot of the dPCA looks more distributed (figure 17). V_1 explains a lesser percentage of variance compared to that in PCA. From the plots of the free energy (18) and the one-dimensional projections of the data (figure 19), we can infer that the dPCA method seeks to maintain the periodicity inherent in the data. However, this comes at a cost of a lack of interpretability of the results.



(a) Original and shifted distributions for ϕ



(b) Original and shifted distributions for ψ

Figure 12: Shifted angles for ϕ and ψ

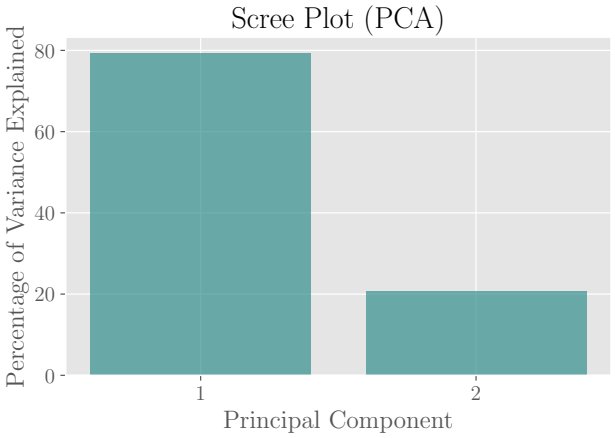


Figure 14: A scree plot of the two principal components obtained from the PCA of ϕ and ψ. PC 1 explains 79.29% of the total variance, while PC 2 explains 20.71% of the total variance.

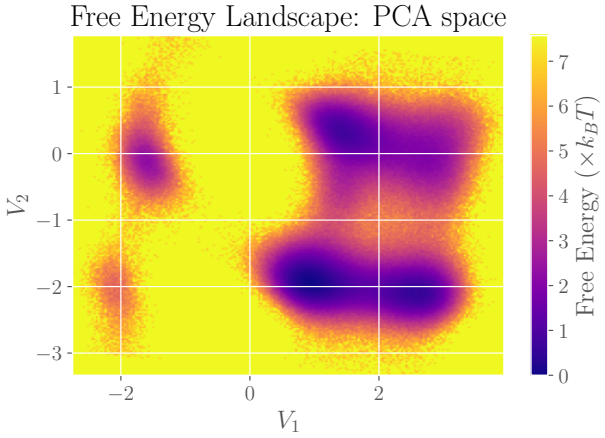


Figure 15

The plot shows a certain level of sharpness in the minima. The dPCA is better suited for capturing the periodic nature of the data, which is inherent in dihedral angles, while PCA might introduce miscalculations since it assumes linearity in the data. Although dPCA attempts to capture the cyclic nature of the dihedral angle data, it introduces new complexity in interpreting the landscape [4].

3.3 dPCA+

Figure 20 shows the variation of the two-dimensional free energy resulting from the dPCA+ analysis. In the original data plot 7, we see that the heatmap gets cut off abruptly at the periodic boundary, for example in the first quadrant. These kinds of abrupt cuts are improved after shifting the data along the maximal gap.

4 Summary and Discussion

This project focused on the analysis of an alanine dipeptide simulation data using the methods of PCA, dPCA, and dPCA+. The data considerations involving trajectory points of dihedral angles (ϕ and ψ). After an overview on the nature of the data points, its periodicity and time evolution, three

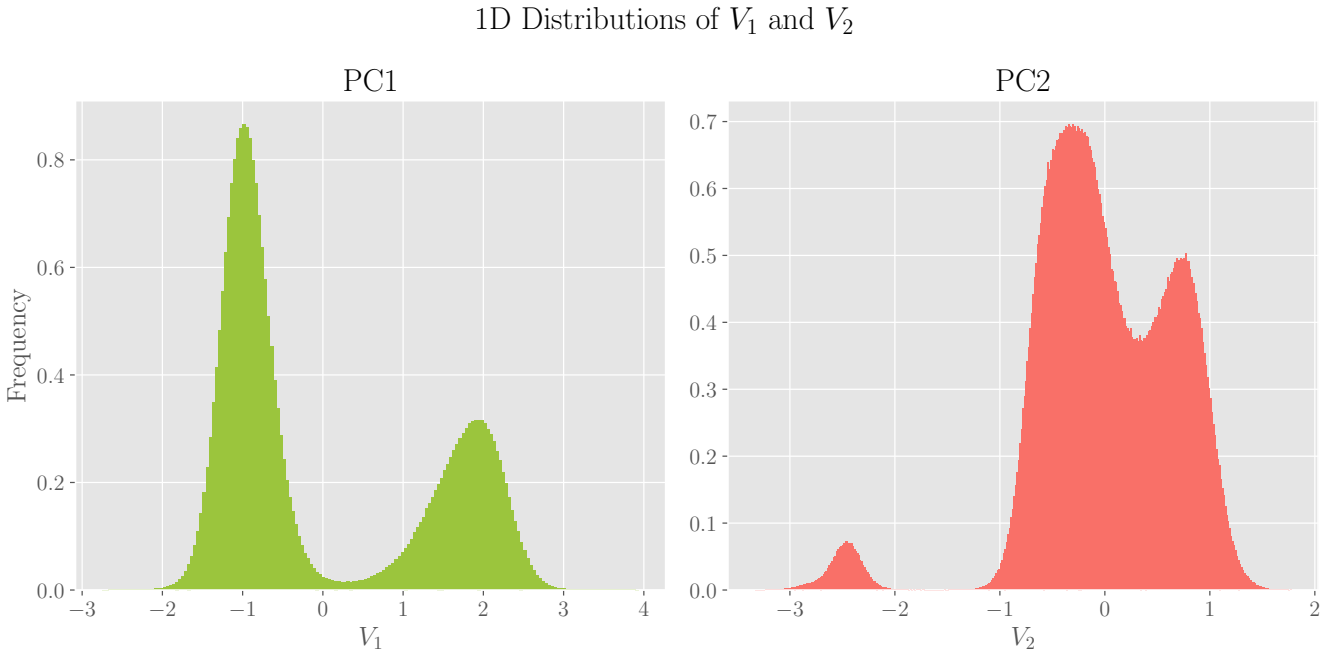


Figure 16

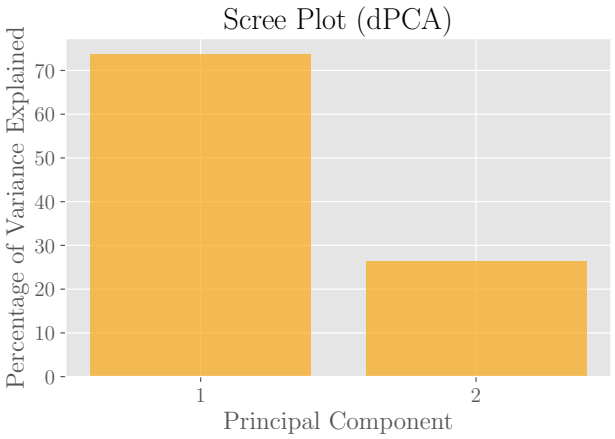


Figure 17: Scree plot from the dPCA: From the code, it was found that the four PCs explain 62.82%, 20.38%, 9.94% and 6.86% of the total variance respectively. Here we projected only to the first two PCs, according to the task guidelines.

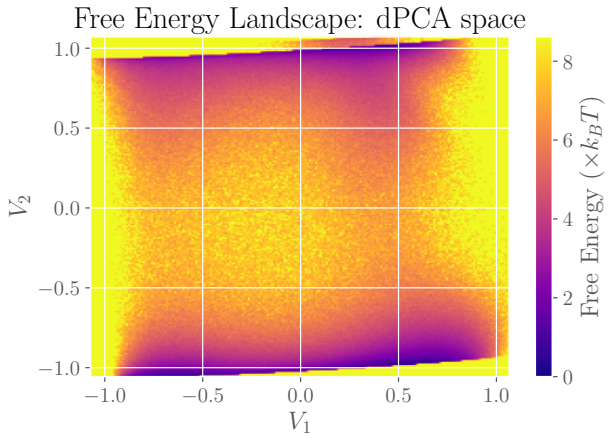


Figure 18: The free energy plot resulting from the dPCA.

analysis techniques were employed to analyze the dihedral angle data.

The PCA technique highlights the overall conformations present in the molecule. Although it is straightforward to implement, in the context of analysis of backbone dihedral angles, traditional PCA struggles with periodic metrics, as it's primarily designed for linear data. Both covariance and variance calculations, which are central to PCA, become flawed.

In contrast, dPCA, transforms these angles using sine and cosine functions, effectively linearizing this circular data, preserving the true relationships and providing a more accurate analysis. This transformation addresses the core issue of the undefined

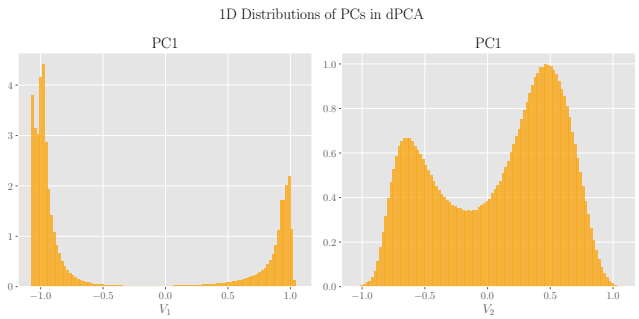


Figure 19: One-dimensional distributions of the PCs from dPCA.

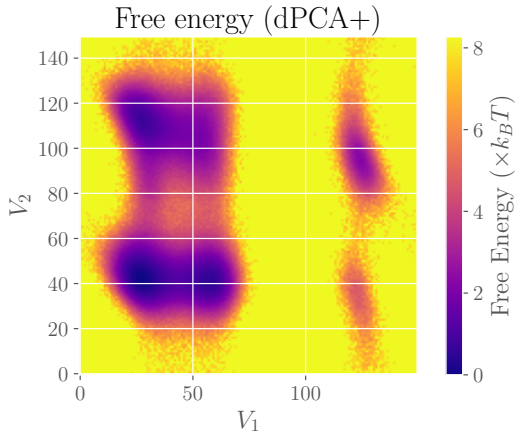


Figure 20

mean in a circular context, ensuring that the resulting analysis represents the actual dynamics of the molecule in study. Although the minima of the free energy landscape look more sharper to distinguish, they may give rise to complicated pattern, which are not so easy to interpret into the actual conformational states of the molecule.

Finally, the dPCA+ technique is designed to preserve the torus topology, and uses a linear transformation that minimizes periodicity-induced errors in covariance estimation and avoids artificial extra dimensions or distortions in probability distribution [6]. This is a comparatively simple algorithm to implement, with the only restriction that the data under consideration should have regions of maximal gap present in them.

A Structure of document and notebook

The former part of this document document is structured in the conventional format of a research article. All code was performed in a Jupyter notebook, which is exported as a PDF and appended after this report. Some of the functions which are not directly significant to the main tasks are saved as a separate Python file `ccs_project_helpers.py`. The styling of the plots were done using the `ggplot` template with additional customizations made in a separate style file `ccs_project.mplstyle`.

B Use of LLMs

The use of Large Language Models (LLMs in short) has become indispensable in assisting various sectors including research, education, and technology, due to their ability to understand and generate human-like text. In this project, ChatGPT was used occasionally, mainly to find word synonyms, clarify specific command syntax and to ease repetitive tasks (like creating labels for subplots), which helped in making the process more efficient. All code developed in the solution was authored independently, and ChatGPT was used responsibly and fairly as a support tool.

Some specific uses:

- Generated a blank LaTeXtemplate for the report with placeholders to add different sections and bibliography entries.
- Generated a function to label ticks in multiples of $\pi/4$ for the plots.
- It was also used in the learning stage to clarify meanings of definitions (like peptides and residues), although it did not prove to be much effective.

References

[1] *Dihedral angle - Wikipedia*. URL: https://en.wikipedia.org/wiki/Dihedral_angle?oldformat=true#Proteins.

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0_Final_Notebook

February 22, 2024

1 Jupter notebook to supplement the report of Task 12

Submitted by: Karthik Jayadevan (Matriculation number: 5582876)

[ ]:
```
import matplotlib.pyplot as plt
import numpy as np
import scipy.constants as sc

from ccs_project_helpers import *

plt.style.use('ggplot')
plt.style.use('./ccs_project.mplstyle')
```

2 Task I

2.1 Importing the data

After importing the data as `numpy` arrays using the `loadtxt` function, the length of the arrays are verified. Then the dihedral angles (which are given in degrees) are converted to radians for later analyses.

[ ]:
```
# Load the data
filename = '../Additional_Files/ala2_3_300dihdt200fs.sec'

# Load the data
data = np.loadtxt(filename)

# Split the data into two arrays
phi, psi = data[:, 0], data[:, 1]


# Check the length of arrays
print(f'Length of arrays: {len(phi):.1e},{len(psi):.2e}')
# checking if any values were lost as 'NaN':
print('Are the array lengths equal?',len(phi)==len(psi))

# Convert degrees to radians
phi_rad = np.radians(phi)
```

```
psi_rad = np.radians(psi)
```

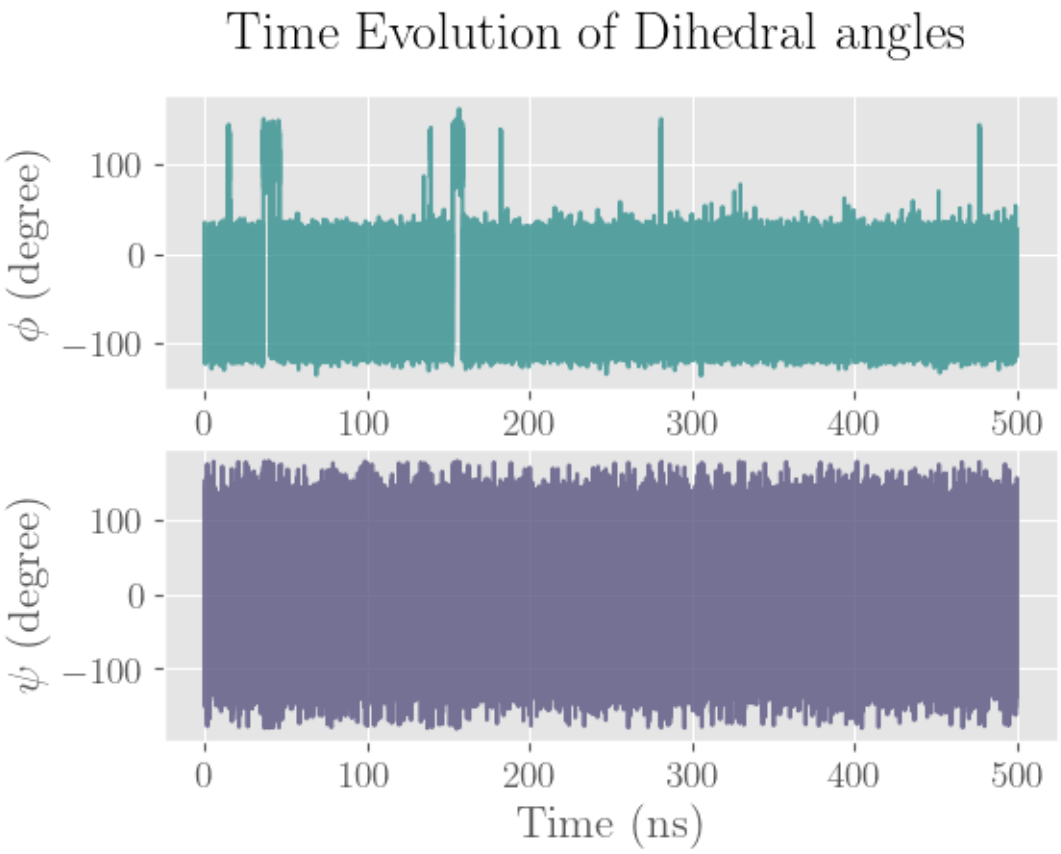
```
Length of arrays: 2.5e+06,2.50e+06
Are the array lengths equal? True
```

[ ]:
```
def timepoints(data):
    """
    To calculate the scale of the time

    Input: the phi or psi array
    Output: time array in nanoseconds
    """
    N = len(data) # number of points
    unit_time = 200e-15 # in seconds

    # array of timepoints in seconds:
    t = np.arange(0,N*unit_time,unit_time)

    # Converting to nanoseconds:
    t /= 1e-9 # in nanoseconds
    return t
```

2.2 Time evolution of dihedral angles

Now, let us visualize the data:

[ ]:
```
fig, (ax1,ax2) = plt.subplots(2,1)
fig.suptitle('Time Evolution of Dihedral angles')

t = timepoints(phi)

ax1.plot(t,phi,alpha=0.8)
ax1.set_ylabel(r'$\phi$ (degree)');

ax2.plot(t,psi,color='C1',alpha=0.8)
ax2.set_xlabel('Time (ns)')
ax2.set_ylabel(r'$\psi$ (degree)');
```



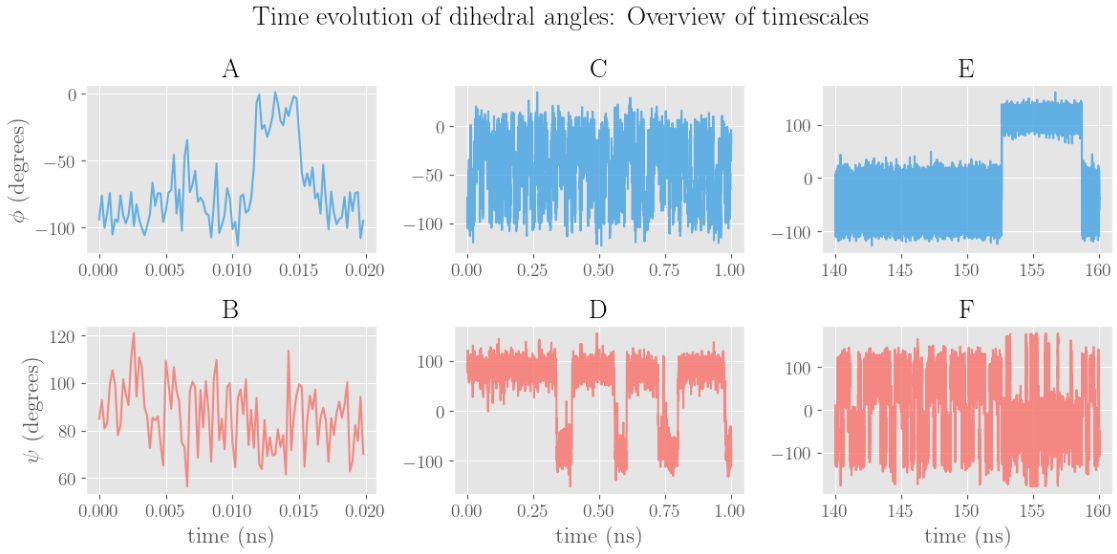
To visualize the evolution of the dihedral angles, we can 'zoom in' to various sections of these plots, as illustrated in the following graphs:

[ ]:
```
# to get the indices where the conformation 'jumps' happen,
# from a visual estimate of the time in nanoseconds:
np.where(((t>=140) & (t<=160)))[0]
```

[ ]:
```
array([700000, 700001, 700002, …, 799998, 799999, 800000])
```

[ ]:
```
fig, axs = plt.subplots(2, 3,figsize=(11.998293,5.999146))

axs[0,0].plot(t[:100],phi[:100],alpha=0.8,color='C5')
axs[1,0].plot(t[:100],psi[:100],alpha=0.8,color='C3')
axs[1,0].set_xlabel('time (ns)')

axs[0,1].plot(t[:5_000],phi[:5_000],alpha=0.8,color='C5')
axs[1,1].plot(t[:5_000],psi[:5_000],alpha=0.8,color='C3')
axs[1,1].set_xlabel('time (ns)')

axs[0,2].plot(t[700_000:800_000],phi[700_000:800_000],alpha=0.8,color='C5')
```

```
axs[1,2].plot(t[700_000:800_000],psi[700_000:800_000],alpha=0.8,color='C3')
axs[1,2].set_xlabel('time (ns)')

axs[0,0].set_ylabel(r'$\phi$ (degrees)')
axs[1,0].set_ylabel(r'$\psi$ (degrees)')

axs[0,0].set_title("A")
axs[1,0].set_title("B")

axs[0,1].set_title("C")
axs[1,1].set_title("D")

axs[0,2].set_title("E")
axs[1,2].set_title("F")

fig.suptitle('Time evolution of dihedral angles: Overview of timescales')
plt.tight_layout()
plt.savefig('./final_plots/dihedral_evolution.pdf')
```

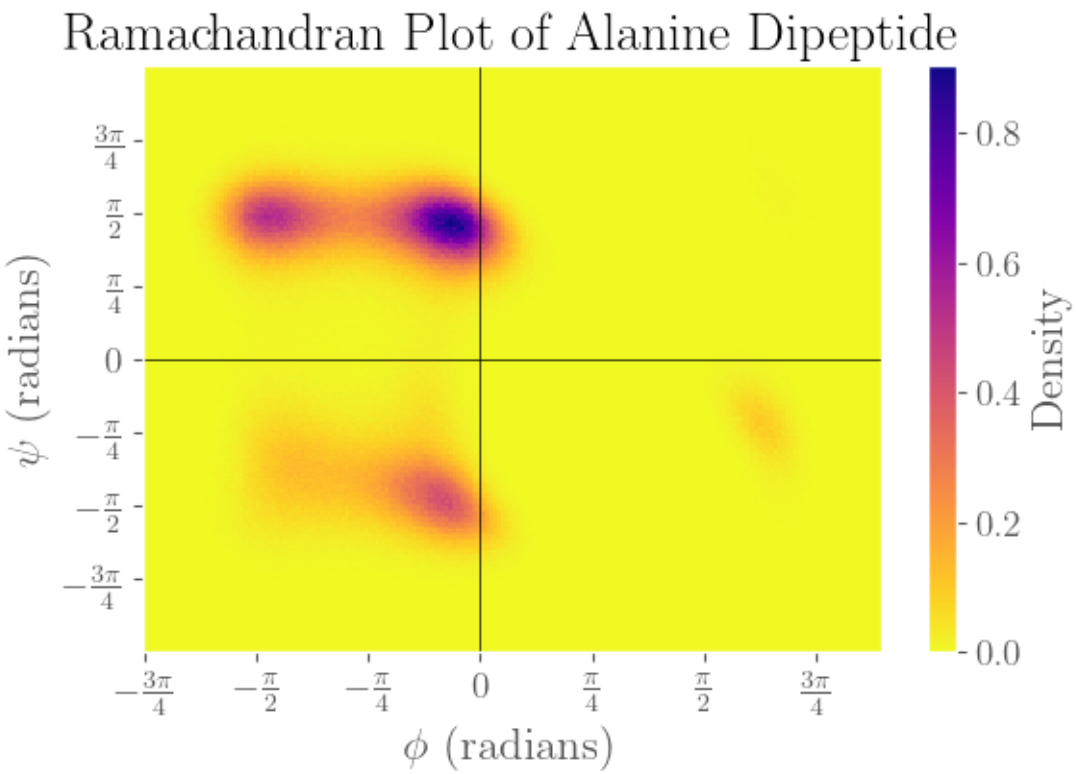


2.3 Ramachandran plot and free energy

Now, we can visualize the 2D-distribution of these angles in a histogram, called the **Ramachandran Plot**:

[ ]:
```
# Setting the bin size for the histogram
bin_size = 200

# Creating the 2D histogram
```

```
histogram, xedges, yedges, image = plt.hist2d(phi_rad, psi_rad, bins=bin_size,␣
 ↪density=True,cmap='plasma_r') # alternate ocean

# Plot settings
plt.colorbar(label='Density')
plt.xlabel(r'$\phi$ (radians)')
plt.ylabel(r'$\psi$ (radians)')
plt.title('Ramachandran Plot of Alanine Dipeptide')
ax = set_ticks()

ax.axhline(0, color='black', lw=0.5)
ax.axvline(0, color='black', lw=0.5)


plt.tight_layout()
plt.savefig('./final_plots/Rama_plot_initial.pdf')

# The density in the plot represents the
# frequency of each angle pair in the trajectory.
# This will help us observe the number of states
# (point accumulations) and compare the barriers between states.
```



We can also create the 2d histogram for the free energy, which due to the logarithmic scale, offers better visibility of the different states.

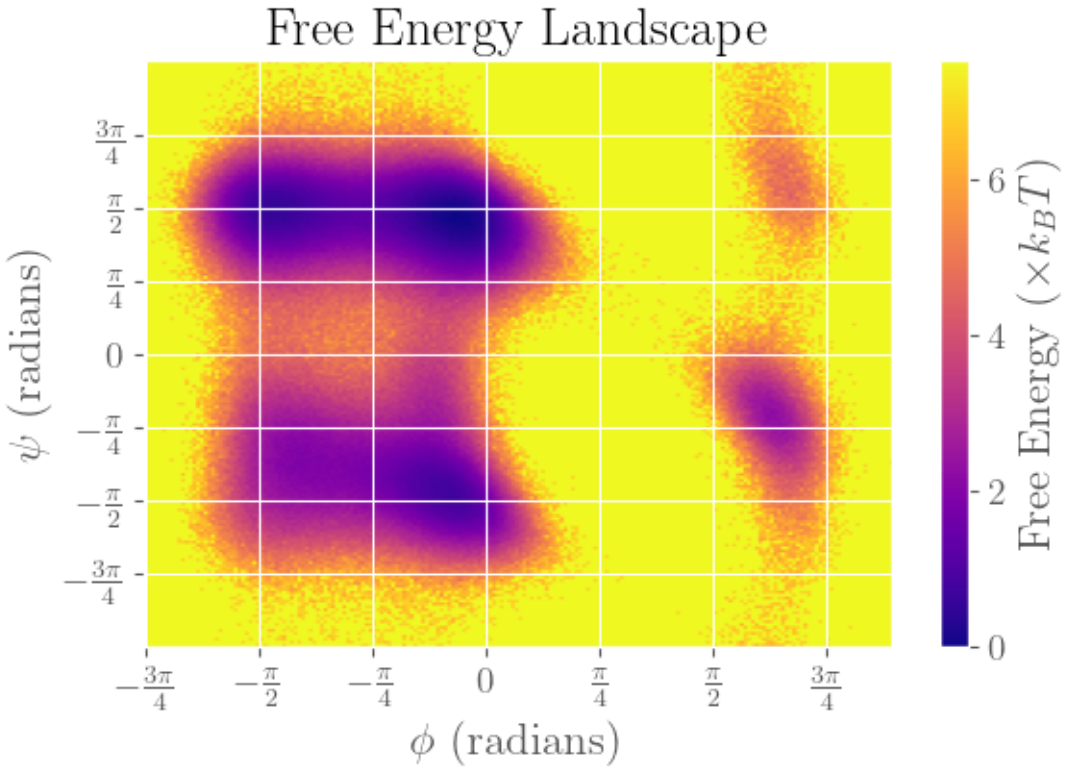
The `calculate_free_energy` computes the free energy of the distribution using the relation:

$$\Delta G(\phi, \psi) = -\ln\left(\frac{P(\phi, \psi) + \rho_{\min}}{\rho_{\max}}\right)$$

The $\rho_{\min}$ is included so as to avoid taking $\ln(0)$, and $\rho_{\max}$ normalizes the distribution.

[ ]:
```
def calculate_free_energy(phi, psi, bin_size):
    """
    Calculate the free energy from phi and psi angles.

    Input: dihedral angles in radians, temperature and bin-size
    Returns: histogram and corresponding x- and y-edges of free energy
    """

    # Compute the 2D distribution (histogram)
    hist, xedges, yedges = np.histogram2d(phi, psi, bins=bin_size, density=True)

    # Compute the free energy ΔG(V1, V2)
    # To avoid taking log of 0, we add a small number inside the log
    rho_min = np.min(hist[hist > 0])  # Minimum non-zero value of the histogram
    rho = hist + rho_min
    rho_max = hist.max()

    delta_G = - np.log(rho / rho_max)

    return hist, delta_G, xedges, yedges

bin_size = 200  # bins defined after trial and error

# Calculate histogram and free energy
hist, delta_G, xedges, yedges = calculate_free_energy(phi_rad, psi_rad,␣
 ↪bin_size)

# Plot the free energy landscape
plt.figure()
# Define the extent of the histogram for plotting
extent = [xedges[0], xedges[-1], yedges[0], yedges[-1]]
plt.imshow(delta_G.T, extent=extent, origin='lower', aspect='auto',␣
 ↪cmap='plasma')
plt.colorbar(label=r'Free Energy ($\times k_B T$)')
plt.xlabel(r'$\phi$ (radians)')
plt.ylabel(r'$\psi$ (radians)')
plt.title('Free Energy Landscape')
```

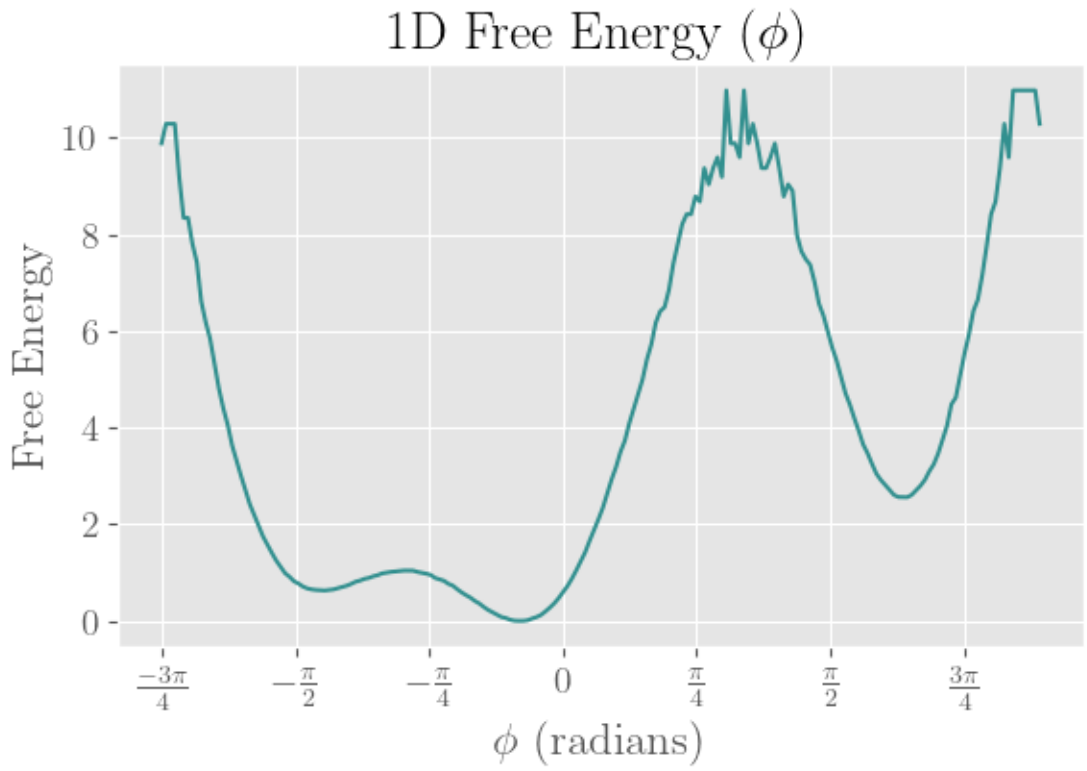
```
ax = set_ticks()

plt.tight_layout()
plt.savefig('./final_plots/free_energy_initial.pdf')
```



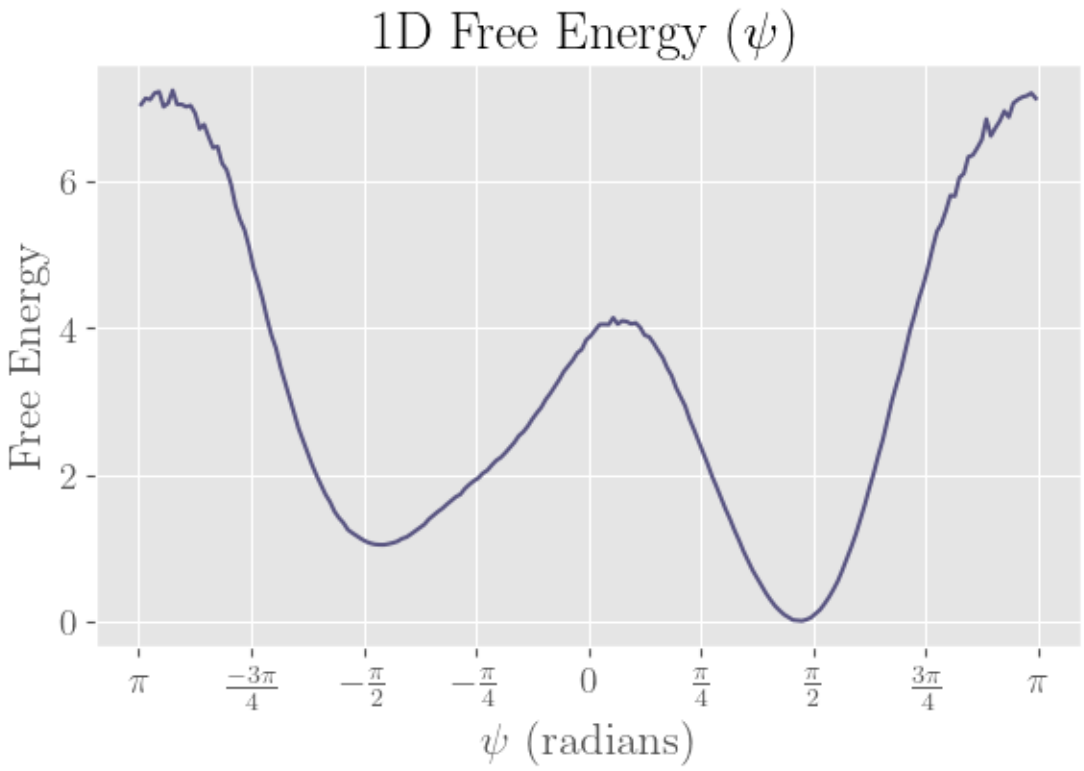
[ ]:
```
def calculate_1d_free_energy(dihedral_angles, bin_size):
    """
    Calculate the 1D free energy from a given array of phi or psi.

    Returns:
    - free_energy: 1D array of free energy values.
    - bin_edges: Edges of the histogram bins.
    """
    # Compute the 1D histogram (distribution)
    hist, bin_edges = np.histogram(dihedral_angles, bins=bin_size, density=True)

    # Compute the free energy F = -kT * ln(hist)
    # To avoid taking log of 0, we add a small number inside the log
    hist_min = np.min(hist[hist > 0])  # Minimum non-zero value of the histogram
    rho = hist + hist_min
    free_energy = -np.log(rho)
```

```
    free_energy -= np.min(free_energy)  # Normalize to set the minimum free energy to zero

    return free_energy, bin_edges
```

[ ]:
```
# Calculate the 1D free energy
phi_free_energy, bin_edges = calculate_1d_free_energy(phi_rad, bin_size=200)

# Get the middle points of the bins for plotting
bin_centers = (bin_edges[:-1] + bin_edges[1:]) / 2

# Plot the 1D free energy distribution
plt.plot(bin_centers, phi_free_energy)
plt.xlabel(r'$\phi$ (radians)')
plt.ylabel('Free Energy')
plt.title(r'1D Free Energy ($\phi$)')

ax=set_ticks_1d()
plt.tight_layout()
plt.savefig('final_plots/1d_phi_initial.pdf')
```



[ ]:
```
# Calculate the 1D free energy
psi_free_energy, bin_edges = calculate_1d_free_energy(psi_rad, bin_size=200)

# Get the middle points of the bins for plotting
bin_centers = (bin_edges[:-1] + bin_edges[1:]) / 2

# Plot the 1D free energy distribution
plt.plot(bin_centers, psi_free_energy,color='C1')
plt.xlabel(r'$\psi$ (radians)')
plt.ylabel('Free Energy')
plt.title(r'1D Free Energy ($\psi$)')

ax=set_ticks_1d()
plt.tight_layout()
plt.savefig('final_plots/1d_psi_initial.pdf')
```

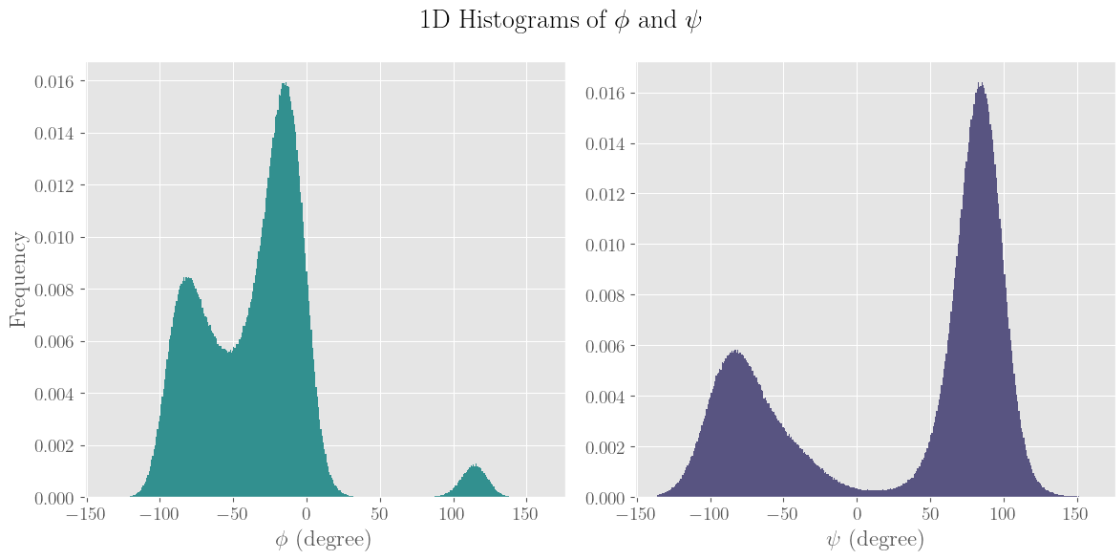


The coordinates of interest can also be seen from a simple 1D distribution of the given dihedral angle data:

[ ]:
```
bins_phi = np.histogram_bin_edges(phi, bins='auto')
bins_psi = np.histogram_bin_edges(psi, bins='auto')
```

```
fig,axs = plt.subplots(1,2,figsize=(11.998293,5.999146))

fig.suptitle('1D Histograms of $\phi$ and $\psi$')

axs[0].hist(phi,bins=bins_phi,color='C0',density=True);
axs[0].set_xlabel(r'$\phi$ (degree)')
axs[0].set_ylabel('Frequency')

axs[1].hist(psi,bins=bins_phi,color='C1',density=True);
axs[1].set_xlabel(r'$\psi$ (degree)')

print(len(bins_phi),len(bins_psi))

plt.tight_layout()
plt.savefig('./final_plots/1d_phi_psi.pdf')
```

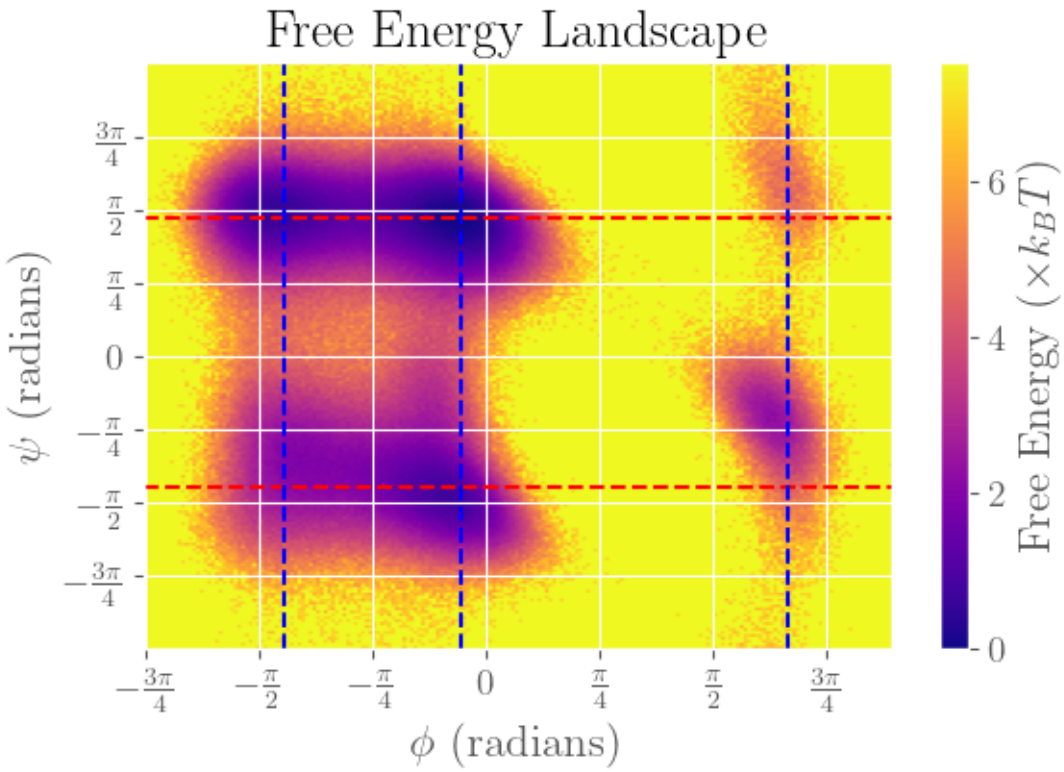
```
367 167
```



[ ]:

[ ]:
```
phi1 = -10
phi2 = -80
phi3 = 120

psi1 = -80
psi2 = 85

phi_minima = np.radians(np.array([phi1,phi2,phi3]))
psi_minima = np.radians(np.array([psi1,psi2]))
```

```
# Calculate histogram and free energy
hist, delta_G, xedges, yedges = calculate_free_energy(phi_rad, psi_rad,␣
 ↪bin_size)

# Plot the free energy landscape
plt.figure()
# Define the extent of the histogram for plotting
extent = [xedges[0], xedges[-1], yedges[0], yedges[-1]]
plt.imshow(delta_G.T, extent=extent, origin='lower', aspect='auto',␣
 ↪cmap='plasma')
plt.colorbar(label=r'Free Energy ($\times k_B T$)')
plt.xlabel(r'$\phi$ (radians)')
plt.ylabel(r'$\psi$ (radians)')
plt.title('Free Energy Landscape')

ax = set_ticks()

plt.tight_layout()

plt.axhline(psi_minima[0],linestyle='--',color='red')
plt.axhline(psi_minima[1],linestyle='--',color='red')
plt.axvline(phi_minima[0],linestyle='--',color='blue')
plt.axvline(phi_minima[1],linestyle='--',color='blue')
plt.axvline(phi_minima[2],linestyle='--',color='blue')

# plt.
 ↪hlines(y=[psi1,psi2],xmin=-100,xmax=150,linestyles='--',colors='red',label=r'minima␣
 ↪of $\psi$')
# plt.
 ↪vlines(x=[phi1,phi2,phi3],ymin=-100,ymax=150,linestyles='--',colors='blue',label=r'minima␣
 ↪of $\phi$')

plt.savefig('./final_plots/free_energy_initial_annotated.pdf')
```



So the energy minima seen from the 1d projections correspond to the states observed in the Ramachandran plot.

3 Task II

This task involves doing a Principal Component Analysis as performed in the Exercise IX of the course. Following similar steps as outlined in the task guidelines, we perform a PCA to the dihedral angle coordinates:

[ ]:
```
# Means
phi_mean = phi_rad.mean()
psi_mean = psi_rad.mean()

# Covariance and variance
phi_variance = phi_rad.var()
psi_variance = psi_rad.var()

# Covariance matrix
covariance_matrix = np.cov(phi_rad,psi_rad)
print(f'Covariance matrix:\n {np.around(covariance_matrix,2)}')

eigenvalues, eigenvectors = np.linalg.eig(covariance_matrix)
```

```
# Reordering eigenvalues and eigenvectors
idx = eigenvalues.argsort()[::-1]
eigenvalues = eigenvalues[idx]
print(f'\nEigen values: {[round(i,2) for i in eigenvalues]}')
eigenvectors = eigenvectors[:, idx]
print(f'Sorted eigen vectors: \n{eigenvectors}\n')

# Principal components:
pc1 = eigenvectors[:, 0]  # First principal component
pc2 = eigenvectors[:, 1]  # Second principal component

print(f'Principal components:\n{pc1,pc2}')
```

```
Covariance matrix:
 [[ 0.49 -0.15]
 [-0.15  1.8 ]]

Eigen values: [1.81, 0.47]
Sorted eigen vectors:
[[ 0.11003329 -0.9939279 ]
 [-0.9939279  -0.11003329]]

Principal components:
(array([ 0.11003329, -0.9939279 ]), array([-0.9939279 , -0.11003329]))
```

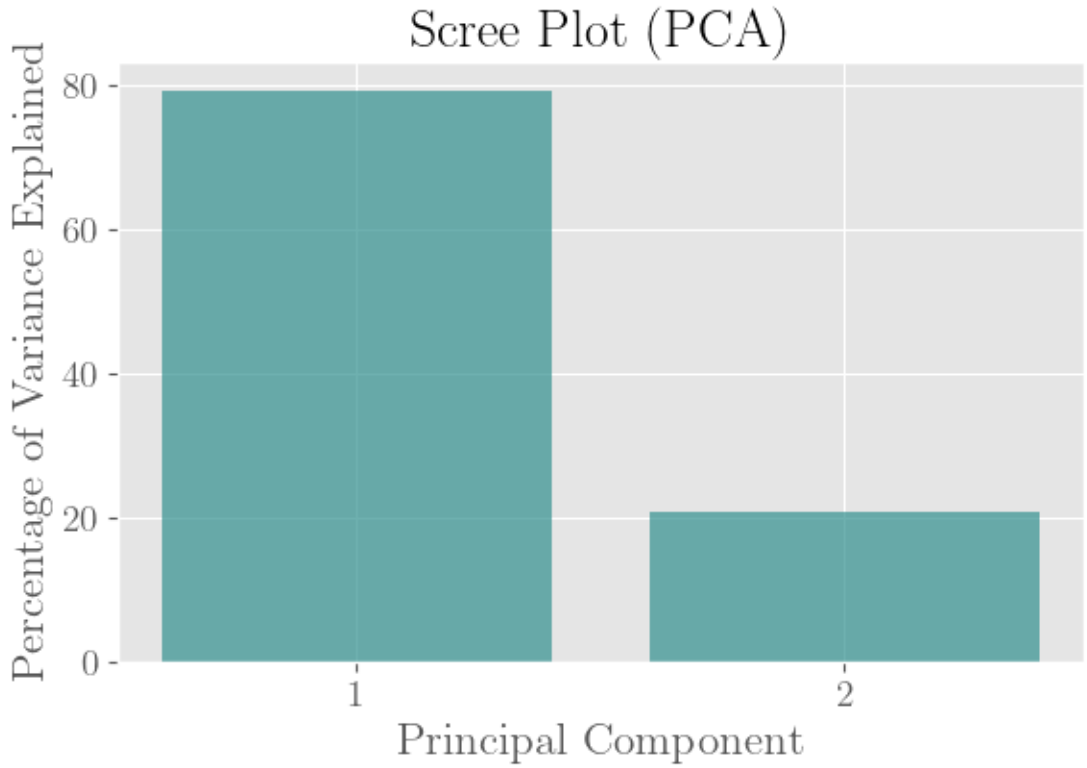
[ ]:
```
# Subtracting the mean from the data
phi_centered = phi_rad - phi_mean
psi_centered = psi_rad - psi_mean

# Stacking the centered data for matrix multiplication
centered_data = np.stack((phi_centered, psi_centered), axis=1)

# Projecting the data onto the principal components
projected_data = np.dot(centered_data, eigenvectors)

V1,V2 = projected_data[:, 0], projected_data[:, 1]
```

[ ]:
```
def scree_data(eigenvalues):
    percent_variance_explained = 100 * eigenvalues / eigenvalues.sum()

    return percent_variance_explained
```

[ ]:
```
# Calculate the percentage of variance explained by each principal component
percent_variance_explained = scree_data(eigenvalues)

# Visualize the PCA results using a scree plot with percentages
plt.bar(range(1, len(eigenvalues) + 1), percent_variance_explained, alpha=0.7)
```

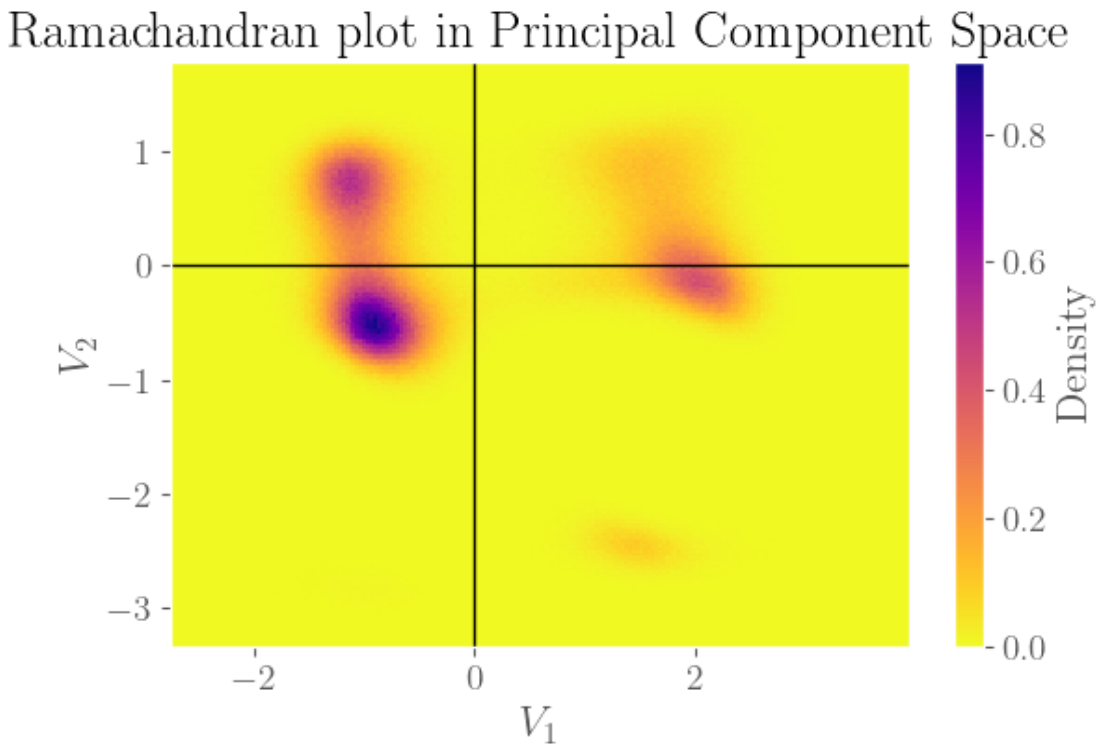
```
plt.ylabel('Percentage of Variance Explained')
plt.xlabel('Principal Component')
plt.title('Scree Plot (PCA)')
plt.xticks(range(1, len(eigenvalues) + 1))

# Print the percentage of the total variance that each principal component␣
 ↪accounts for
for i, variance in enumerate(percent_variance_explained):
    print(f'Principal Component {i+1}: {variance:.2f}% of the total variance')

plt.tight_layout()
plt.savefig('./final_plots/scree_PCA.pdf')
```

```
Principal Component 1: 79.29% of the total variance
Principal Component 2: 20.71% of the total variance
```



[ ]:
```
plt.figure()
plt.hist2d(V1,V2, bins=200, density=True,cmap='plasma_r')
plt.colorbar(label='Density')
plt.xlabel(r'$V_1$')
plt.ylabel(r'$V_2$')
plt.title('Ramachandran plot in Principal Component Space')
```

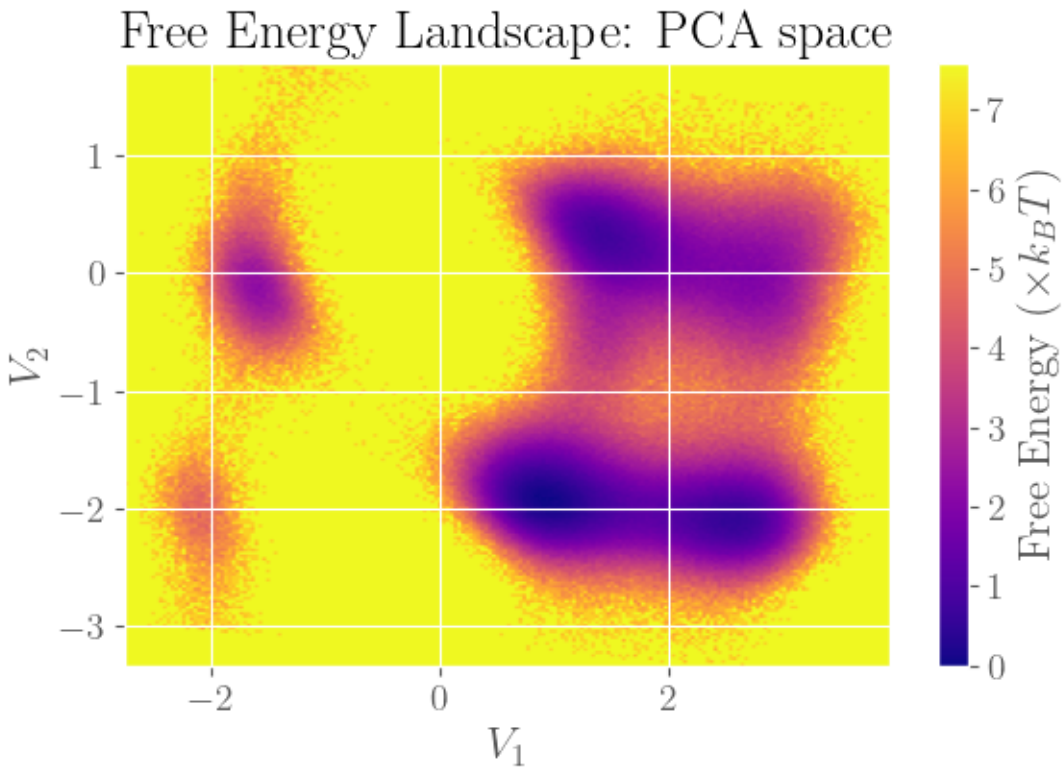
```
plt.grid(True)
plt.tight_layout()

ax = plt.gca()
ax.axvline(0,color='black',lw=1)
ax.axhline(0,color='black',lw=1)

plt.tight_layout()
plt.savefig('./final_plots/Rama_PCA.pdf')

plt.show()
```



Again, we can take a look at the free energy for better visibility:

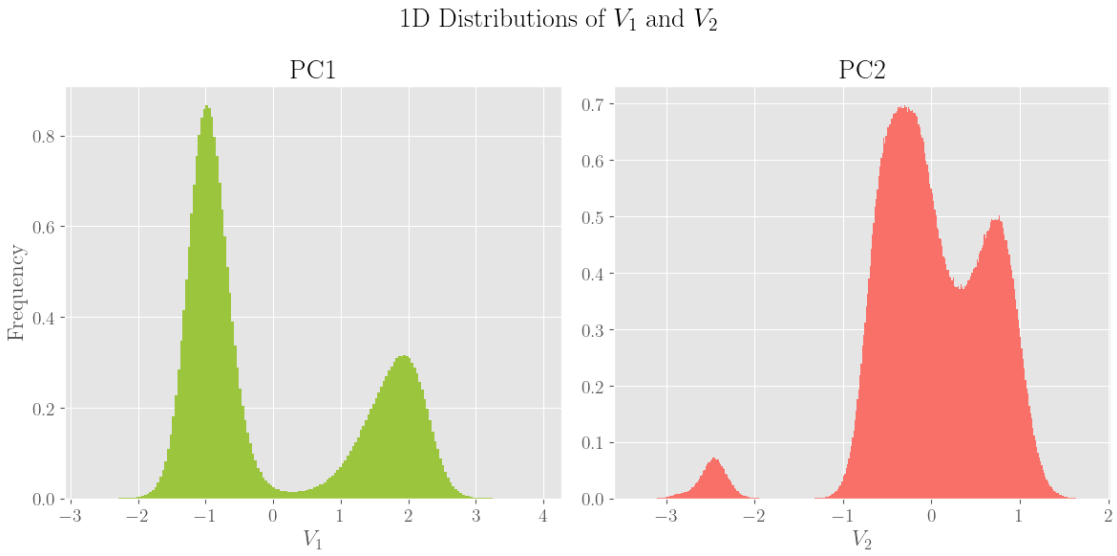
[ ]:
```
# Calculate histogram and free energy
hist_pca, delta_G_pca, xedges_pca, yedges_pca = calculate_free_energy(V1, V2,␣
 ↪bin_size)

# Plot the free energy landscape
plt.figure()
# Define the extent of the histogram for plotting
extent = [xedges_pca[0], xedges_pca[-1], yedges_pca[0], yedges_pca[-1]]
```

```
plt.imshow(delta_G_pca, extent=extent, origin='lower', aspect='auto',␣
 ↪cmap='plasma')
plt.colorbar(label=r'Free Energy ($\times k_B T$)')
plt.xlabel(r'$V_1$')
plt.ylabel(r'$V_2$')
plt.title('Free Energy Landscape: PCA space')

# ax = set_ticks()

plt.tight_layout()
plt.savefig('./final_plots/free_energy_PCA.pdf')
```



[ ]:
```
bins_V1 = np.histogram_bin_edges(V1, bins='auto')
bins_V2 = np.histogram_bin_edges(V2, bins='auto')

fig,axs = plt.subplots(1,2,figsize=(11.998293,5.999146))

fig.suptitle('1D Distributions of $V_1$ and $V_2$')

axs[0].hist(V1,bins=bins_V1,color='C2',density=True);
axs[0].set_xlabel(r'$V_1$')
axs[0].set_ylabel('Frequency')
```

```
axs[0].set_title('PC1')

axs[1].hist(V2,bins=bins_V2,color='C3',density=True);
axs[1].set_xlabel(r'$V_2$')
axs[1].set_title('PC2')

plt.tight_layout()
plt.savefig('./final_plots/1d_v1_v2.pdf')
```



[ ]:

[ ]:

4 Task III

[ ]:

[ ]:
```
# Project the angles onto sine and cosine space
sin_phi = np.sin(phi_rad)
cos_phi = np.cos(phi_rad)
sin_psi = np.sin(psi_rad)
cos_psi = np.cos(psi_rad)
```

[ ]:
```
# Means
sin_phi_mean = sin_phi.mean()
cos_phi_mean = cos_phi.mean()
sin_psi_mean = sin_psi.mean()
cos_psi_mean = cos_psi.mean()
```

```python
# Covariance matrix
stacked_arr = np.vstack([sin_phi,cos_phi,sin_psi,cos_psi])
print(stacked_arr.shape)
covariance_matrix = np.cov(stacked_arr)
print(f'Covariance matrix:\n {covariance_matrix}')
print(f'Dimension: {covariance_matrix.shape}')

eigenvalues, eigenvectors = np.linalg.eig(covariance_matrix)

# Reordering eigenvalues and eigenvectors
idx = eigenvalues.argsort()[::-1]
eigenvalues = eigenvalues[idx]
print(f'\nEigen values: {[round(i,2) for i in eigenvalues]}')
eigenvectors = eigenvectors[:, idx]
print(f'Sorted eigen vectors: \n{eigenvectors}\n')

# Principal components:
pc1 = eigenvectors[:, 0]  # First principal component
pc2 = eigenvectors[:, 1]  # Second principal component
pc3 = eigenvectors[:, 2]  # Third principal component
pc4 = eigenvectors[:, 3]  # Fourth principal component

print(f'Principal components:\n{pc1}\n{pc2}\n{pc3}\n{pc4}')
```

```
(4, 2500000)
Covariance matrix:
 [[ 0.18429202  0.07555427 -0.0390987   0.01756248]
 [ 0.07555427  0.16486931 -0.00904187 -0.01042206]
 [-0.0390987  -0.00904187  0.7597456  -0.04233677]
 [ 0.01756248 -0.01042206 -0.04233677  0.1098412 ]]
Dimension: (4, 4)

Eigen values: [0.77, 0.25, 0.12, 0.08]
Sorted eigen vectors:
[[ 0.071886    0.74479202  0.39101899 -0.53593041]
 [ 0.02287625  0.66315674 -0.47374502  0.57902113]
 [-0.99497704  0.07057578  0.06934195  0.01521352]
 [ 0.06580106  0.02295746  0.78604166  0.6142326 ]]

Principal components:
[ 0.071886    0.02287625 -0.99497704  0.06580106]
[0.74479202 0.66315674 0.07057578 0.02295746]
[ 0.39101899 -0.47374502  0.06934195  0.78604166]
[-0.53593041  0.57902113  0.01521352  0.6142326 ]
```

[ ]:
```
# Calculate the percentage of variance explained by each principal component
percent_variance_explained = scree_data(eigenvalues)

# Visualize the PCA results using a scree plot with percentages
plt.bar(range(1, len(eigenvalues) + 1), percent_variance_explained, color='C4',alpha=0.7)
plt.ylabel('Percentage of Variance Explained')
plt.xlabel('Principal Component')
plt.title('Scree Plot (dPCA)')
plt.xticks(range(1, len(eigenvalues) + 1))
# plt.show()

# Print the percentage of the total variance that each principal component accounts for
for i, variance in enumerate(percent_variance_explained):
    print(f'Principal Component {i+1}: {variance:.2f}% of the total variance')

plt.tight_layout()
plt.savefig('./final_plots/scree_dPCA.pdf')
```

```
Principal Component 1: 73.62% of the total variance
Principal Component 2: 26.38% of the total variance
```

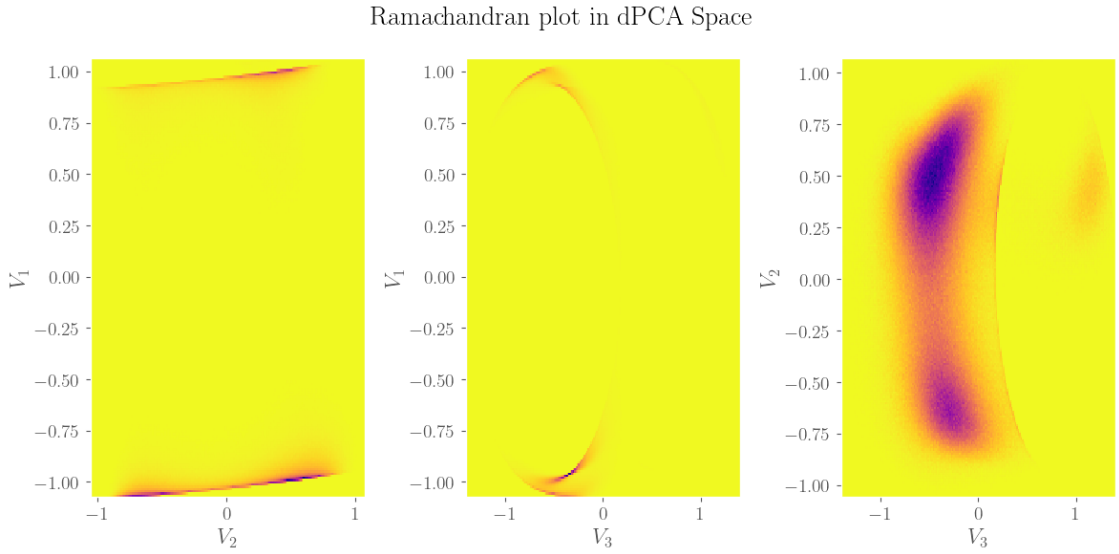
Here we clearly see how the method of PCA reduces the dimensionality. Although we mapped our $2N$ set of data to a $4N$ space, the method of PCA helps reduce the extra dimensionality introduced.

From the above plot, we see that about 63% of the total variance can be explained by PC1 alone. If PC2 is included, 83% of the variance can be explained, and so on.

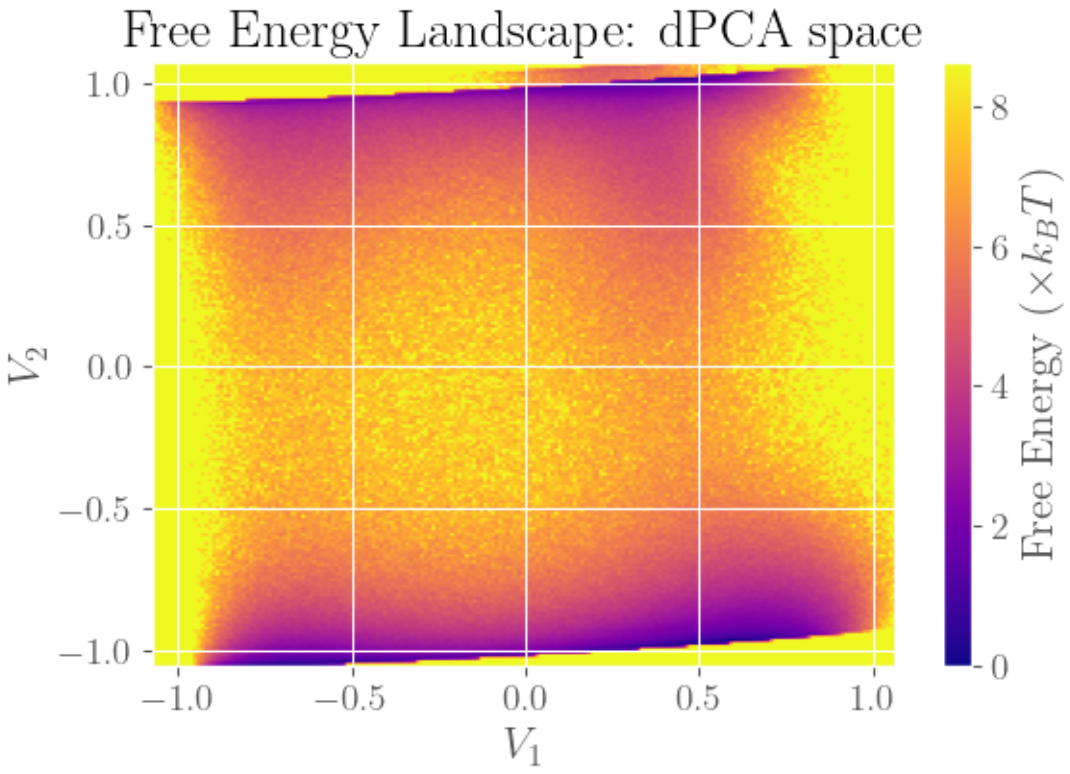
[ ]:
```
# Subtracting the mean from the data
sin_phi_centered = sin_phi #- sin_phi_mean
cos_phi_centered = cos_phi #- cos_phi_mean
sin_psi_centered = sin_psi #- sin_psi_mean
cos_psi_centered = cos_psi #- cos_psi_mean

# Stacking the centered data for matrix multiplication
centered_data = np.
 ↪stack((sin_phi_centered,cos_phi_centered,sin_psi_centered,cos_psi_centered),␣
 ↪axis=1)

# Projecting the data onto the principal components
projected_data = np.dot(centered_data, eigenvectors)

V1,V2,V3,V4 = projected_data[:, 0], projected_data[:, 1], projected_data[:,␣
 ↪2],projected_data[:, 3]
```

[ ]:
```
fig,axs = plt.subplots(1,3,figsize=(11.998293,5.999146))

fig.suptitle('Ramachandran plot in dPCA Space')

axs[0].hist2d(V2,V1, bins=200, density=True,cmap='plasma_r')
axs[0].set_xlabel(r'$V_2$')
axs[0].set_ylabel(r'$V_1$')
# axs[0].set_aspect('equal')

axs[1].hist2d(V3,V1, bins=200, density=True,cmap='plasma_r')
axs[1].set_xlabel(r'$V_3$')
axs[1].set_ylabel(r'$V_1$')
# axs[1].set_aspect('equal')

axs[2].hist2d(V3,V2, bins=200, density=True,cmap='plasma_r')
axs[2].set_xlabel(r'$V_3$')
axs[2].set_ylabel(r'$V_2$')
# axs[2].set_aspect('equal')

# ax = plt.gca()
# ax.axvline(0,color='black',lw=1)
# ax.axhline(0,color='black',lw=1)

plt.tight_layout()
plt.savefig('./final_plots/Rama_dPCA_V1_V2.pdf')
```

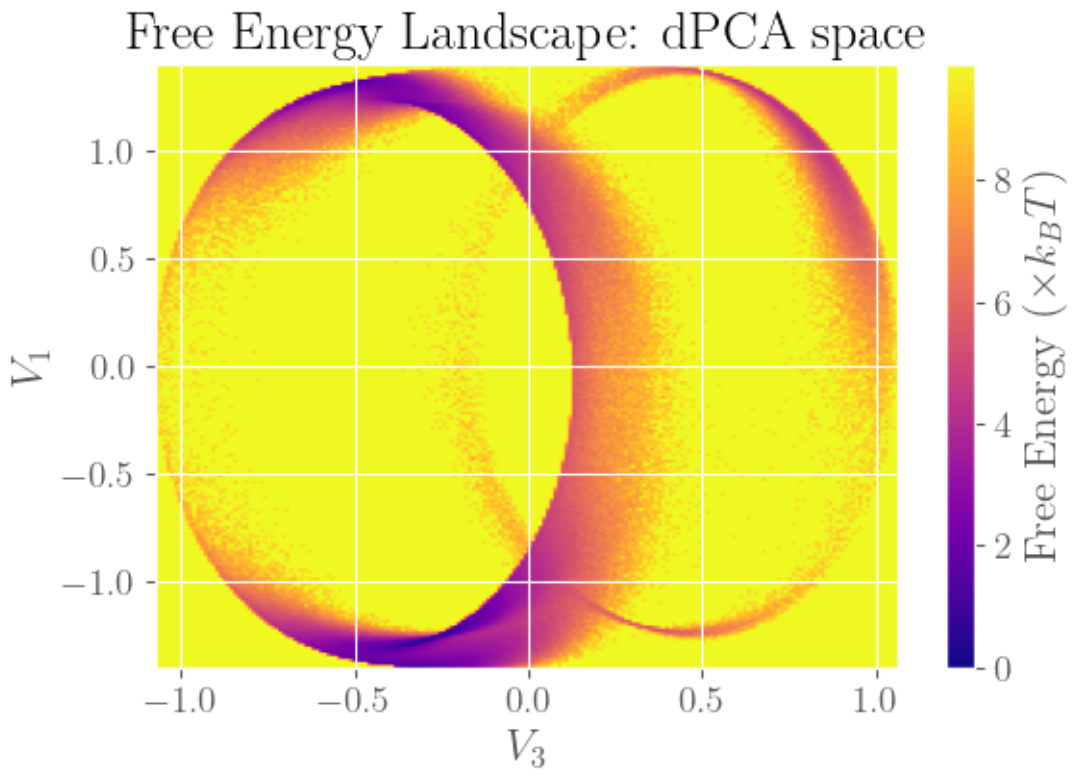
```
plt.show()
```



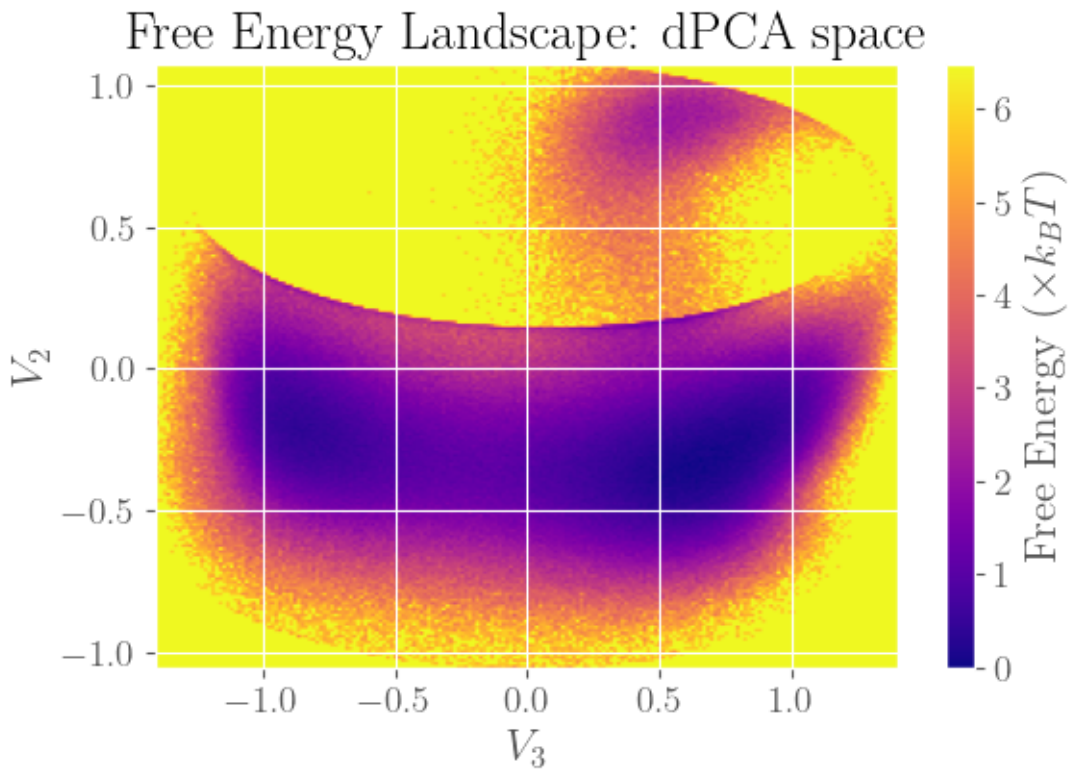
[ ]:
```
# Calculate histogram and free energy
hist1_dpca, delta_G1_dpca, xedges1_dpca, yedges1_dpca =␣
 ↪calculate_free_energy(V1, V2, bin_size)
hist2_dpca, delta_G2_dpca, xedges2_dpca, yedges2_dpca =␣
 ↪calculate_free_energy(V1, V3, bin_size)
hist3_dpca, delta_G3_dpca, xedges3_dpca, yedges3_dpca =␣
 ↪calculate_free_energy(V3, V2, bin_size)

# Plot the free energy landscape
plt.figure()
# Define the extent of the histogram for plotting
extent = [xedges1_dpca[0], xedges1_dpca[-1], yedges1_dpca[0], yedges1_dpca[-1]]
plt.imshow(delta_G1_dpca, extent=extent, origin='lower', aspect='auto',␣
 ↪cmap='plasma')
plt.colorbar(label=r'Free Energy ($\times k_B T$)')
plt.xlabel(r'$V_1$')
plt.ylabel(r'$V_2$')
plt.title('Free Energy Landscape: dPCA space')

# ax = set_ticks()

plt.tight_layout()
plt.savefig('./final_plots/free_energy_dPCA_V1_V2.pdf')
```



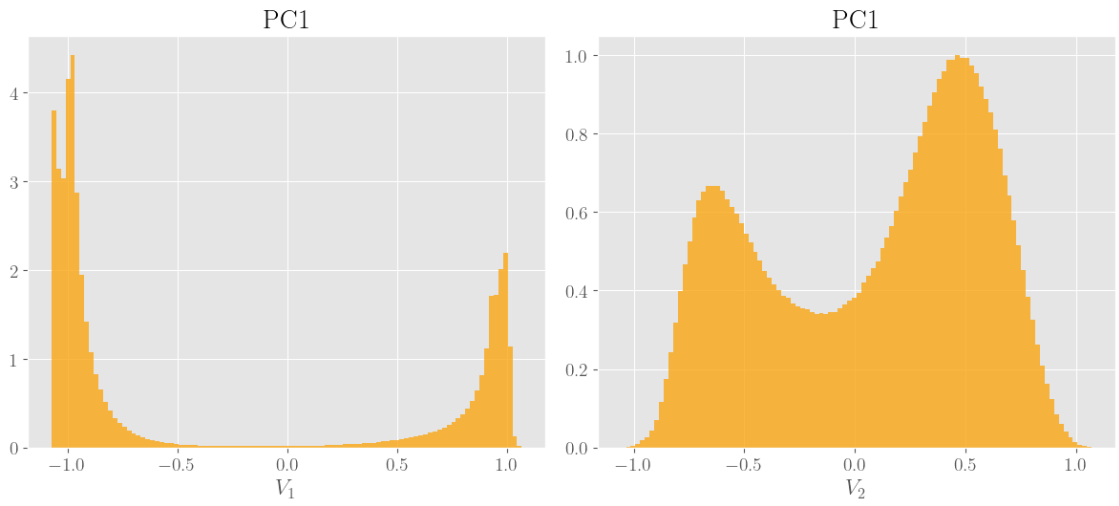
[ ]:
```
extent = [xedges2_dpca[0], xedges2_dpca[-1], yedges2_dpca[0], yedges2_dpca[-1]]
plt.imshow(delta_G2_dpca, extent=extent, origin='lower', aspect='auto',␣
  ↪cmap='plasma')
plt.colorbar(label=r'Free Energy ($\times k_B T$)')
plt.xlabel(r'$V_3$')
plt.ylabel(r'$V_1$')
plt.title('Free Energy Landscape: dPCA space')

# ax = set_ticks()

plt.tight_layout()
plt.savefig('./final_plots/free_energy_dPCA_V1_V3.pdf')
```



[ ]:
```
extent = [xedges3_dpca[0], xedges3_dpca[-1], yedges3_dpca[0], yedges3_dpca[-1]]
plt.imshow(delta_G3_dpca, extent=extent, origin='lower', aspect='auto',␣
  ↪cmap='plasma')
plt.colorbar(label=r'Free Energy ($\times k_B T$)')
plt.xlabel(r'$V_3$')
plt.ylabel(r'$V_2$')
plt.title('Free Energy Landscape: dPCA space')

# ax = set_ticks()

plt.tight_layout()
plt.savefig('./final_plots/free_energy_dPCA_V2_V3.pdf')
```

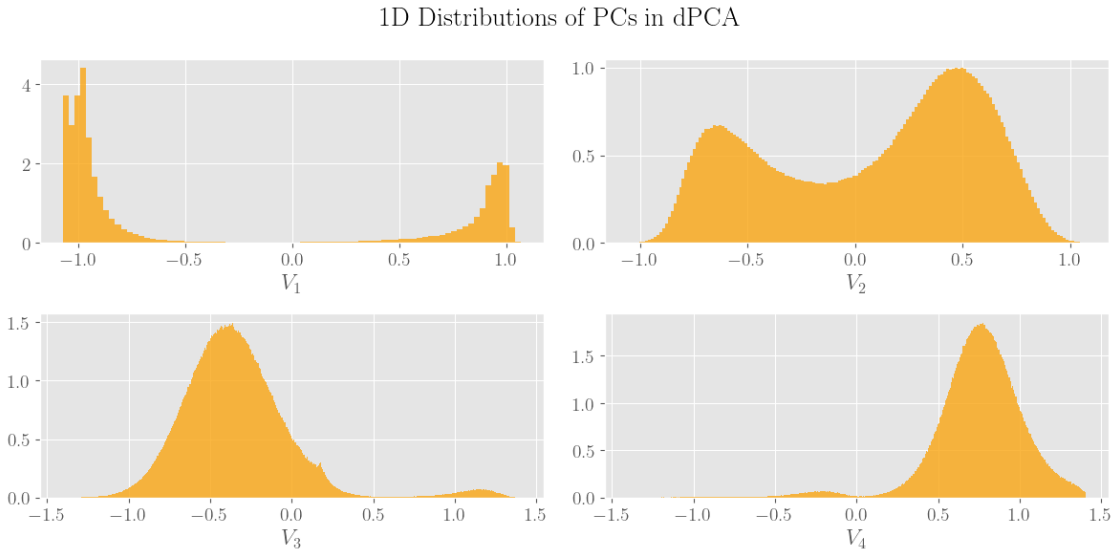


[ ]:
```
bins_V1 = np.histogram_bin_edges(V1, bins=100)
bins_V2 = np.histogram_bin_edges(V2, bins=100)

fig,axs = plt.subplots(1,2,figsize=(11.998293,5.999146))

fig.suptitle('1D Distributions of PCs in dPCA')

axs[0].hist(V1,bins=bins_V1,color='C4',density=True,alpha=0.8)
axs[1].hist(V2,bins=bins_V2,color='C4',density=True,alpha=0.8)

axs[0].set_xlabel(r'$V_1$')
axs[0].set_title(r'PC1')
axs[1].set_title(r'PC1')
axs[1].set_xlabel(r'$V_2$')

plt.tight_layout()
plt.savefig('./final_plots/1d_dPCA_V1_V2.pdf')
```



[ ]:

[ ]:
```
bins_V1 = np.histogram_bin_edges(V1, bins='auto')
bins_V2 = np.histogram_bin_edges(V2, bins='auto')
bins_V3 = np.histogram_bin_edges(V3, bins='auto')
bins_V4 = np.histogram_bin_edges(V4, bins='auto')

fig,axs = plt.subplots(2,2,figsize=(11.998293,5.999146))

fig.suptitle('1D Distributions of PCs in dPCA')

axs[0,0].hist(V1,bins=bins_V1,color='C4',density=True,alpha=0.8)
axs[0,1].hist(V2,bins=bins_V2,color='C4',density=True,alpha=0.8)
axs[1,0].hist(V3,bins=bins_V3,color='C4',density=True,alpha=0.8)
axs[1,1].hist(V4,bins=bins_V4,color='C4',density=True,alpha=0.8)

axs[0,0].set_xlabel(r'$V_1$')
axs[0,1].set_xlabel(r'$V_2$')
axs[1,0].set_xlabel(r'$V_3$')
axs[1,1].set_xlabel(r'$V_4$')

plt.tight_layout()
plt.savefig('./final_plots/1d_dPCA_all_four.pdf')
```

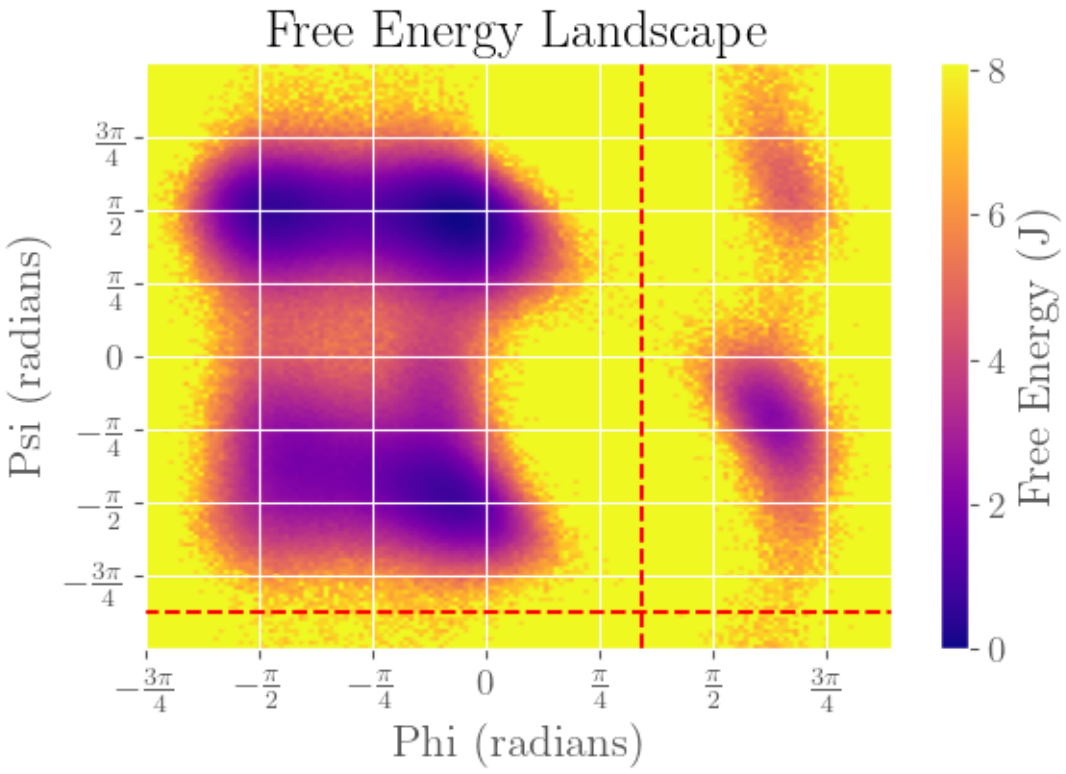


5 Task IV

An initial visual guess of the offset angle is made, by looking at the density of points in different regions of the 2D heatmap of the free energy. The guessed 'cut' values are annotated in the plot below:

[ ]:
```
bin_size = 150

# Calculate histogram and free energy
hist, delta_G, xedges, yedges = calculate_free_energy(phi_rad, psi_rad,␣
 ↪bin_size)

# Plot the free energy landscape
plt.figure()
# Define the extent of the histogram for plotting
extent = [xedges[0], xedges[-1], yedges[0], yedges[-1]]
plt.imshow(delta_G.T, extent=extent, origin='lower', aspect='auto',␣
 ↪cmap='plasma')
plt.colorbar(label='Free Energy (J)')
plt.xlabel('Phi (radians)')
plt.ylabel('Psi (radians)')
plt.title('Free Energy Landscape')

plt.axvline((11/32)*np.pi,color='red',linestyle='--')
plt.axhline(-(7/8)*np.pi,color='red',linestyle='--')

ax = set_ticks()
```

```
plt.tight_layout()
plt.savefig('./final_plots/free_energy_max_gap.pdf')
```

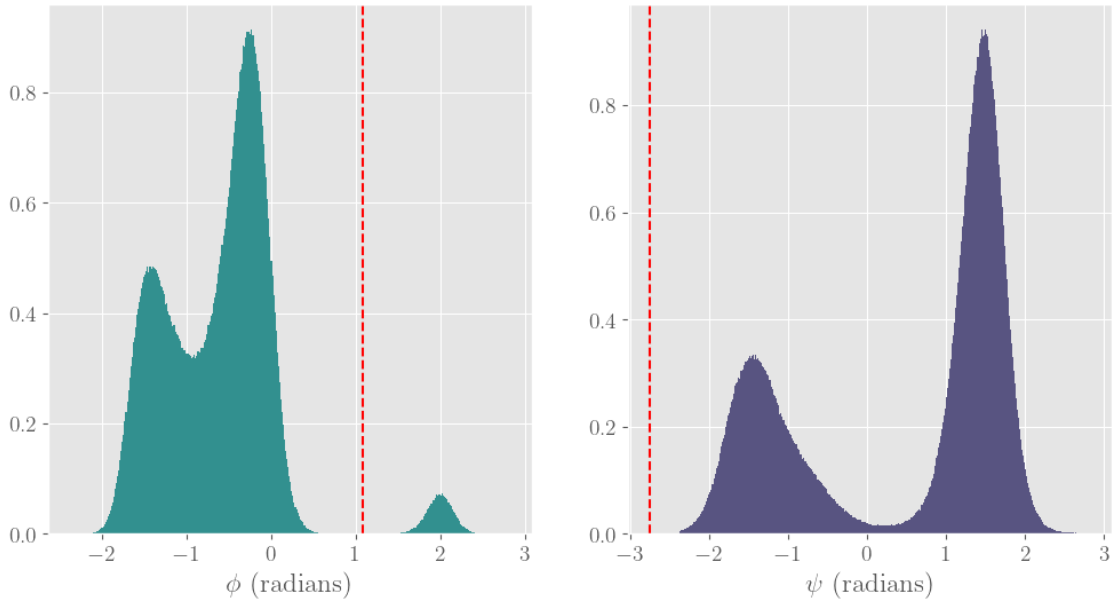


The guessed cut points can also be visualized in the 1D distributions:

[ ]:
```
guess_cut1=(11/32)*np.pi # naming the cuts
guess_cut2=-(7/8)*np.pi

# Re-generate the density histograms for phi and psi

bins_phi = np.histogram_bin_edges(phi_rad, bins='auto')
bins_psi = np.histogram_bin_edges(psi_rad, bins='auto')

print(len(bins_phi),len(bins_psi))

fig,axs = plt.subplots(1,2,figsize=(11.998293,5.999146))

axs[0].hist(phi_rad,bins=bins_phi,color='C0',density=True);
axs[0].axvline(guess_cut1,color='red',linestyle='--')
axs[0].set_xlabel(r'$\phi$ (radians)')

axs[1].hist(psi_rad,bins=bins_phi,color='C1',density=True);
```

```
axs[1].axvline(guess_cut2,color='red',linestyle='--')
axs[1].set_xlabel(r'$\psi$ (radians)')

plt.savefig('./final_plots/1d_maximal_gaps.pdf')
```

```
367 167
```



Now, the guessed cut value is optimized by defining the following search function `find_best_maximal_gap` which takes in the histogram data and identifies the best bin to shift the data. The numpy function `searchsorted` is utilized for this purpose. This function takes a sorted array (`bin_edges` in this case) and a value (`guess_value`) and returns the index at which this value should be inserted to maintain the order of the array.

[ ]:
```
def find_best_maximal_gap(hist, guess_value):
    """
    Find the best value of the variable for the maximal gap based
    on the guessed value.
    """
    counts, bin_edges = hist
    bin_width = bin_edges[1] - bin_edges[0]

    # Find the index of the bin which contains the guess value
    guess_index = np.searchsorted(bin_edges, guess_value, side='right') - 1

    ## Look for the bin with the minimal count near the guess value
    search_range = 20
    start = max(0, guess_index - search_range)
    end = min(len(counts), guess_index + search_range)
```

```
    # Locate the index of the bin with the lowest count
    #  within the specified range.
    min_count_index = np.argmin(counts[start:end]) + start

    # Calculate the midpoint of the bin with the minimal count
    best_value = bin_edges[min_count_index] + bin_width / 2

    print(f'Guessed cut:{guess_value:.3f},\n Optimized cut:{best_value:.3f}')

    return best_value
```

The side='right' argument in the above function specifies that the insertion index should be such that the `guess_value` is inserted just after any existing entries of the same value in `bin_edges`. In other words, it finds the index where guess_value should go if all values in bin_edges are considered to be the left edges of the intervals. For example, if `guess_value` is 3.5 and `bin_edges` has a bin edge exactly at 3, then searchsorted with `side='right'` would return the index after 3.

[ ]:
```
cut1=find_best_maximal_gap(np.histogram(phi_rad,bins='auto'),guess_cut1)
cut2=find_best_maximal_gap(np.histogram(psi_rad,bins='auto'),guess_cut2)
```

```
Guessed cut:1.080,
 Optimized cut:0.922
Guessed cut:-2.749,
 Optimized cut:-3.007
```

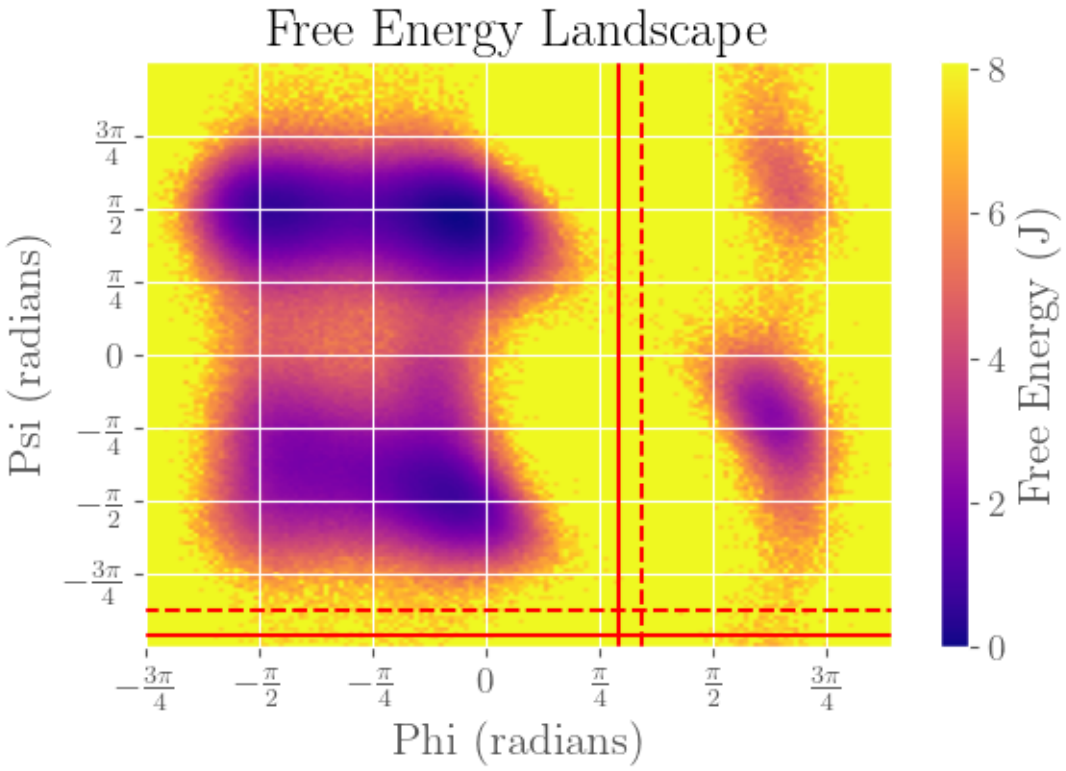
Visualizing the optimized cuts in comparison to the original cuts:

[ ]:
```
np.rad2deg(cut1),np.rad2deg(cut2)
```

[ ]:
```
(52.81541803278686, -172.31668373493977)
```

[ ]:
```
bin_size = 150

# Calculate histogram and free energy
hist, delta_G, xedges, yedges = calculate_free_energy(phi_rad, psi_rad,␣
 ↪bin_size)

# Plot the free energy landscape
plt.figure()
# Define the extent of the histogram for plotting
extent = [xedges[0], xedges[-1], yedges[0], yedges[-1]]
plt.imshow(delta_G.T, extent=extent, origin='lower', aspect='auto',␣
 ↪cmap='plasma')
plt.colorbar(label='Free Energy (J)')
plt.xlabel('Phi (radians)')
plt.ylabel('Psi (radians)')
plt.title('Free Energy Landscape')
```

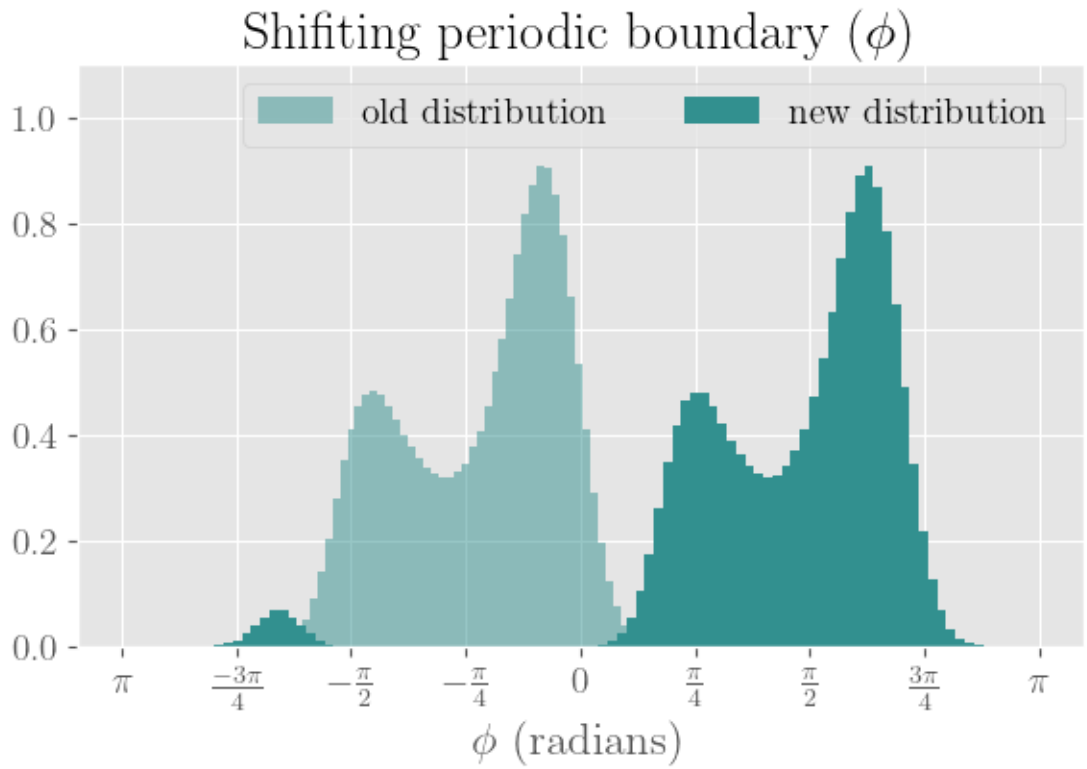
```
plt.axvline(guess_cut1,color='red',linestyle='--')
plt.axvline(cut1,color='red',linestyle='-')
plt.axhline(guess_cut2,color='red',linestyle='--')
plt.axhline(cut2,color='red',linestyle='-')

ax = set_ticks()

plt.tight_layout()
plt.savefig('./final_plots/free_energy_max_gap_best.pdf')
```



Now we write a function to shift the offset angles by the periodic boundary.

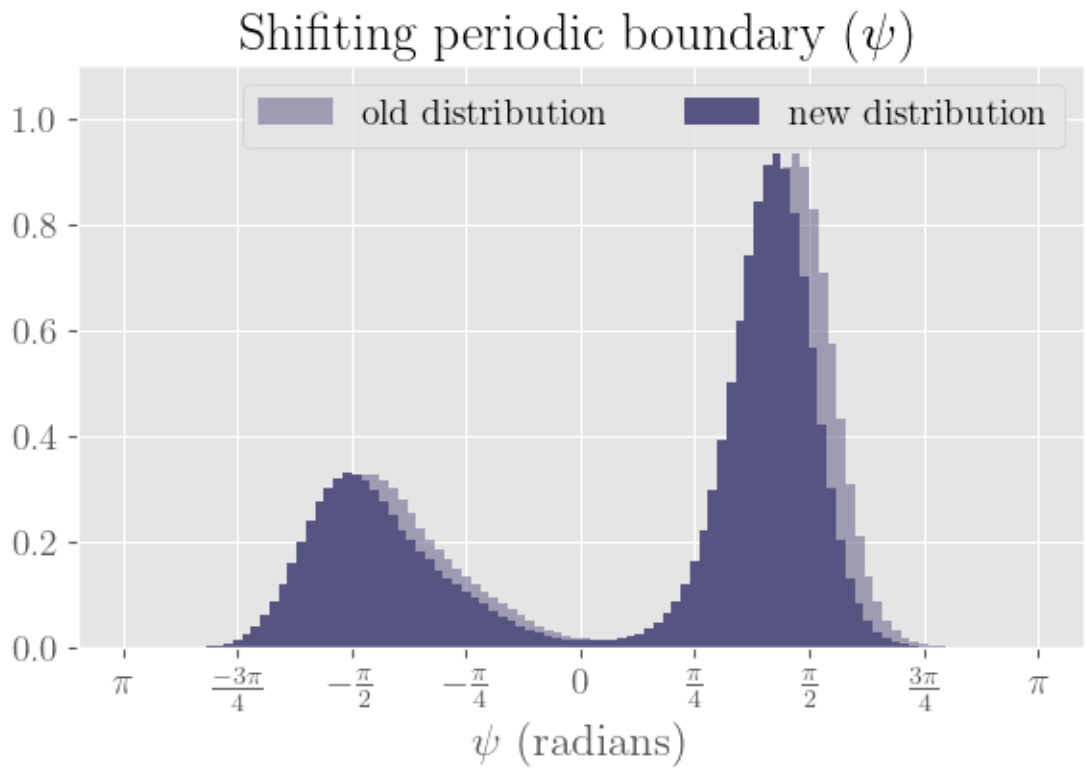
[ ]:
```
def shift_angles(angles,cut):
    transformed_angles = np.zeros_like(angles)

    # Shift the angles based on the cut point
    shifted_angles = (angles - cut) % (2 * np.pi) - np.pi
    # The periodic boundary is ensured by using the modulo operatiom,
    # mapping the angles to a range 0 to pi first, and then
    # subtracting by pi to map them back to the [-pi,pi) range.

    return shifted_angles
```

[ ]:
```
plt.hist(phi_rad,bins=100,color='C0',alpha=0.5,density=True,label='old␣
 ↪distribution');

# updating the phi
new_phi = shift_angles(phi_rad,cut1)

plt.hist(new_phi,bins=100,color='C0',alpha=1,density=True,label='new␣
 ↪distribution');
plt.ylim(0,1.1)
plt.legend(ncols=2)
plt.title(r'Shifiting periodic boundary ($\phi$)')
plt.xlabel(r'$\phi$ (radians)')
ax = set_ticks_1d()

plt.tight_layout()
plt.savefig('./final_plots/shifting_PB_phi.pdf')
```



[ ]:
```
plt.hist(psi_rad,bins=100,color='C1',alpha=0.5,density=True,label='old␣
 ↪distribution');

# updating the psi
```

```
new_psi = shift_angles(psi_rad,cut2)

plt.hist(new_psi,bins=100,color='C1',alpha=1,density=True,label='new␣
 ↪distribution');
plt.ylim(0,1.1)
plt.legend(ncols=2)
plt.title(r'Shifiting periodic boundary ($\psi$)')
plt.xlabel(r'$\psi$ (radians)')
ax = set_ticks_1d()

plt.tight_layout()
plt.savefig('./final_plots/shifting_PB_psi.pdf')
```



[ ]:

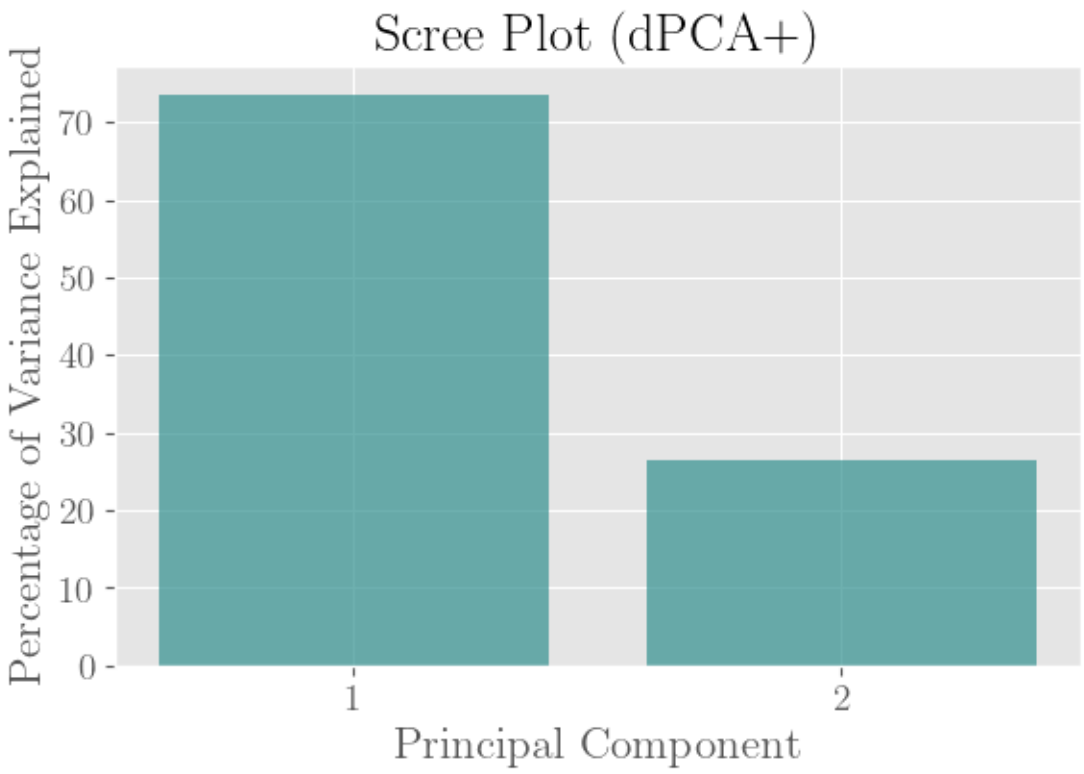
[ ]:
```
# Means
phi_mean = new_phi.mean()
psi_mean = new_psi.mean()

# Covariance and variance
phi_variance = new_phi.var()
psi_variance = new_psi.var()
```

```
# Covariance matrix
covariance_matrix = np.cov(new_phi,new_psi)

eigenvalues, eigenvectors = np.linalg.eig(covariance_matrix)

# Reordering eigenvalues and eigenvectors
idx = eigenvalues.argsort()[::-1]
eigenvalues = eigenvalues[idx]
print(f'Eigen values: {[round(i,2) for i in eigenvalues]}')
eigenvectors = eigenvectors[:, idx]

# Principal components:
pc1 = eigenvectors[:, 0]  # First principal component
pc2 = eigenvectors[:, 1]  # Second principal component

# Subtracting the mean from the data
phi_centered = new_phi - phi_mean
psi_centered = new_psi - psi_mean

# Stacking the centered data for matrix multiplication
centered_data = np.stack((phi_centered, psi_centered), axis=1)

# Projecting the data onto the principal components
projected_data = np.dot(centered_data, eigenvectors)
```

```
Eigen values: [1.8, 0.64]
```

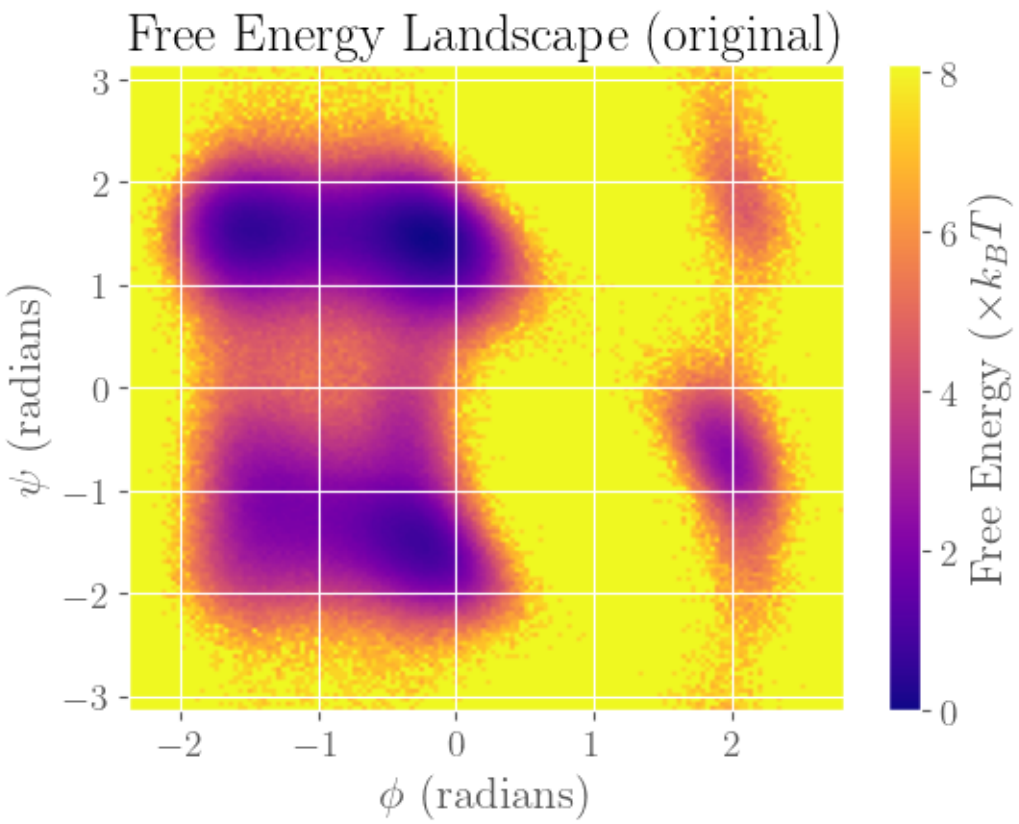
[ ]:
```
dpcaPlus_scree = scree_data(eigenvalues=eigenvalues)

# Visualize the PCA results using a scree plot with percentages
plt.bar(range(1, len(eigenvalues) + 1), dpcaPlus_scree, alpha=0.7)
plt.ylabel('Percentage of Variance Explained')
plt.xlabel('Principal Component')
plt.title('Scree Plot (dPCA+)')
plt.xticks(range(1, len(eigenvalues) + 1))

# Print the percentage of the total variance that each principal component␣
 ↪accounts for
for i, variance in enumerate(dpcaPlus_scree):
    print(f'Principal Component {i+1}: {variance:.2f}% of the total variance')

plt.tight_layout()
plt.savefig('./final_plots/scree_dPCAplus.pdf')
```

```
Principal Component 1: 73.62% of the total variance
Principal Component 2: 26.38% of the total variance
```

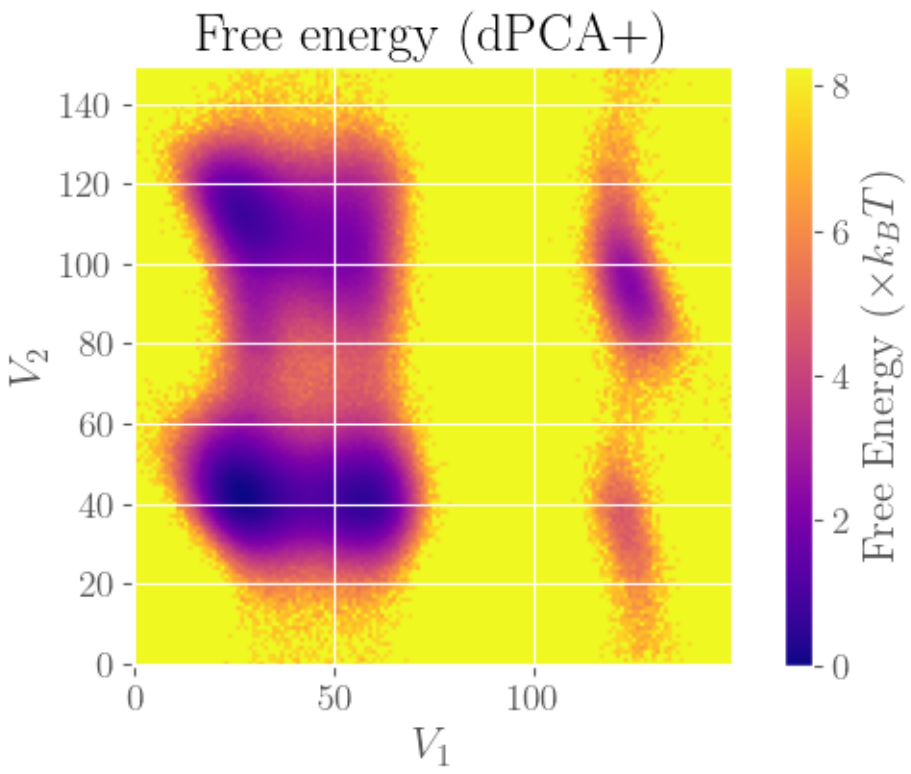


[ ]:
```
# Calculate histogram and free energy
hist, delta_G, xedges, yedges = calculate_free_energy(phi_rad, psi_rad,␣
 ↪bin_size)

# Plot the free energy landscape
plt.figure()
# Define the extent of the histogram for plotting
extent = [xedges[0], xedges[-1], yedges[0], yedges[-1]]
plt.imshow(delta_G.T, extent=extent, origin='lower', aspect='auto',␣
 ↪cmap='plasma')
plt.colorbar(label=r'Free Energy ($\times k_B T$)')
plt.xlabel(r'$\phi$ (radians)')
plt.ylabel(r'$\psi$ (radians)')
plt.title('Free Energy Landscape (original)')
```

[ ]:
```
Text(0.5, 1.0, 'Free Energy Landscape (original)')
```



[ ]:
```
hist_dpcaPlus, delta_G_dpcaPlus, xedges_dpcaPlus, yedges_dpcaPlus =␣
 ↪calculate_free_energy(projected_data[:,0],projected_data[:,1], bin_size)
extent = [xedges_dpcaPlus[0], xedges_dpcaPlus[-1], yedges_dpcaPlus[0],␣
 ↪yedges_dpcaPlus[-1]]

plt.figure()
plt.grid('False')
plt.imshow(delta_G_dpcaPlus,origin='lower',cmap='plasma')
plt.colorbar(label=r'Free Energy ($\times k_B T$)')

plt.title('Free energy (dPCA+)')
plt.xlabel(r'$V_1$')
plt.ylabel(r'$V_2$')

plt.tight_layout()
plt.savefig('./final_plots/free_energy_dPCAPlus.pdf')
```



[ ]:

6 Appendix

Contents of the `ccs_project_helpers.py` python file:

[ ]:
```python
import numpy as np
import matplotlib.pyplot as plt

def angle_difference(a1, a2):
    """
    To calculate the smallest difference between two angles
    """
    # Convert angles to radians
    a1_rad = np.radians(a1)
    a2_rad = np.radians(a2)

    # Calculate difference
    diff = np.arctan2(np.sin(a1_rad-a2_rad), np.cos(a1_rad-a2_rad))

    # Convert the smallest difference back to degrees
```

```
    diff_deg = np.degrees(diff)

    # Ensure the difference is within 0-180 degrees
    return np.abs(diff_deg)

# Example angles
a1 = 150
a2 = -150

angle_difference(a1,a2)

def set_ticks(): # majorly generated by ChatGPT
    ax = plt.gca()  # Get current axes
    xmin, xmax = ax.get_xlim()  # Get the limits of the x-axis

    # Convert the limits to multiples of pi/4
    xmin_pi = np.ceil(xmin / (np.pi/4)) * (np.pi/4)
    xmax_pi = np.floor(xmax / (np.pi/4)) * (np.pi/4)

    # Set ticks at multiples of pi/4 within the limits
    ticks_x = np.arange(xmin_pi, xmax_pi + np.pi/4, np.pi/4)

    # Set labels corresponding to the ticks_x
    labels = []
    for tick in ticks_x:
        numerator = int(4*tick/np.pi)
        denominator = 4

        # Simplify the fraction using modulo operation
        while numerator % 2 == 0 and denominator % 2 == 0:
            numerator /= 2
            denominator /= 2

        if numerator == 0:
            labels.append('0')
        elif denominator == 1:
            labels.append(r'$\pi$')
        elif numerator == 1:
            labels.append(fr'$\frac{{\pi}}{{ {int(denominator)} }}$')
        elif numerator == -1:
            labels.append(fr'$-\frac{{\pi}}{{ {int(denominator)} }}$')
        else:
            labels.append(fr'$\frac{{ {int(numerator)} \pi}}{{␣
 ↪{int(denominator)} }}$')

    ymin, ymax = ax.get_ylim()  # Get the limits of the x-axis
```

```
    # Convert the limits to multiples of pi/4
    ymin_pi = np.ceil(ymin / (np.pi/4)) * (np.pi/4)
    ymax_pi = np.floor(ymax / (np.pi/4)) * (np.pi/4)

    # Set ticks at multiples of pi/4 within the limits
    ticks_y = np.arange(ymin_pi, ymax_pi + np.pi/4, np.pi/4)

    # Set labels corresponding to the ticks_y
    labels = []
    for tick in ticks_y:
        numerator = int(4*tick/np.pi)
        denominator = 4

        # Simplify the fraction using modulo operation
        while numerator % 2 == 0 and denominator % 2 == 0:
            numerator /= 2
            denominator /= 2

        sign = "-" if numerator < 0 else ""
        numerator = abs(numerator)

        if numerator == 0:
            labels.append('0')
        elif denominator == 1:
            labels.append(fr'${sign}\pi$')
        elif numerator == 1:
            labels.append(fr'${sign}\frac{{\pi}}{{ {int(denominator)} }}$')
        else:
            labels.append(fr'${sign}\frac{{ {int(numerator)} \pi}}{{␣
 ↪{int(denominator)} }}$')

    ax.set_xticks(ticks_x)
    ax.set_yticks(ticks_y)
    ax.set_xticklabels(labels)
    ax.set_yticklabels(labels)
    # plt.show()

    return ax

def set_ticks_1d():
    ax = plt.gca()  # Get current axes
    xmin, xmax = ax.get_xlim()  # Get the limits of the x-axis

    # Convert the limits to multiples of pi/4
    xmin_pi = np.ceil(xmin / (np.pi/4)) * (np.pi/4)
    xmax_pi = np.floor(xmax / (np.pi/4)) * (np.pi/4)
```

```
    # Set ticks at multiples of pi/4 within the limits
    ticks_x = np.arange(xmin_pi, xmax_pi + np.pi/4, np.pi/4)

    # Set labels corresponding to the ticks_x
    labels = []
    for tick in ticks_x:
        numerator = int(4*tick/np.pi)
        denominator = 4

        # Simplify the fraction using modulo operation
        while numerator % 2 == 0 and denominator % 2 == 0:
            numerator /= 2
            denominator /= 2

        if numerator == 0:
            labels.append('0')
        elif denominator == 1:
            labels.append(r'$\pi$')
        elif numerator == 1:
            labels.append(fr'$\frac{{\pi}}{{ {int(denominator)} }}$')
        elif numerator == -1:
            labels.append(fr'$-\frac{{\pi}}{{ {int(denominator)} }}$')
        else:
            labels.append(fr'$\frac{{ {int(numerator)} \pi}}{{␣
↪{int(denominator)} }}$')

    ax.set_xticks(ticks_x)
    ax.set_xticklabels(labels)
    # plt.show()

    return ax
```

The following function was used to test the PCA implementation using the built-in scikitlearn library.

```
[ ]: def perform_pca(sin_phi, cos_phi, sin_psi, cos_psi):
    """
    Perform PCA on the sine and cosine transformations of the dihedral angles␣
↪phi and psi.
    """

    # Stack the input arrays into a single matrix for PCA
    data = np.column_stack((sin_phi, cos_phi, sin_psi, cos_psi))

    # Initialize the PCA model with 4 components
    pca = PCA(n_components=4)
```

```
    # Fit the PCA model and transform the data
    projected_data = pca.fit_transform(data)

    v1,v2,v3,v4 = projected_data.T

    # Return the projected data
    return v1,v2,v3,v4
```

[ ]:
```
from sklearn.decomposition import PCA

V1,V2,V3,V4 = perform_pca(sin_phi,cos_phi,sin_psi,cos_psi)
```

Contents of the `ccs_project.mplstyle` template file:

```
text.usetex: True
text.latex.preamble: \usepackage{amsmath}\usepackage{amssymb}\usepackage{nicefrac}\usepackage{s

figure.figsize : 5.9991,4.3630 # or (11.998293,5.999146)
figure.titlesize: x-large

font.size: 14.0
font.family: serif
font.serif: cmbright
#font.family: sans-serif
#font.sans-serif: cmbright

axes.prop_cycle : cycler('color', ["#32908F", "#585481", "#9BC53D", "#F97068", "#FAA613", "#40A

axes.formatter.use_mathtext:True
axes.titlesize: x-large

xtick.labelsize: medium
ytick.labelsize: medium
```

[ ]:
```

```