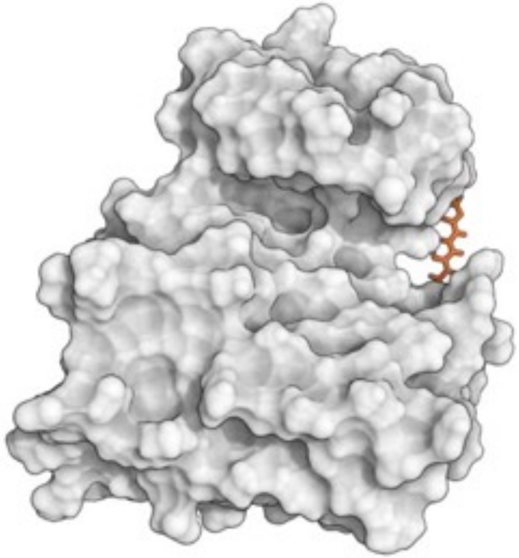
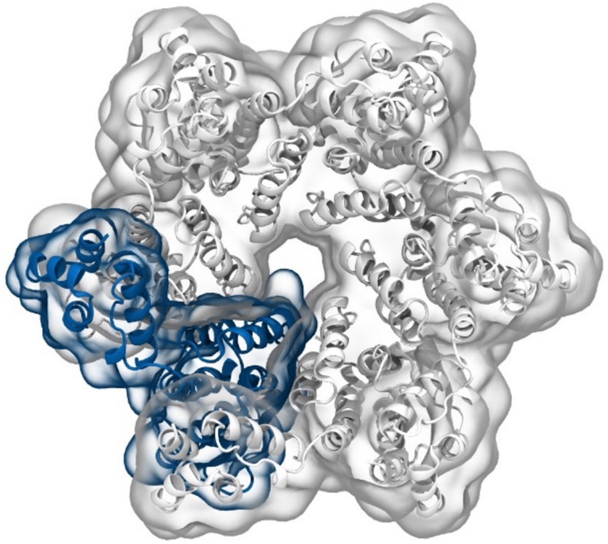
Simulation of Biomolecules



Dimensionality Reduction



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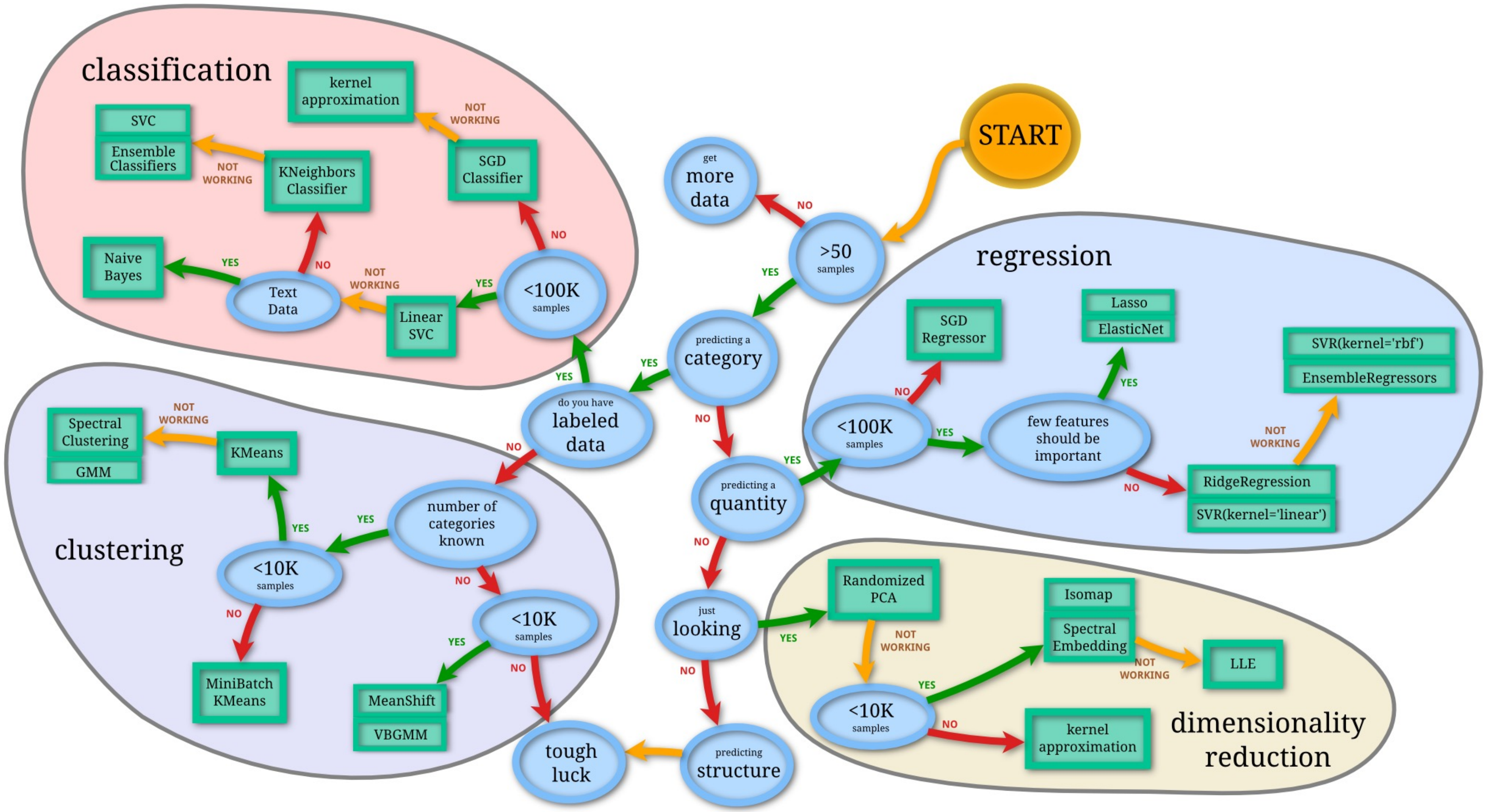
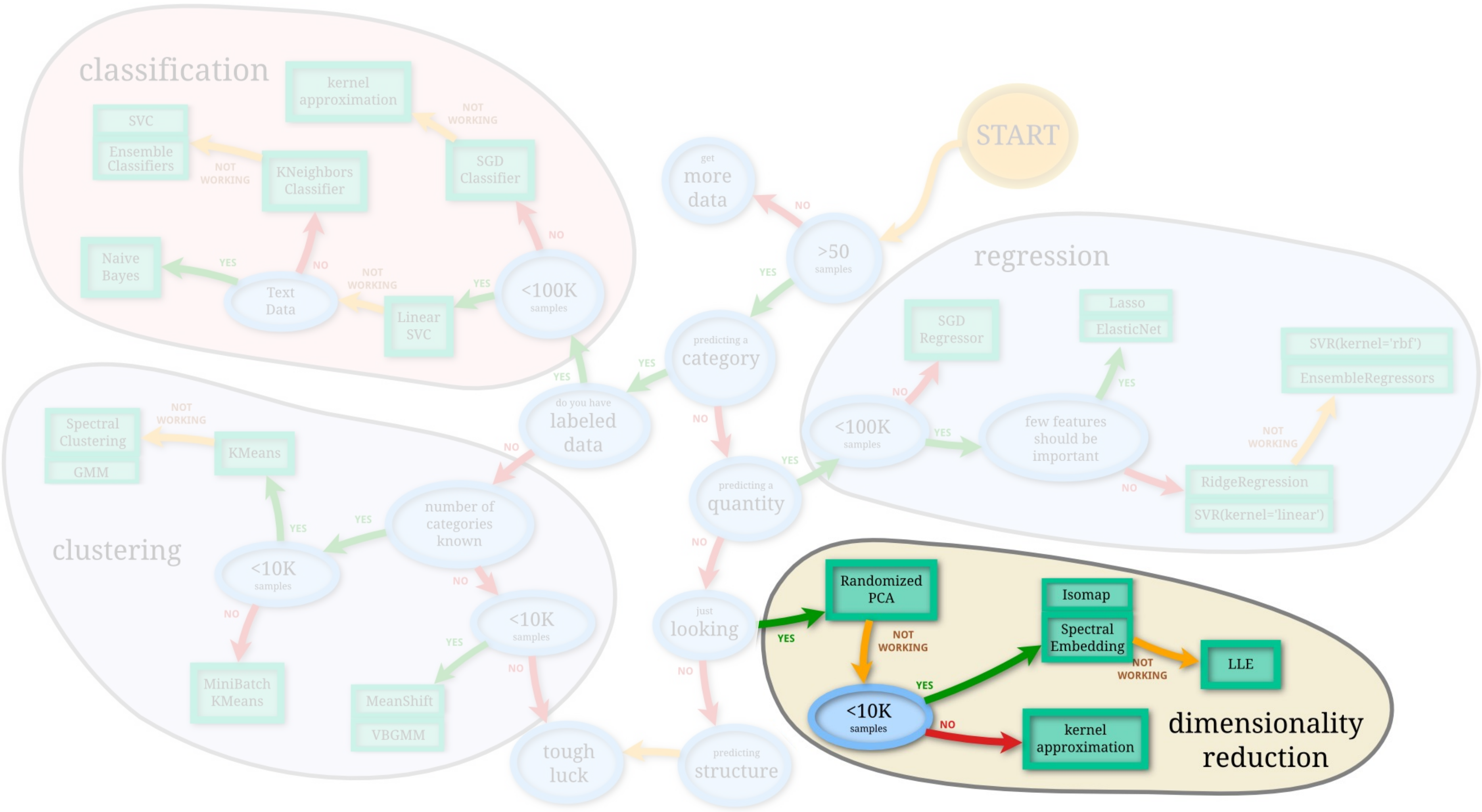
The Data Mining world



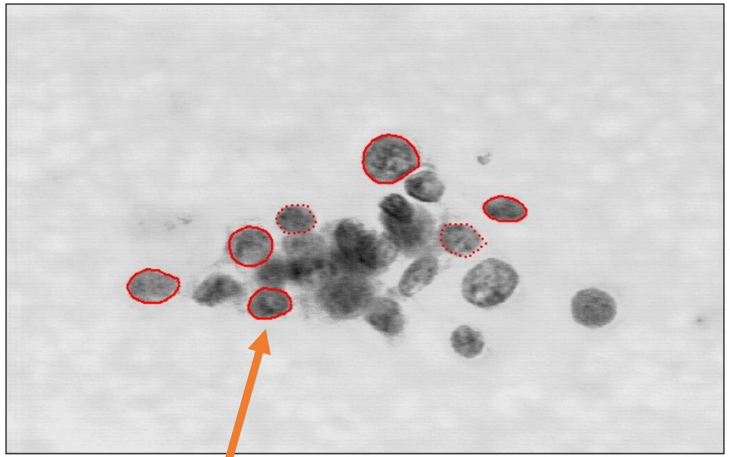
From **scikit-learn.org**

The Data Mining world



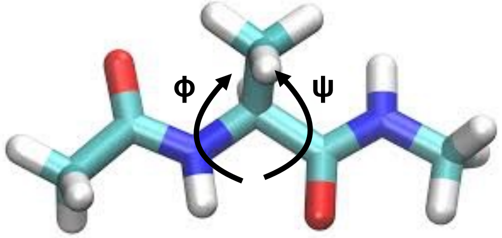
From **scikit-learn.org**

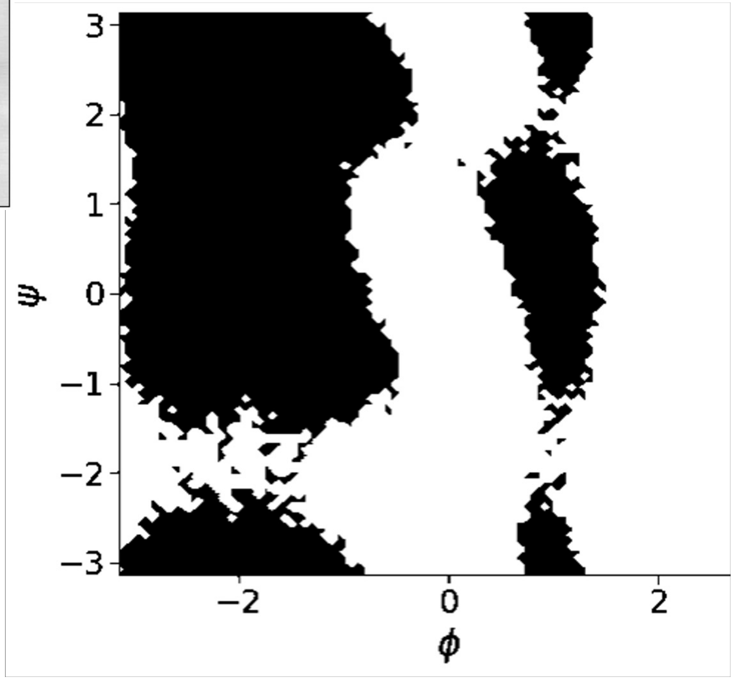
features are possible ways to represent data



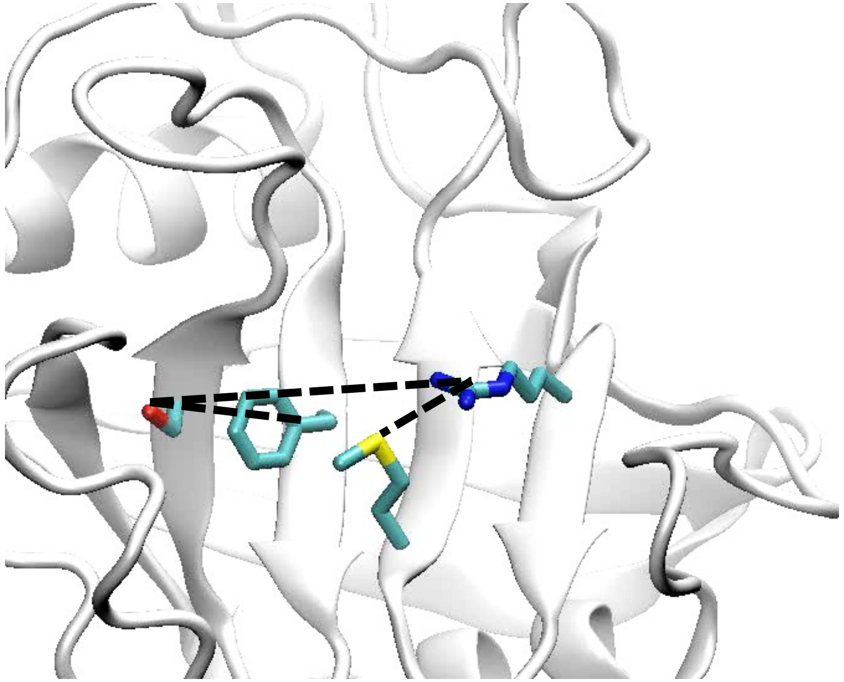
Sphericity (***1***)

Pixels colour
(28x28 = ***784***)





Torsional angles (***2***)



atomic positions (***459***)
atomic distances (***3***)

Not all features are useful

Task: predict the weather in Edinburgh using historical data

data = {X, Y, Z} → sun, rain, snow

{Temperature (C), ~~Temperature (K)~~, Humidity (g/m^3)}

2 decorrelated features

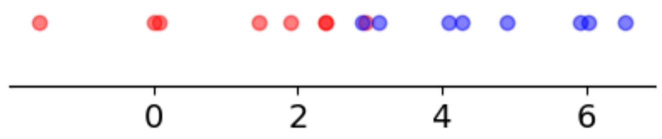
{Temperature (C), ~~Swiss cheese export (£)~~, Humidity (g/m^3)}

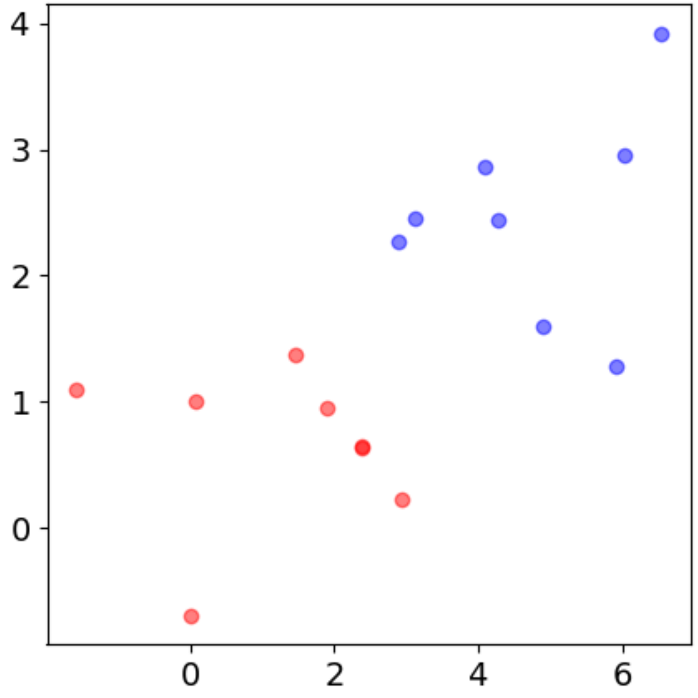
2 relevant features

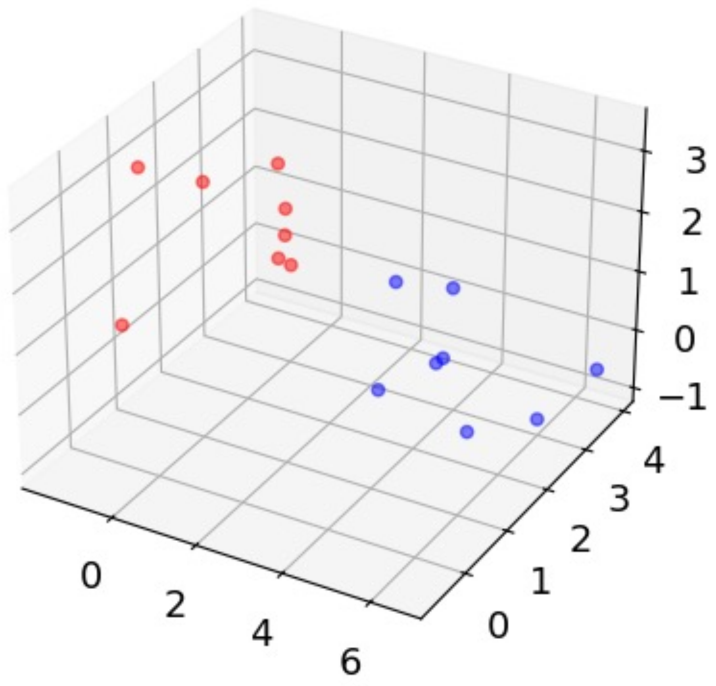
{Avg. gas expenditure (£), Heat strokes (#), Slipping accidents (#), Sunscreen sold (£)}

4 features connected to another quantity temperature

Curse of dimensionality





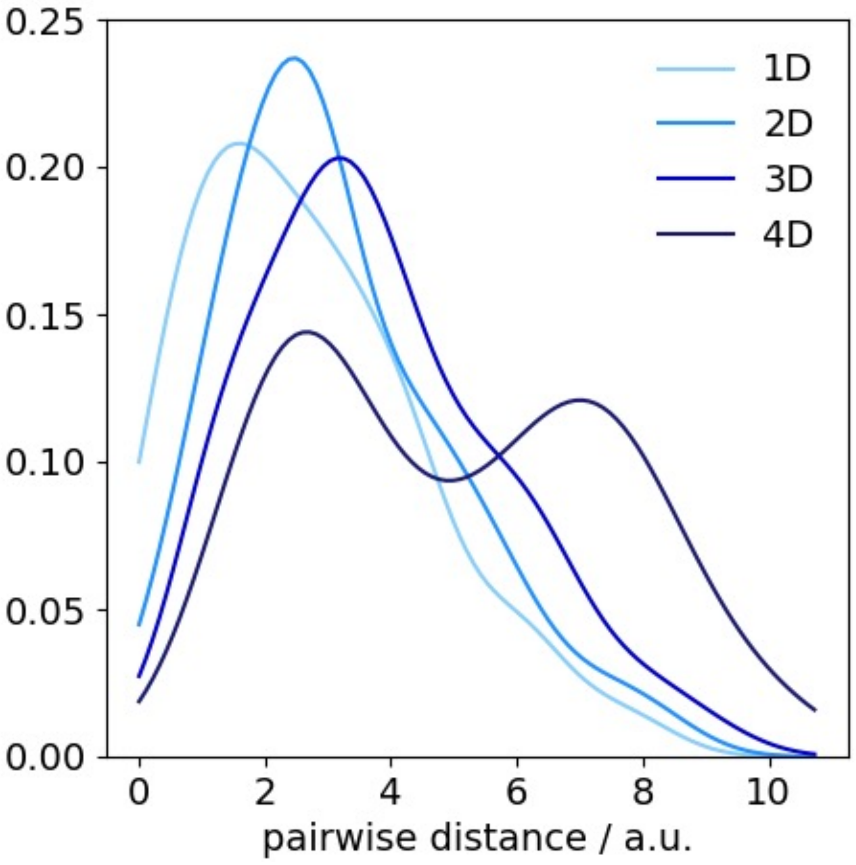


$$\|x\|_2 = \sqrt{\sum_{i=1}^{N} x_i^2}$$

Distances between M data points $\boldsymbol{x} \in \mathbb{R}^N$ increase, when N increases

Problem: less data density increases uncertainty on underlying data structure

[Extra] Curse of dimensionality



Distribution of pairwise distances between points shown in previous slide

$$\|x\|_2 = \sqrt{\sum_{i=1}^{N} x_i^2}$$

Distances between M data points $\boldsymbol{x} \in \mathbb{R}^N$ increase, when N increases

Problem: less data density increases uncertainty on underlying data structure

Reducing features increases data density

- Chose appropriate features [expert user]

- Remove features

- Find a lower dimensional representation *E* of features *X*

$$\{ X_1 , \ X_2 , \ldots , X_N \}$$

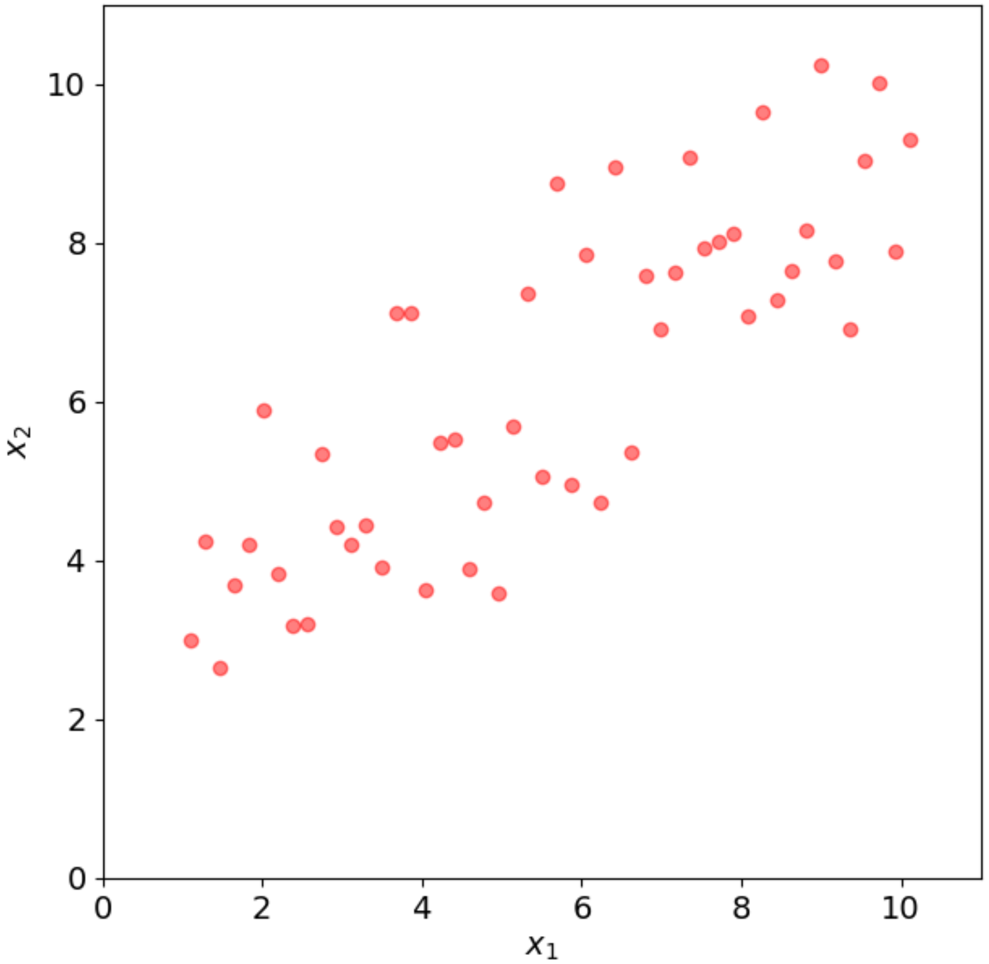
$$\{ E_1 , E_2 , \ldots , E_K \}$$

$E_i = f(\{X\})$

where $K < N$

Principal Components Analysis (PCA)

Let $\boldsymbol{X}$ a dataset of M datapoints in N dimensions (here, M=50 and N=2)



- Center data:

$$\boldsymbol{X}' = \boldsymbol{X} - \mu$$

- Compute data covariance matrix $\boldsymbol{C}$:

$$c_{i,j} = \frac{1}{M}\sum_{k=1}^{M} \boldsymbol{x}'_i \boldsymbol{x}'_j$$

- Calculate eigenvalue decomposition:

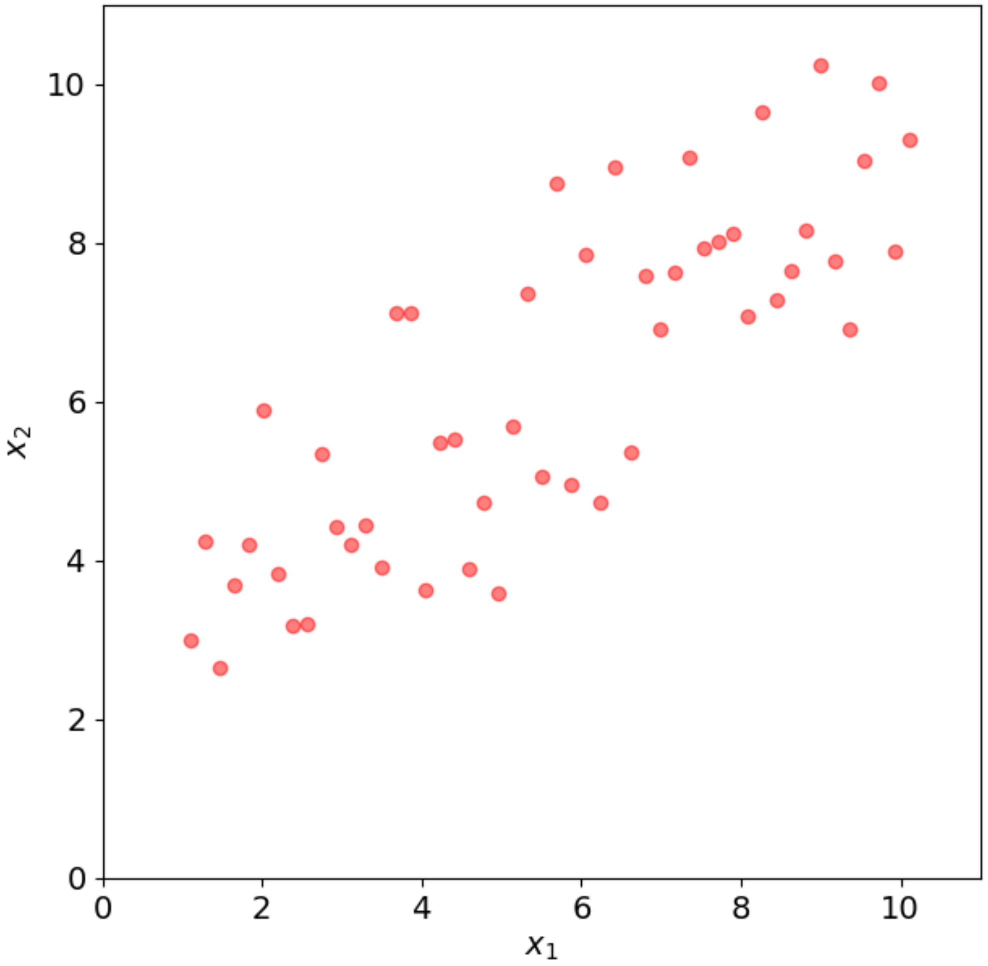
$$\boldsymbol{C} = \boldsymbol{V}\boldsymbol{\lambda}\boldsymbol{V}^{-1}$$

*N*x*N* matrix of ***eigenvectors***

*N*x*N* diagonal matrix of ***eigenvalues***

[Extra] Principal Components Analysis (PCA)

Let $\boldsymbol{X}$ a dataset of M datapoints in N dimensions (here, M=50 and N=2)



An eigenvector $\boldsymbol{v}$ of $\boldsymbol{C}$ respects:

$$\boldsymbol{C}\boldsymbol{v} = \boldsymbol{\lambda}\boldsymbol{v}$$

Find eigenvalues as the roots of the characteristic polynomial:

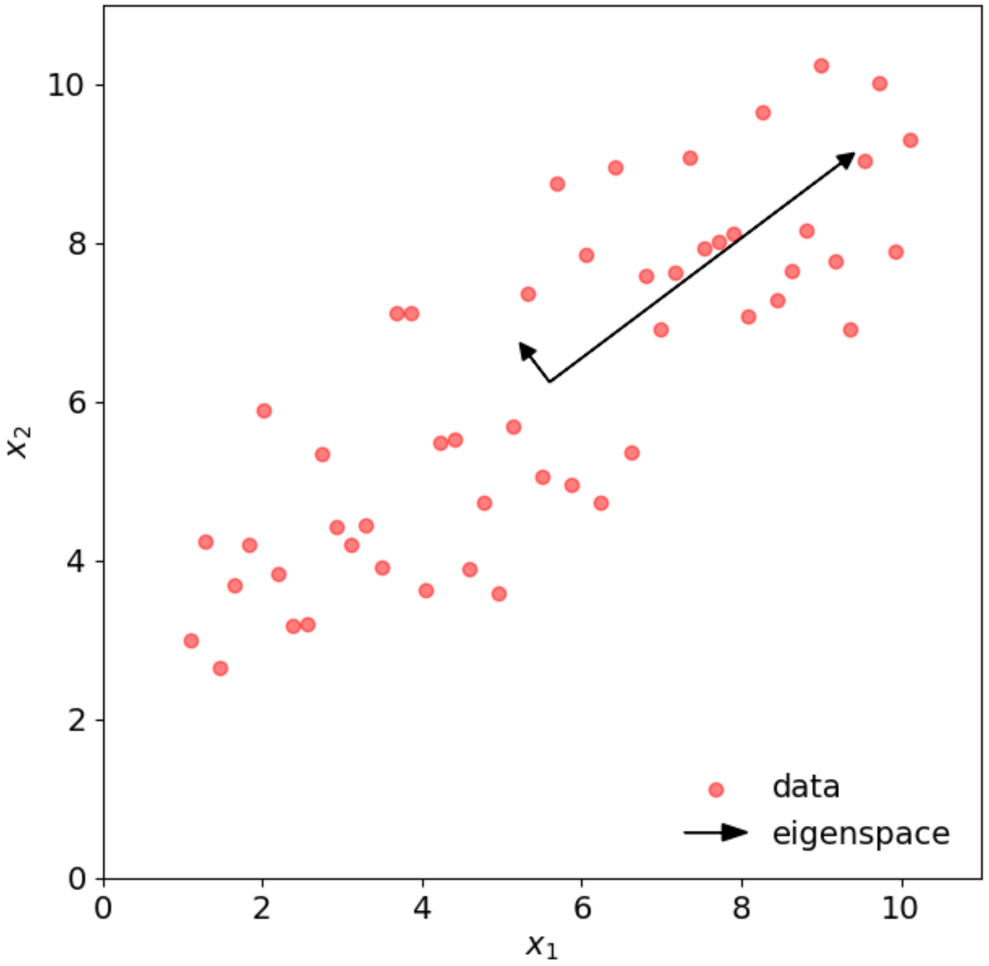
$$p(\boldsymbol{\lambda}) = \det(\boldsymbol{C} - \boldsymbol{\lambda}\boldsymbol{I}) = 0$$

The i-th eigenvector $\boldsymbol{v_i}$ is found by solving:

$$\boldsymbol{C}\boldsymbol{v_i} = \boldsymbol{\lambda_i}\boldsymbol{v_i}$$

Principal Components Analysis (PCA)

Let $\boldsymbol{X}$ a dataset of M datapoints in N dimensions (here, M=50 and N=2)



$$\boldsymbol{C} = \boldsymbol{V}\boldsymbol{\lambda}\boldsymbol{V}^{-1}$$

$\boldsymbol{V} = [\boldsymbol{v}_1 \dots \boldsymbol{v}_N]$ eigenvectors: orthonormal base

$\boldsymbol{\lambda}$ eigenvalues: scalars defining the importance of each eigenvector

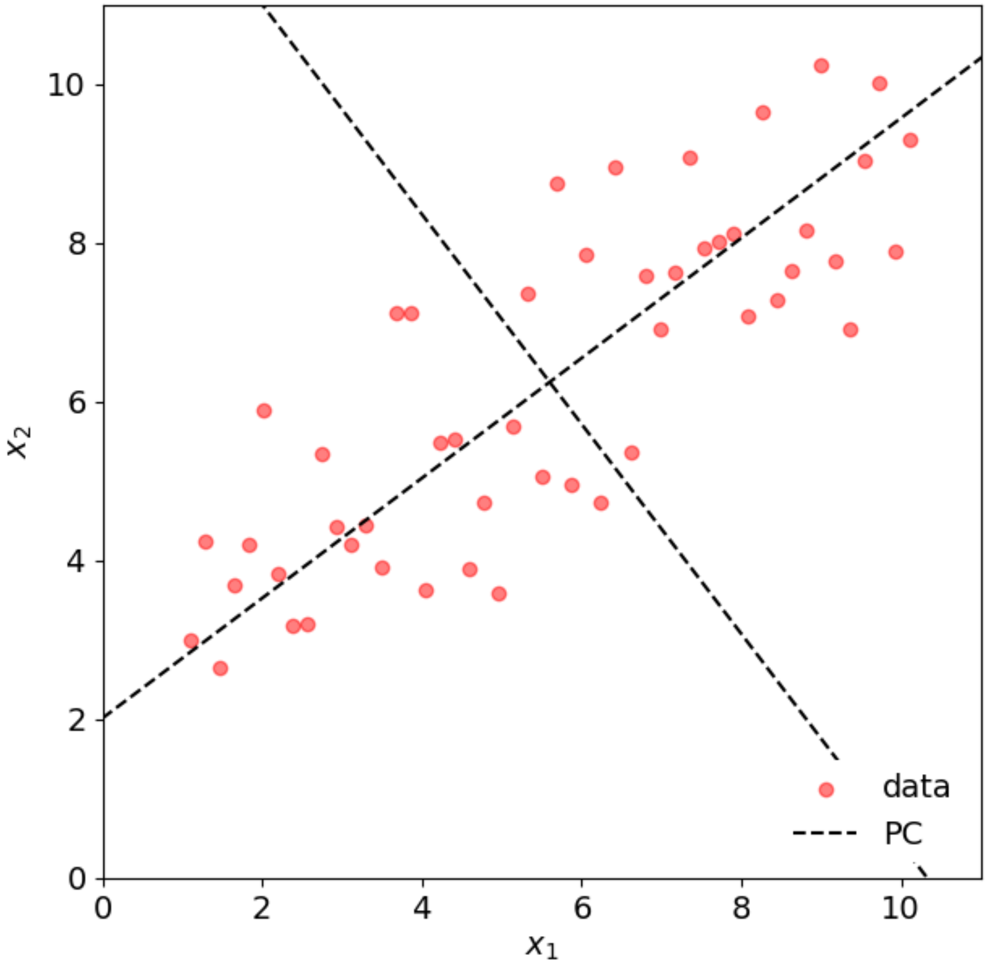
Importance $\boldsymbol{r}_i$ of each eigenvector $\boldsymbol{v}_i$:

$$\boldsymbol{r}_i = \frac{\boldsymbol{\lambda}_i}{\sum \boldsymbol{\lambda}}$$

Sort $\boldsymbol{V}$ and $\boldsymbol{\lambda}$ according to $\boldsymbol{\lambda}$

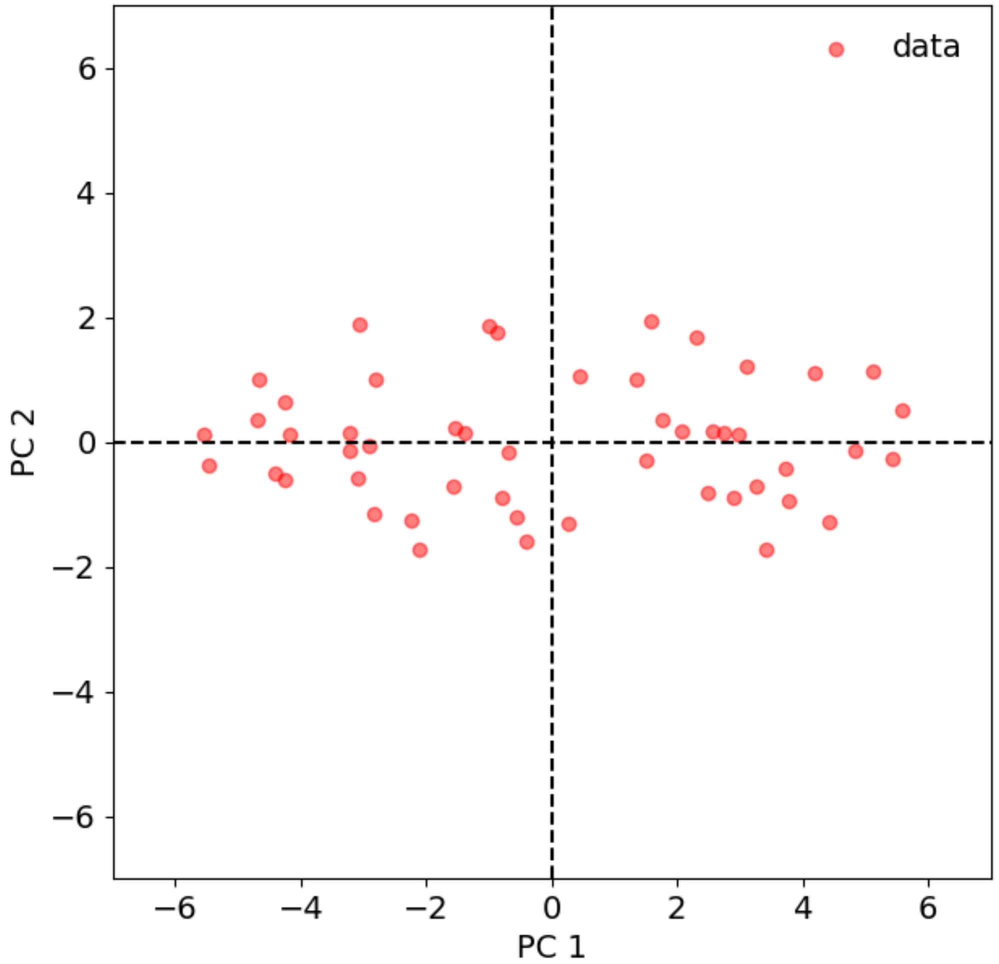
Projection into the eigenspace

Let **X** a dataset of *M* datapoints in *N* dimensions (here, *M*=50 and *N*=2)



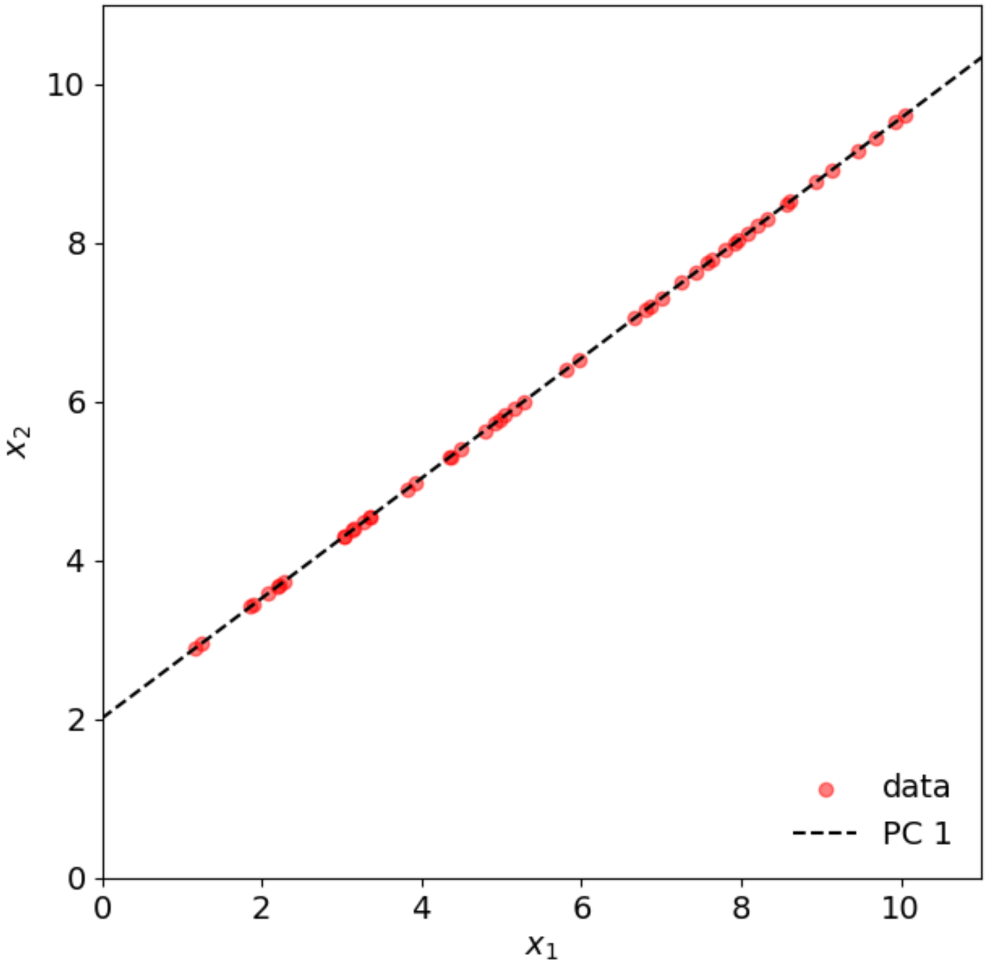
$$p = \boldsymbol{V}^T(\boldsymbol{x} - \mu)$$

transform



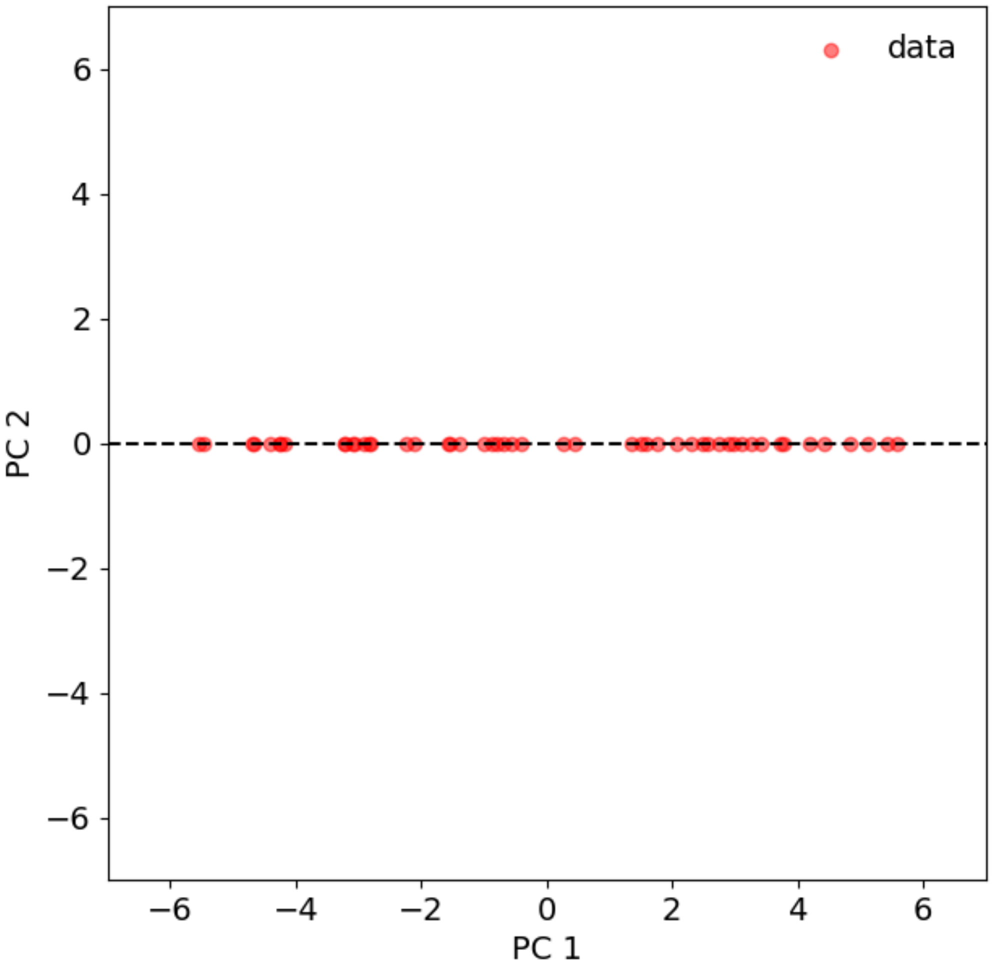
Dimensionality reduction

Remove dimensions that least contribute to data variance



$$p = \boldsymbol{V}^T(\boldsymbol{x} - \mu)$$

transform

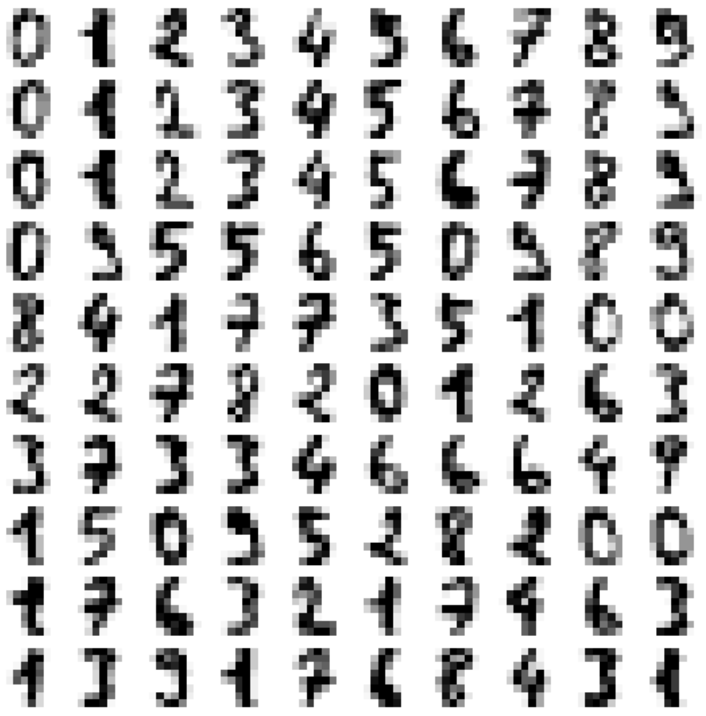


[Example 1] Representing written digits

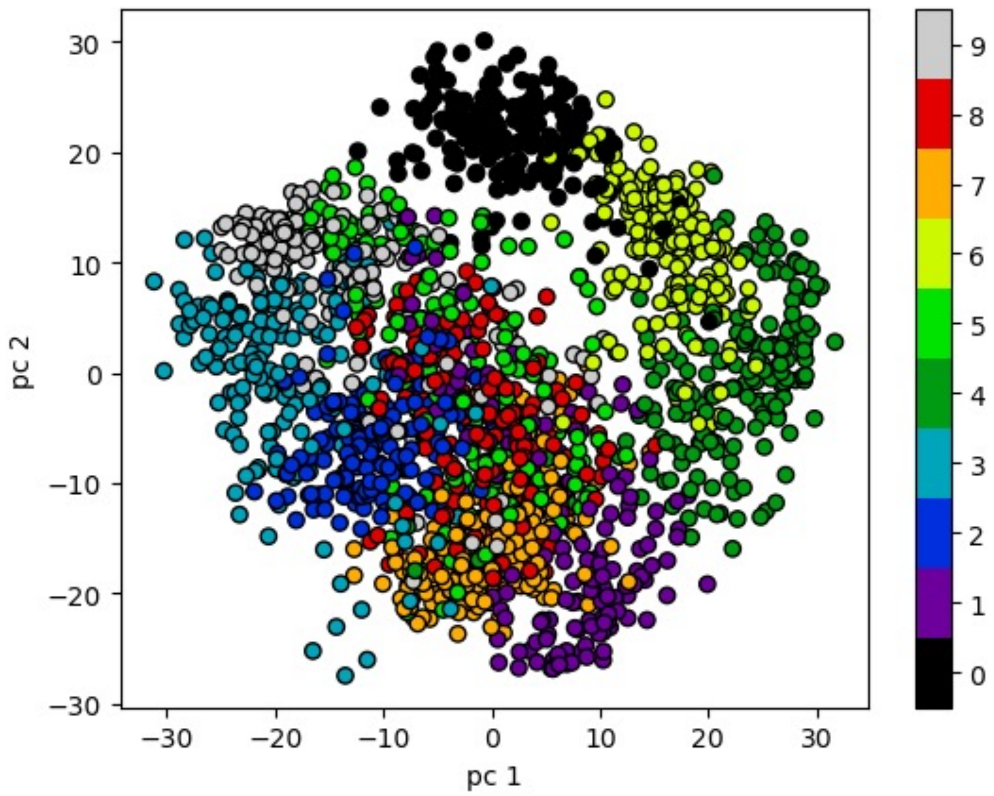
MNIST database of written digits

Input is a vector of 64 dimensions

8x8 pixel digits

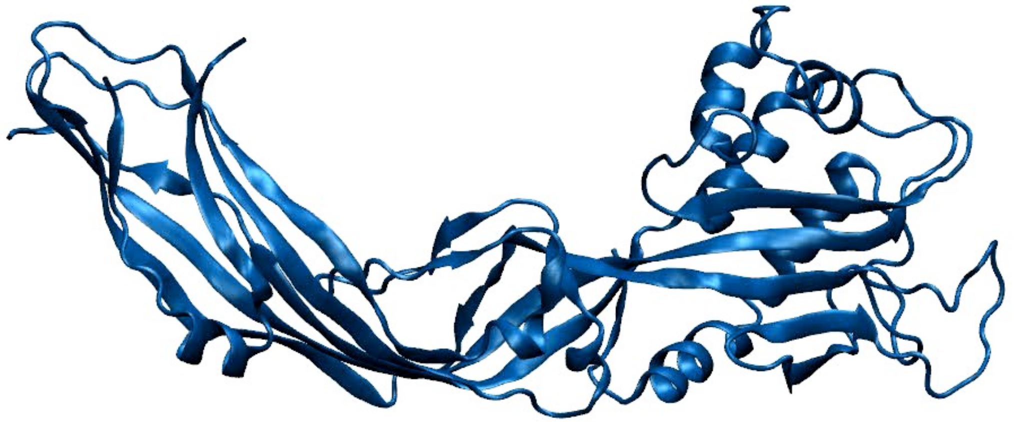


2 principal components manage to project a few of the digits in a similar area of space!

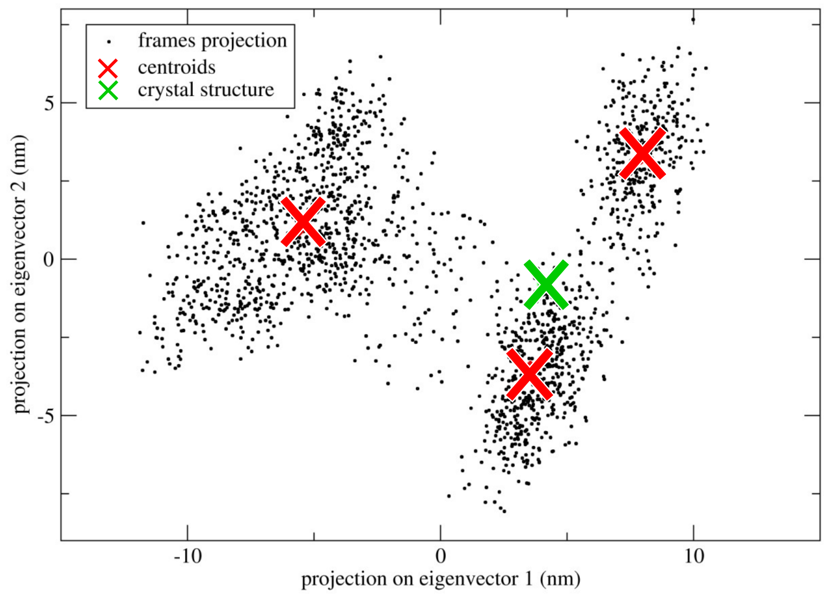


[Example] Identifying dominant motions in proteins

Protein MD simulation

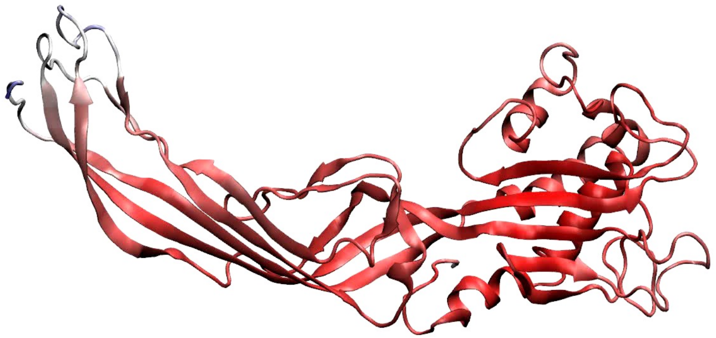


Eigenspace of Cα coordinates



- Simulations are complex and noisy

- select only first few PC (eigenvectors) to separate signal from noise



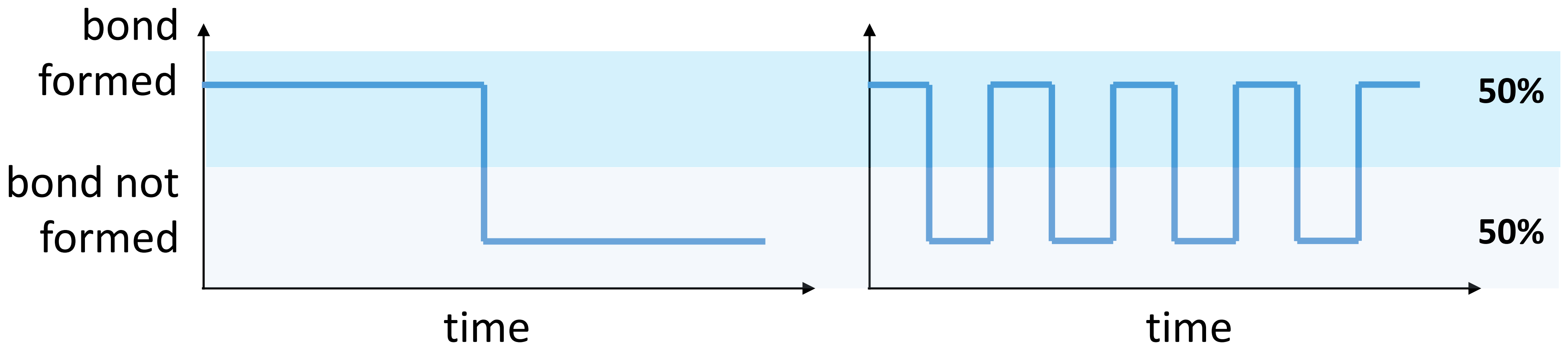
Degiacomi, M.T. & Dal Peraro, M.. *Macromolecular symmetric assembly prediction using swarm intelligence dynamic modeling*. ***Structure***, 2013

Time-lagged independent component analysis (tICA)

tICA is a **linear transform** similar to PCA

The transform is chosen such that, amongst all linear transforms, tICA **maximizes the autocorrelation** of transformed coordinates.

Thought experiment: typically hydrogen bond is considered established if donor-acceptor distance <2.5 Å, and donor-acceptor-hydrogen angle <20°.



reporting % time a bond is established in simulation can be misleading!

Time-lagged independent component analysis (tICA)

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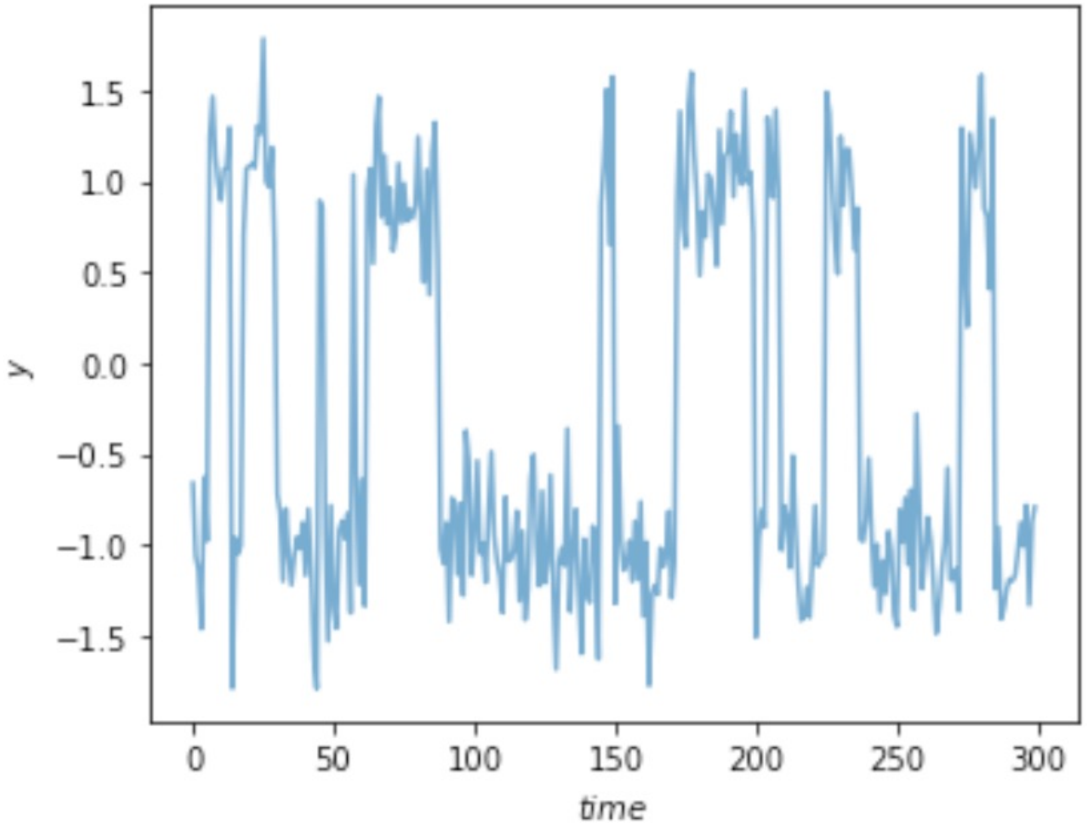
$\mathbf{r}(t) = (r_i(t))_{i=1,\ldots,D}$

D-dimensional input data vector that is mean free, i.e., $\mathbf{r}(t) = \mathbf{r}(t) - \langle \mathbf{r}(t) \rangle_t$

Computing the covariance of the data at $t = 0$ and $t = \tau$ which is the lag-time chosen

$c_{ij}(\tau) = \langle r_i(t) r_j(t+\tau) \rangle_t$

enables computing two covariance matrices: $\mathbf{C}(0)$ and $\mathbf{C}(\tau)$



F. Nüske, […], A. S. J. S. Mey and F. Noé: ***JCTC***, 2014 G. Perez-Hernandez, et al., ***JCTC***, 2013 C. R. Schwantes et al., ***JCTC***, 2013

Time-lagged independent component analysis (tICA)

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The transform is chosen such that, amongst all linear transforms, tICA **maximizes the autocorrelation** of transformed coordinates.

Entries of the covariance matrix can be computed as:

$$c_{ij}(\tau) = \frac{1}{N-\tau-1}\sum_{t=1}^{N-\tau} r_i(t) r_j(t+\tau)$$

$\mathbf{C}(0)$ will be a symmetric matrix. The symmetry of $\mathbf{C}(\tau)$ will need to be enforced with:

$$\mathbf{C}(\tau) = \frac{1}{2}(\mathbf{C}_d(\tau) + \mathbf{C}_d^{\mathsf{T}}(\tau))$$

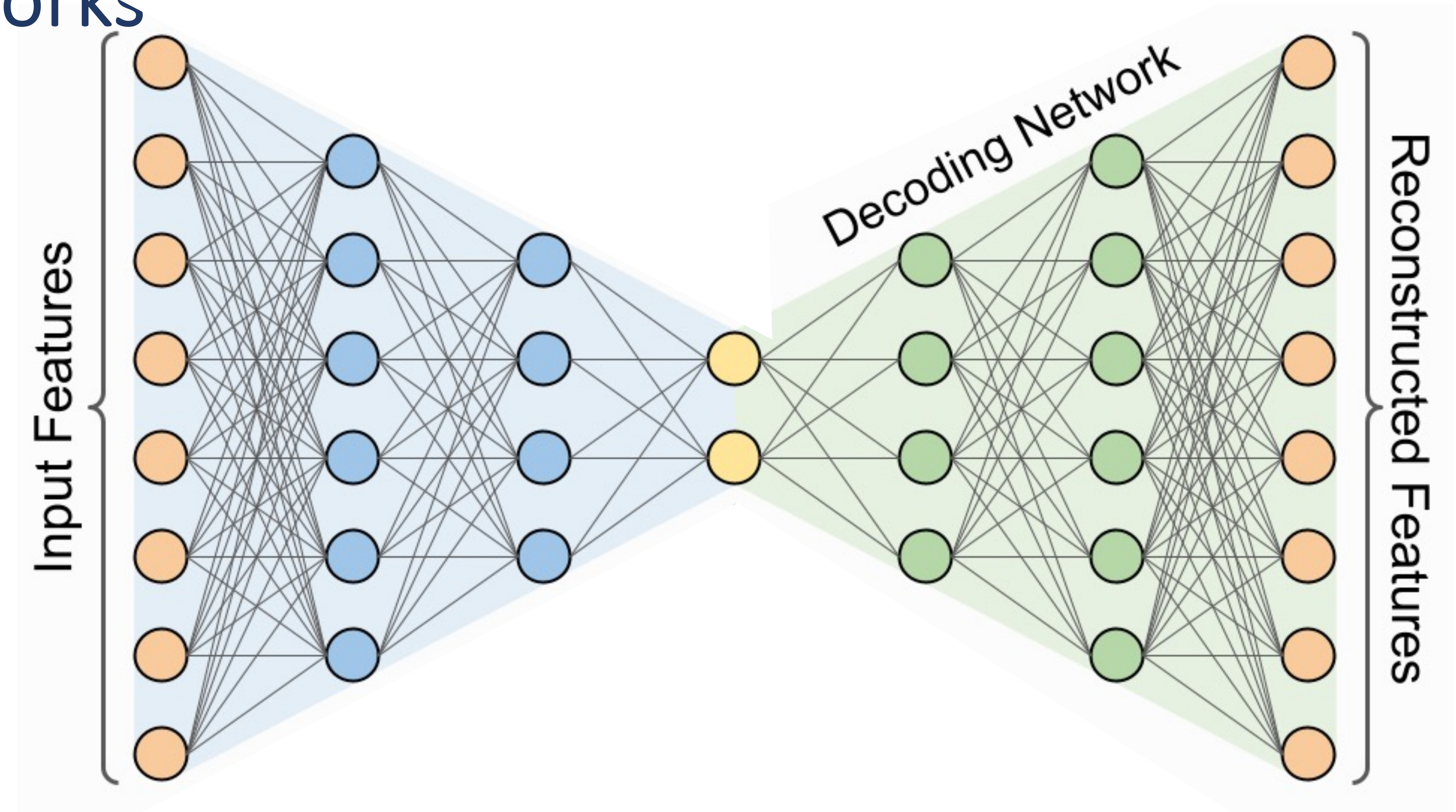
We can now solve the generalised eigenvalue problem:

$$\mathbf{C}(\tau)\mathbf{U} = \mathbf{C}(0)\mathbf{U}\mathbf{\Lambda} \longrightarrow \mathbf{z}^{\mathsf{T}}(t) = \mathbf{r}^{\mathsf{T}}(t)\mathbf{U}$$

Eigenvector matrix containing ICs **Diagonal matrix with eigenvalues** **M columns of full rank U for DR**

F. Nüske, […], A. S. J. S. Mey and F. Noé: *JCTC*, 2014 G. Perez-Hernandez, et al., ***JCTC***, 2013 C. R. Schwantes et al., ***JCTC***, 2013

[Extra] Dimensionality reduction with neural networks



PCA dimensionality reduction is *interpretable,* that of t-SNE and neural networks is not.