

RMSD

PDB IDs

1. **3bqc**: High pH-value crystal structure of emodin in complex with the catalytic subunit of protein kinase CK2 (1.5A)
2. **3h30**: Crystal structure of the catalytic subunit of human protein kinase CK2 with 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole (1.56 Å)
3. **3mb7**: Human CK2 catalytic domain in complex with a difurane derivative inhibitor (AMR) (1.65 Å)
4. **3nsz**: Human CK2 catalytic domain in complex with AMPPN (1.30 Å)
5. **3pe1**: Crystal structure of human protein kinase CK2 alpha subunit in complex with the inhibitor CX-4945 (1.6 Å)
6. **3war**: Crystal structure of human CK2a (1.04 Å)
7. **4kwp**: Crystal Structure of Human CK2-alpha in complex with a benzimidazole inhibitor (K164) at 1.25 Å resolution (1.25 Å)
8. **5csv**: Crystal Structure of CK2alpha with Compound 6 bound (1.375 Å)
9. **5cu4**: Crystal Structure of CK2alpha with Compound 10 bound (1.56 Å)
10. **5cu6**: Crystal Structure of CK2alpha (1.36 Å)
11. **2pvr**: Crystal structure of the catalytic subunit of protein kinase CK2 (C-terminal deletion mutant 1-335) in complex with two sulfate ions
12. **5clp**: Crystal Structure of CK2alpha with 3,4-dichlorophenethylamine bound
13. **5csp**: Crystal Structure of CK2alpha with Compound 5 bound
14. **5cvg**: Crystal Structure of CK2alpha with a novel closed conformation of the aD loop
15. **3r0t**: Crystal structure of human protein kinase CK2 alpha subunit in complex with the inhibitor CX-5279
16. **3q9w**: Crystal structure of human CK2 alpha in complex with emodin at pH 8.5
17. **3q04**: Crystal structure of the apo-form of human CK2 alpha at pH 8.5
18. **5cs6**: Crystal Structure of CK2alpha with Compound 3 bound
19. **3owk**: Human CK2 catalytic domain in complex with a benzopyridoindole derivative inhibitor
20. **4rl1**: Crystal structure of human CK2alpha in complex with the ATP-competitive inhibitor 4-[(E)-(fluoren-9-ylidene)hydrazinylidene]-methyl] benzoate

MSA

Files:

sequences_pdb20.pir
sequences_pdb20.fasta

Input file for alignment using Bio.Align; MSA generated

Set Reference: 3war - Crystal structure of human CK2a (1.04 Å)

Set Sample: x – any of the other 19 structures

Define Ranges, Extract CA co-ordinates from Reference and Sample

- 30-300 bps
- Biopython script

RMSD Calculation

$$RMSD = \sqrt{\frac{1}{N} \sum_{i=1}^n (x_{ci} - x_{di})^2 + (y_{ci} - y_{di})^2 + (z_{ci} - z_{di})^2}$$

$$= \sqrt{\frac{1}{N} \sum_{i=1}^n d_x^2 + d_y^2 + d_z^2}$$

$$= \sqrt{\frac{1}{N} \sum_{i=1}^n \vec{d}}$$

where (x_{ci}, y_{ci}, z_{ci}) are the coordinates of Reference Structure CAs

(x_{di}, y_{di}, z_{di}) are the coordinates of Sample Structure CAs

Superimposition of structures (backbone)

Optimal movement of one structure over another to minimize RMSD

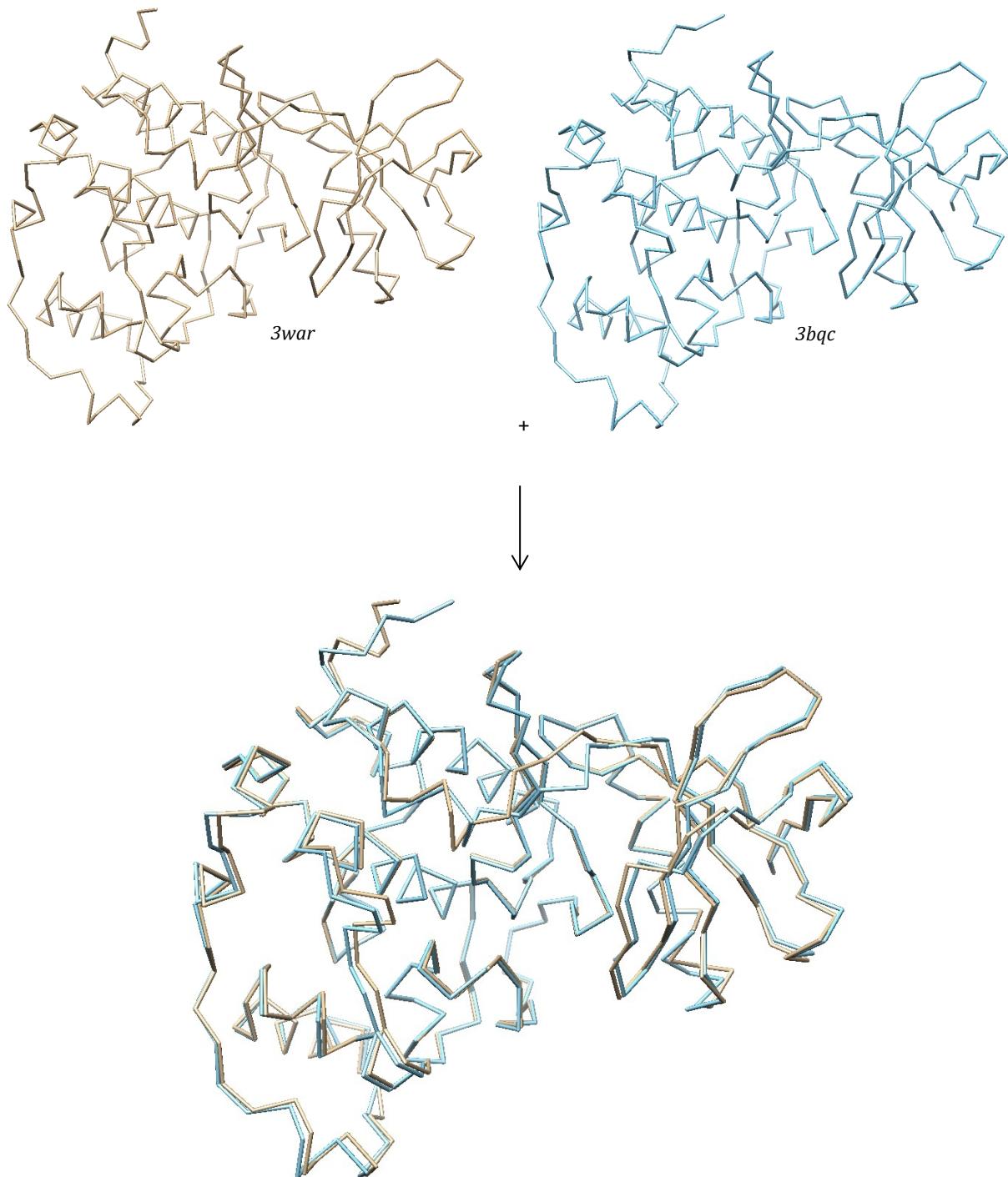
Method: Rigid Body Rotation and translation of B (sample) on A (reference)

Reference: 3war

Sample: 3bqc

Structures: 3war, 3bqc

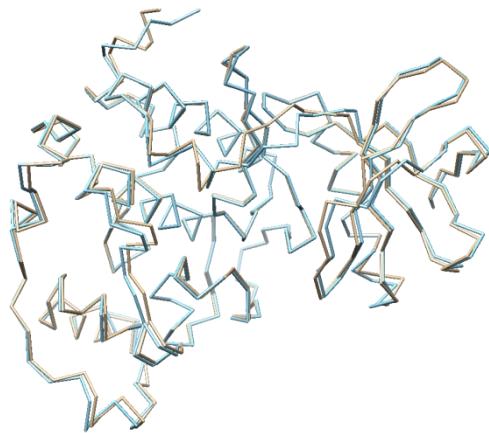
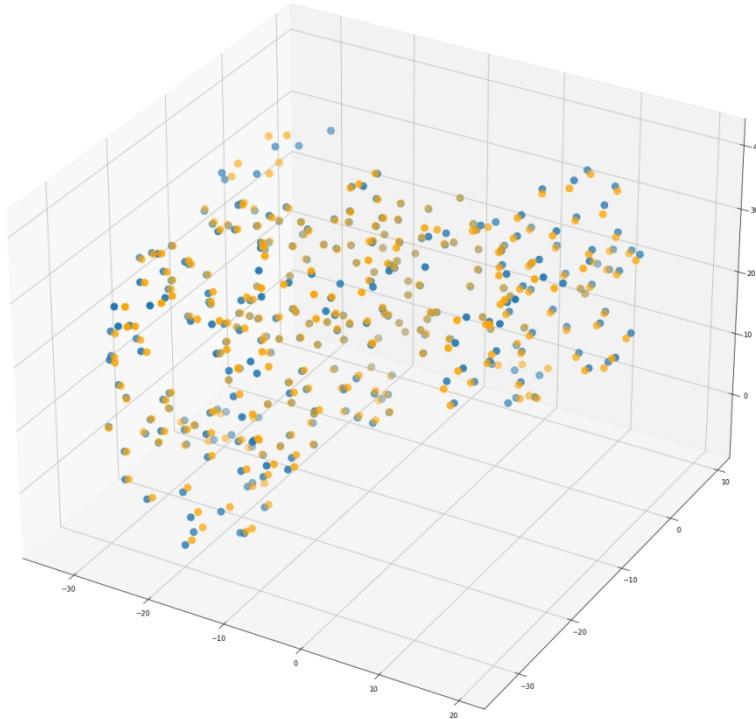
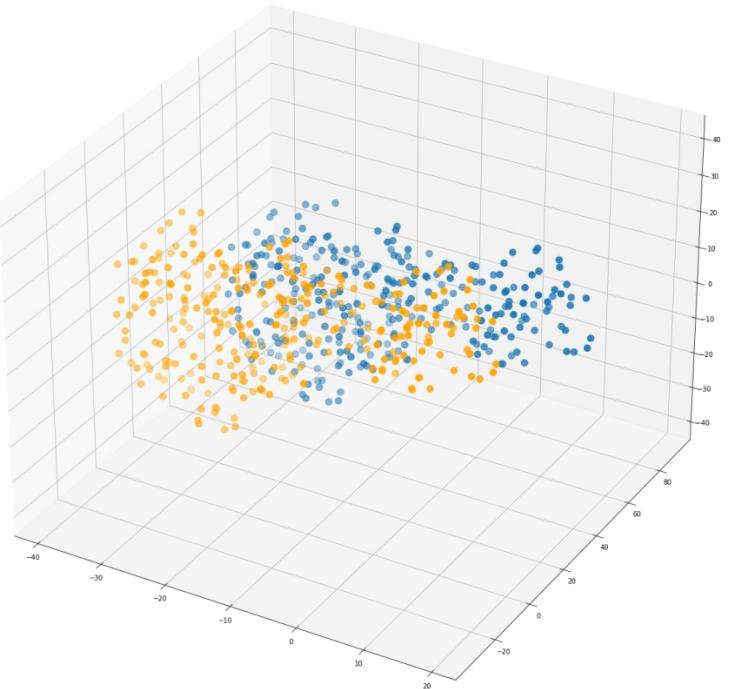
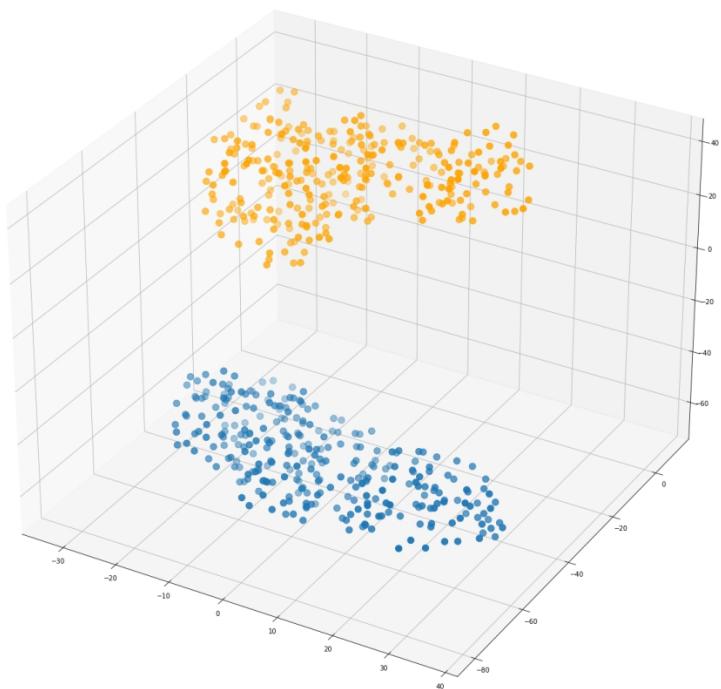
Chain traces



Python implementation:

Reference: 3war (30-330 bps)

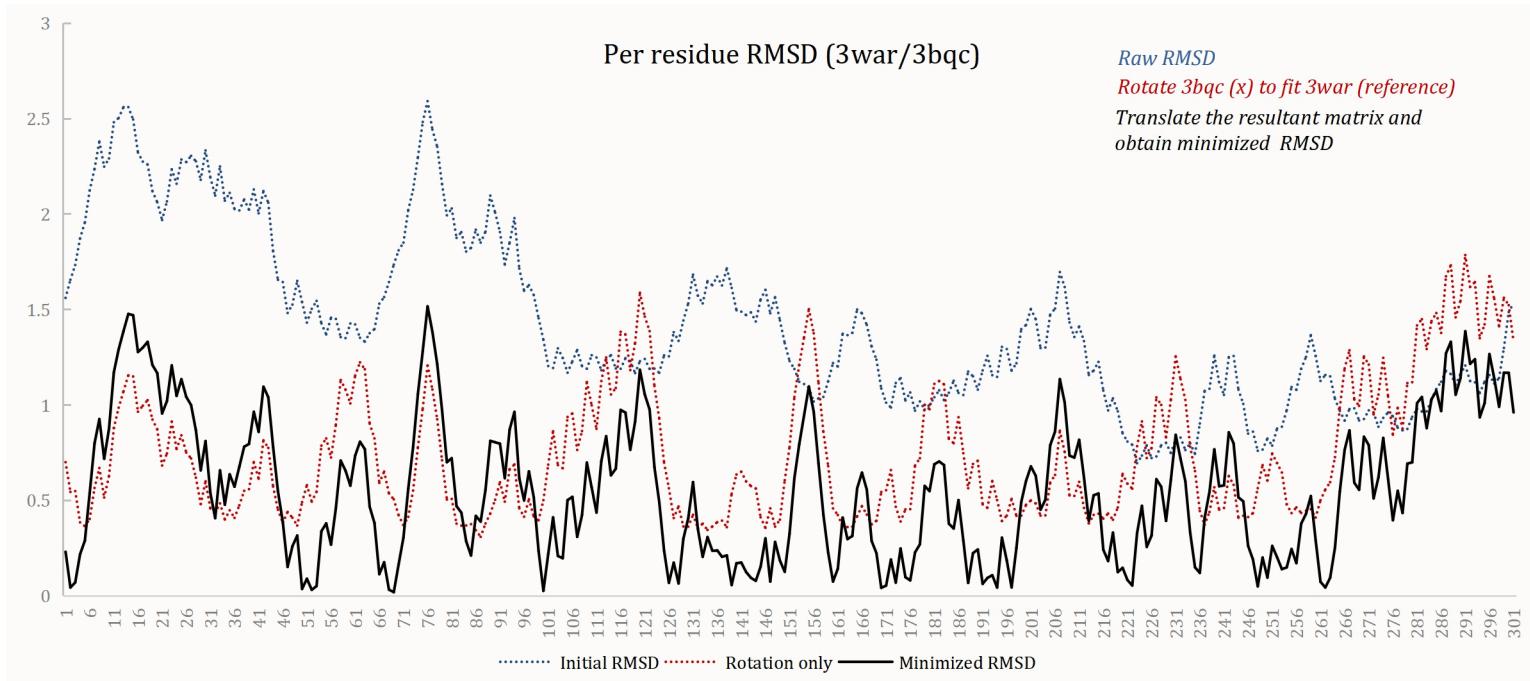
Sample: 3bqc (30-330 bps)



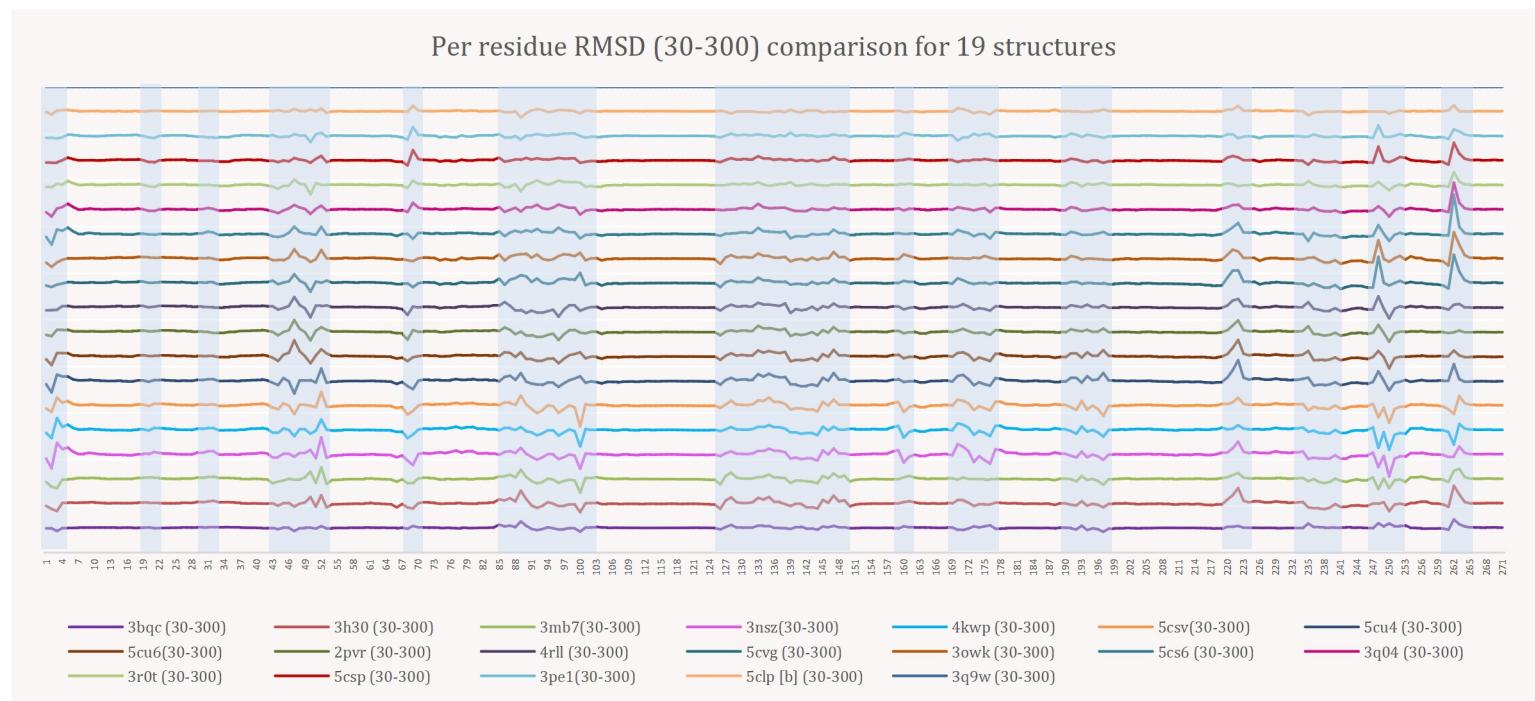
Initial average RMSD (3war/3bqc): **1.4168445841471353**

Minimized average RMSD (3war/3bqc): **0.5565493265787761**

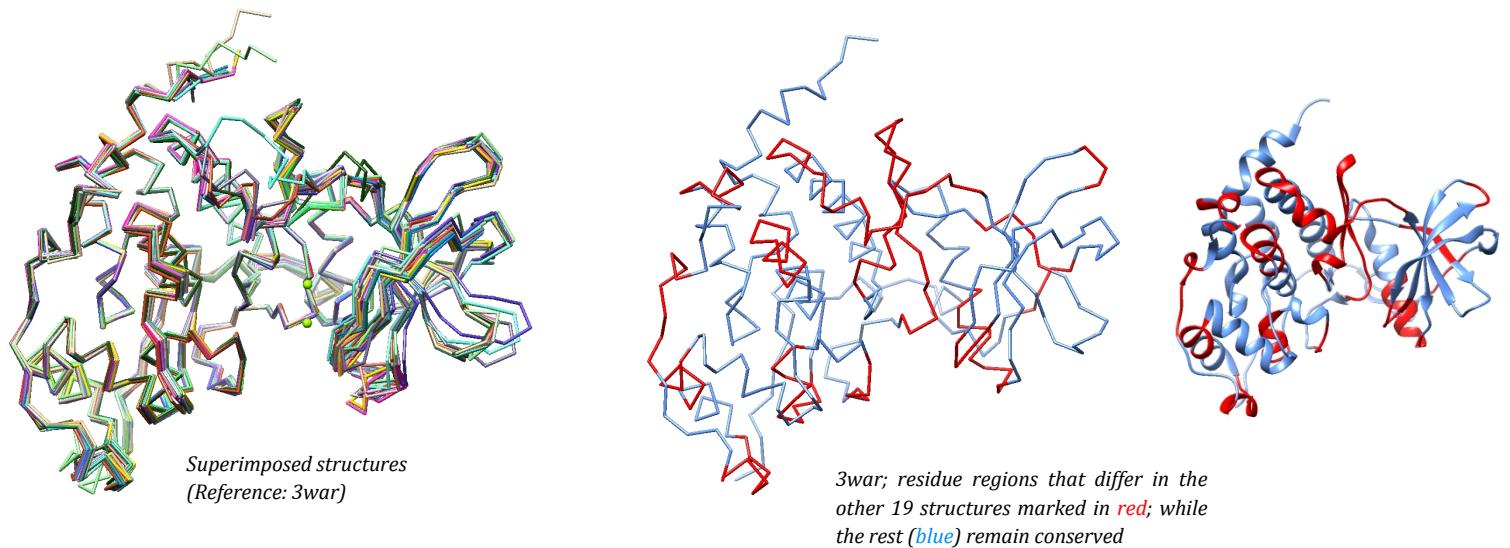
Per residue RMSD (3war/3bqc)



Per residue RMSD (Reference: 3war, Sample: x)



Regions of variability of samples with respect to reference structure (3war)



Principle Component Analysis

1. Standardize dataset (order $m \times n$) :

$$x_{new} = \frac{x - \mu}{\sigma}$$

$$\begin{bmatrix} x_{11} & \cdots & x_{1n} \\ \vdots & \ddots & \vdots \\ x_{m1} & \cdots & x_{mn} \end{bmatrix} \quad \dots(i)$$

2. Find Covariance Matrix for the whole dataset (order $n \times n$):

$$cov(x, y) = \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{N}$$

$$\begin{bmatrix} x_{11} & \cdots & x_{1n} \\ \vdots & \ddots & \vdots \\ x_{n1} & \cdots & x_{nn} \end{bmatrix} \quad \dots(ii)$$

3. Calculate Eigenvalues and Eigenvectors:

Let A be a square matrix (the covariance matrix), v be a vector and λ a scalar such that:

$$\begin{aligned} Av &= \lambda v \\ Av - \lambda v &= 0 \\ A - \lambda I &= 0 \end{aligned}$$

$$|A - \lambda I| = 0 \quad \dots(iii)$$

To get Eigenvectors, substitute λ and solve for :

$$(A - \lambda I) \cdot v = 0$$

$$\begin{pmatrix} x_{11} & \cdots & x_{1n} \\ \vdots & \ddots & \vdots \\ x_{n1} & \cdots & x_{nn} \end{pmatrix} \cdot \begin{pmatrix} v_1 \\ \vdots \\ v_n \end{pmatrix} = 0 \quad \dots(iv)$$

Now, a Eigenvector matrix can be build from changing λ values:

$$\begin{pmatrix} e_{11} & \cdots & e_{1n} \\ \vdots & \ddots & \vdots \\ e_{n1} & \cdots & e_{nn} \end{pmatrix} \dots(v)$$

Sort eigenvalues and their corresponding eigenvectors: and pick k eigenvalues to form a matrix of eigenvectors:

$$\begin{pmatrix} e_{11} & \cdots & e_{1(n-k)} \\ \vdots & \ddots & \vdots \\ e_{n1} & \cdots & e_{n(n-k)} \end{pmatrix} \dots(vi)$$

The data set can now be transformed using the original standardized dataset of order $(m \times n)$ and the eigenvector matrix of order $(n \times k)$:

$$\begin{bmatrix} x_{11} & \cdots & x_{1n} \\ \vdots & \ddots & \vdots \\ x_{m1} & \cdots & x_{mn} \end{bmatrix} \cdot \begin{bmatrix} e_{11} & \cdots & e_{1(n-k)} \\ \vdots & \ddots & \vdots \\ e_{n1} & \cdots & e_{n(n-k)} \end{bmatrix} = \begin{bmatrix} e_{11} & \cdots & e_{1k} \\ \vdots & \ddots & \vdots \\ e_{m1} & \cdots & e_{mk} \end{bmatrix} \dots(vii)$$

$\begin{bmatrix} e_{11} & \cdots & e_{1k} \\ \vdots & \ddots & \vdots \\ e_{m1} & \cdots & e_{mk} \end{bmatrix}$ is now the transformed matrix of the desired order.