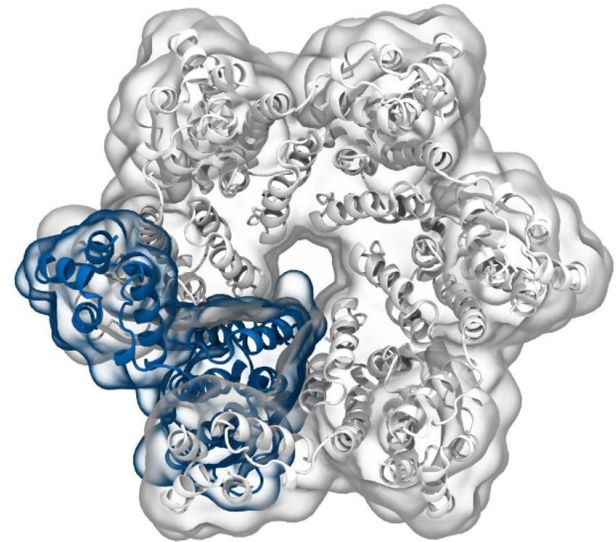
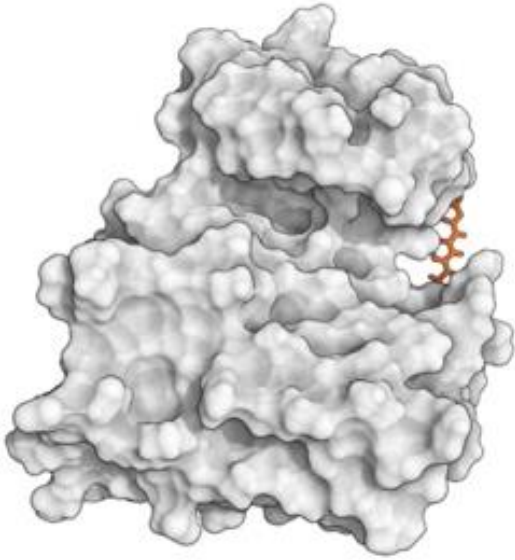


Simulation of Biomolecules

Dimensionality Reduction



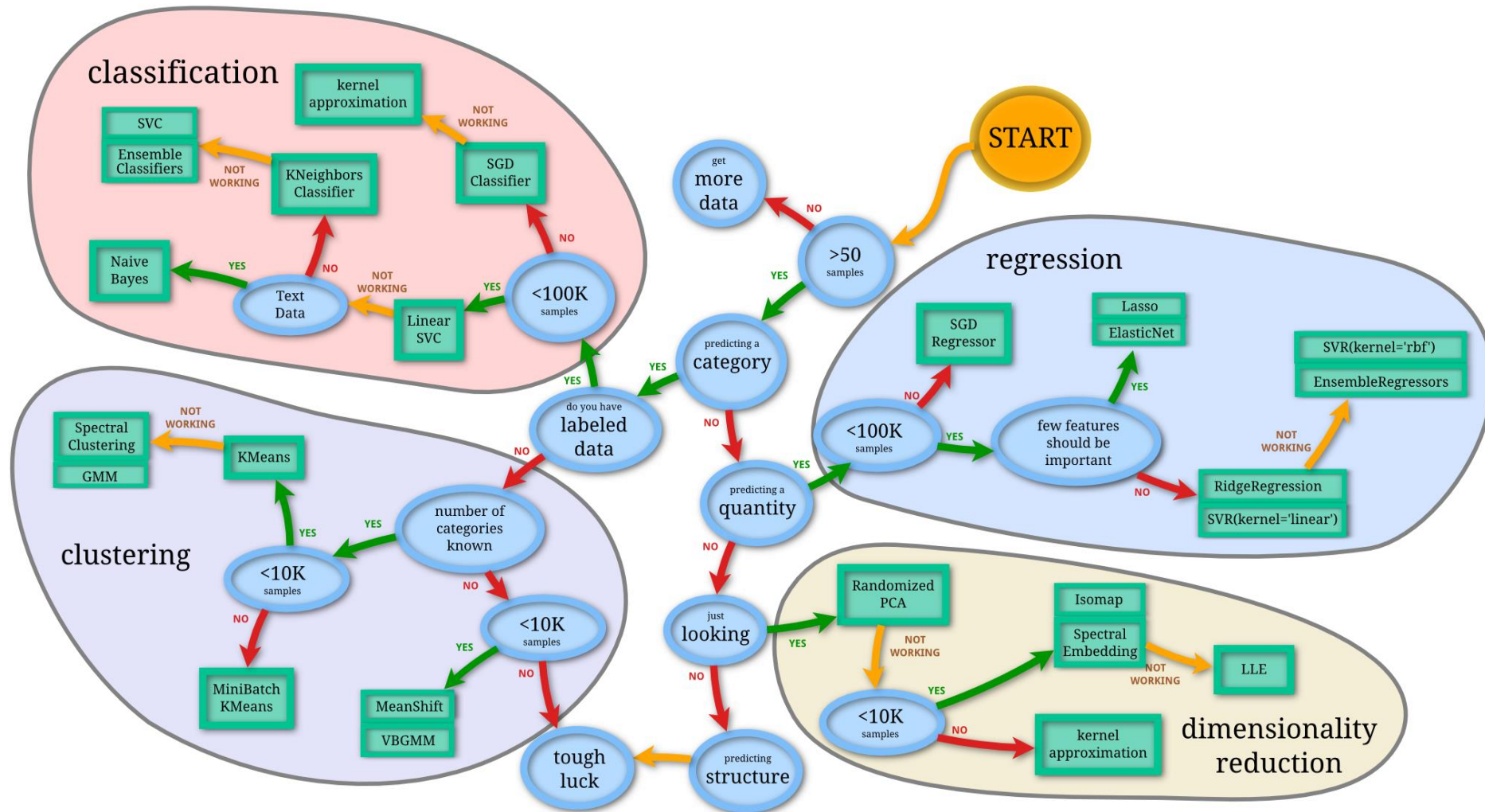
Dr Matteo Degiacomi
Durham University

matteo.t.degiacomini@durham.ac.uk

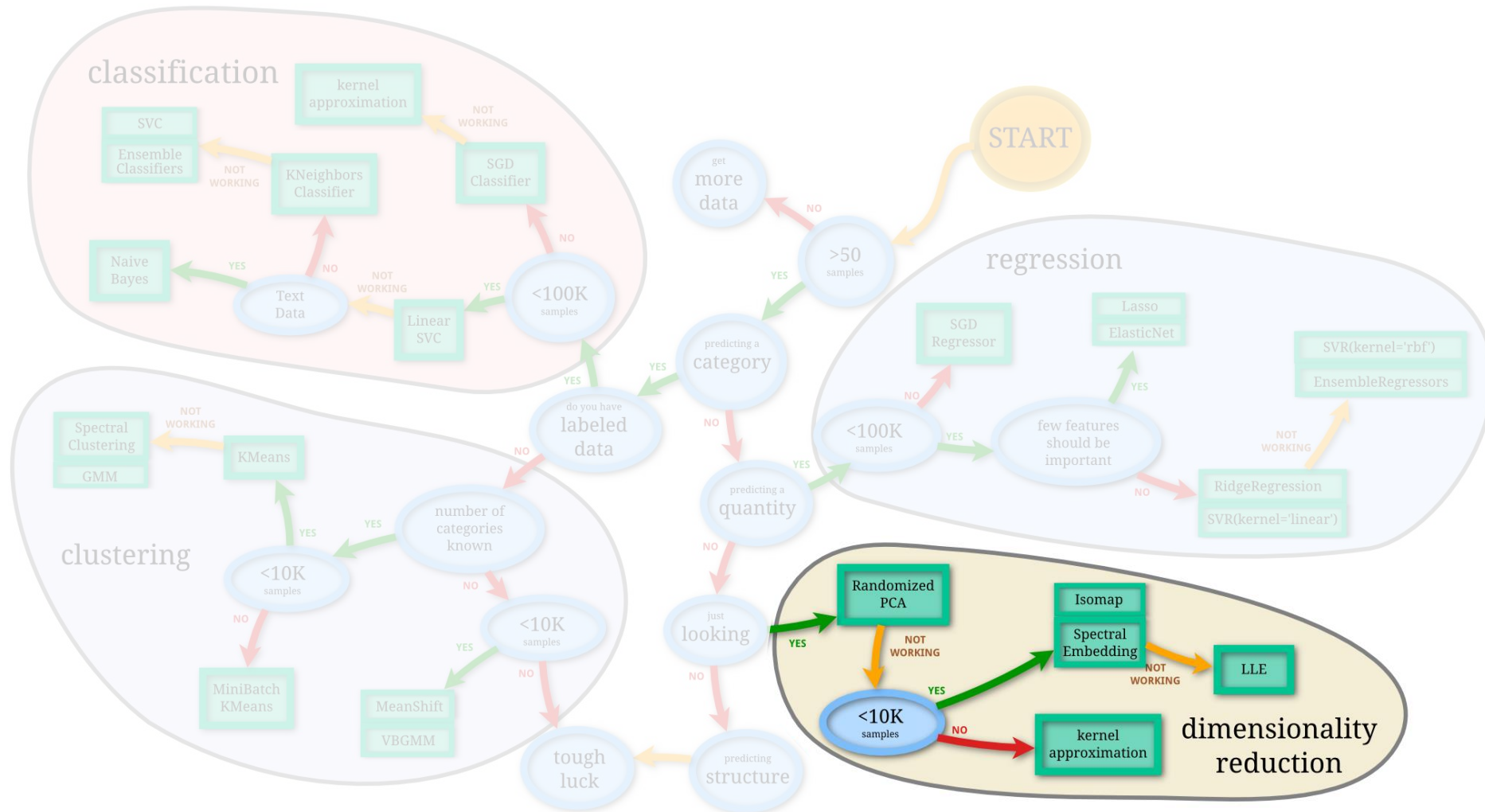
Dr Antonia Mey
University of Edinburgh

antonia.mey@ed.ac.uk

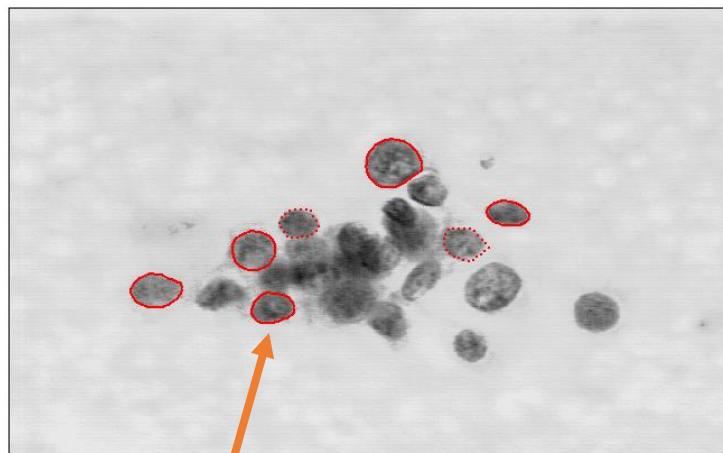
The Data Mining world



The Data Mining world

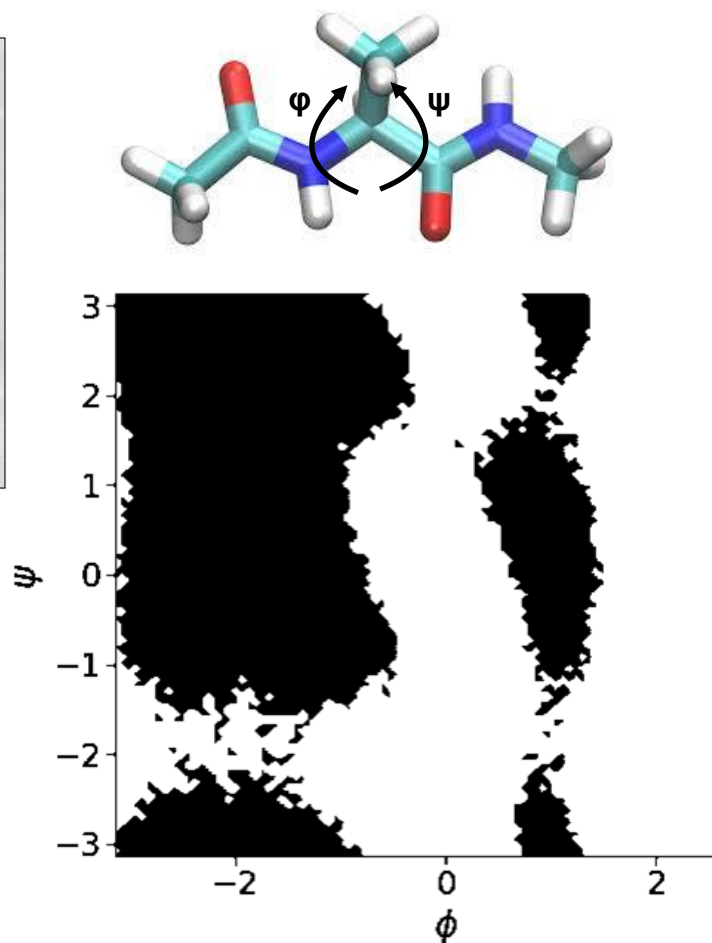


features are possible ways to represent data

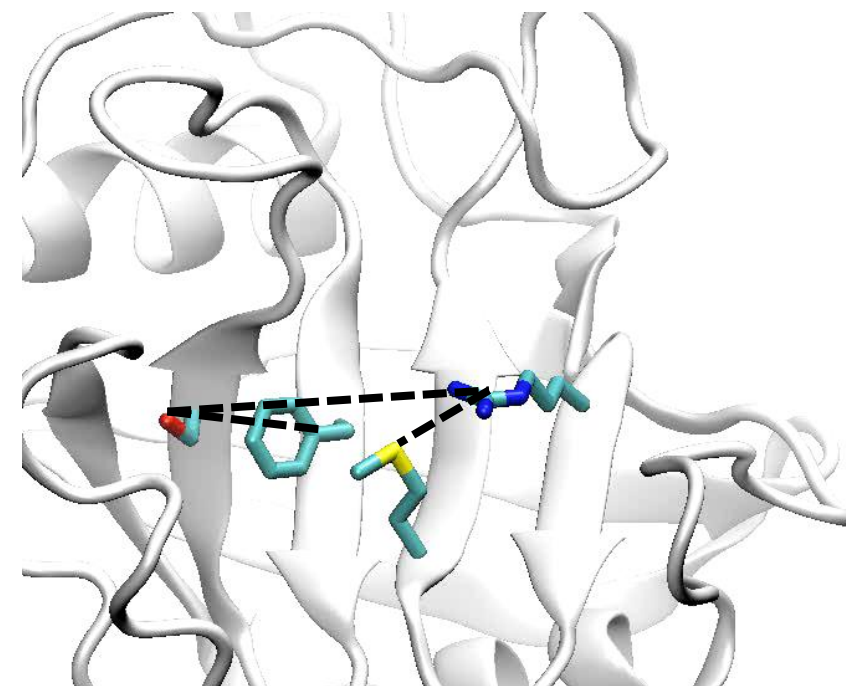


Sphericity (**1**)

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/m³)}

2 decorrelated
features

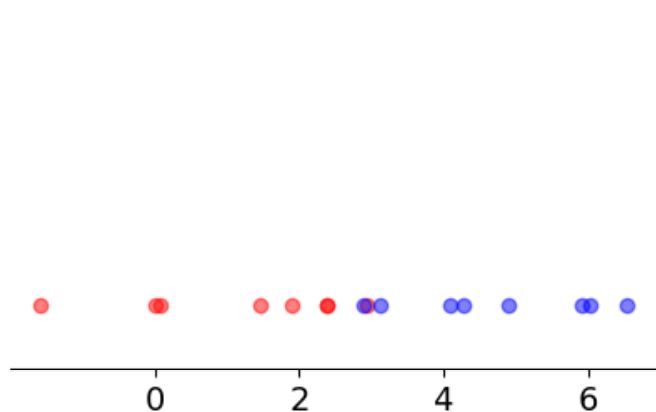
{Temperature (C),
~~Swiss cheese export (£)~~,
Humidity (g/m³)}

2 relevant
features

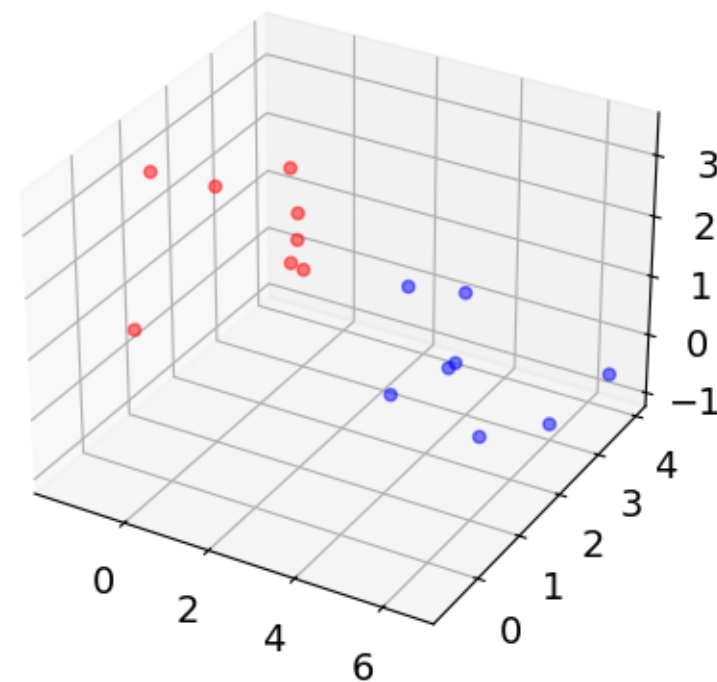
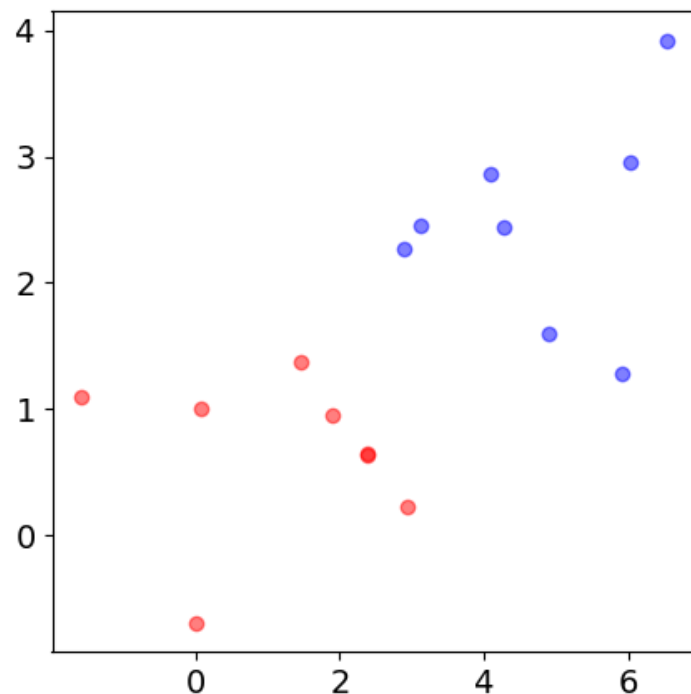
{Avg. gas expenditure (£),
Heat strokes (#),
Slipping accidents (#),
Sunscreen sold (£)}

4 features connected to
another quantity
temperature

Curse of dimensionality



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

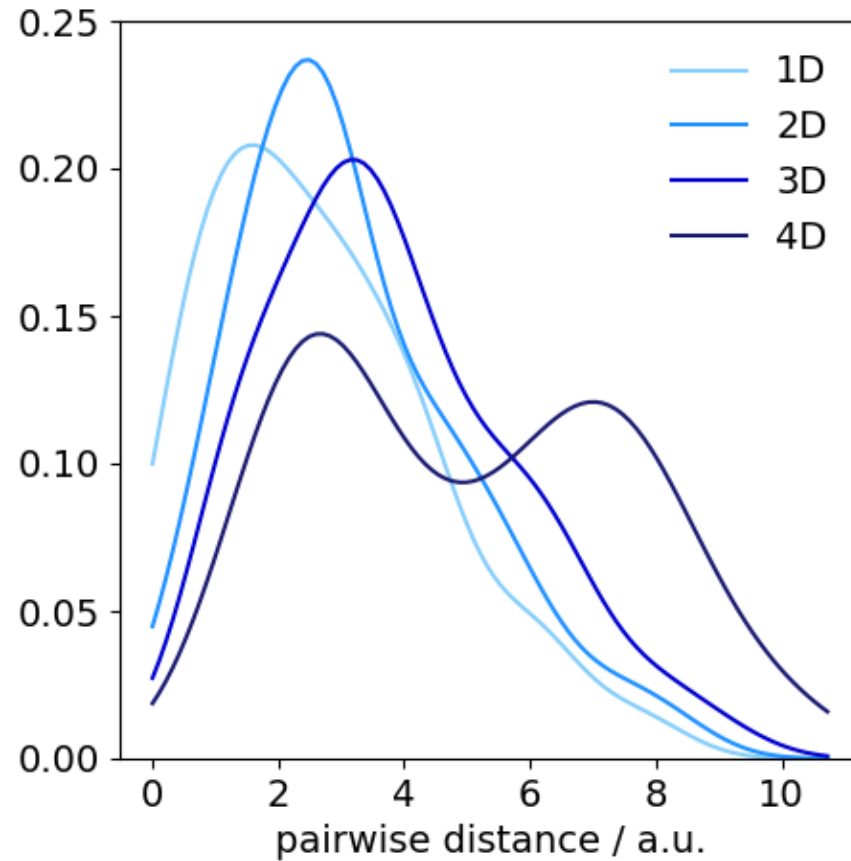


Distances between M data points $x \in \mathbb{R}^N$ increase, when N increases

Problem: less data density increases uncertainty on underlying data structure

[Extra] Curse of dimensionality

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



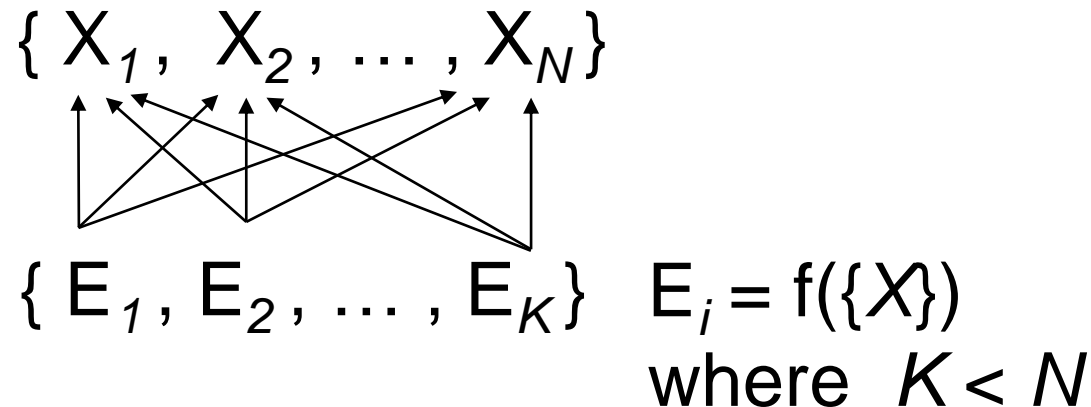
Distribution of pairwise distances between points shown in previous slide

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

Problem: less data density increases uncertainty on underlying data structure

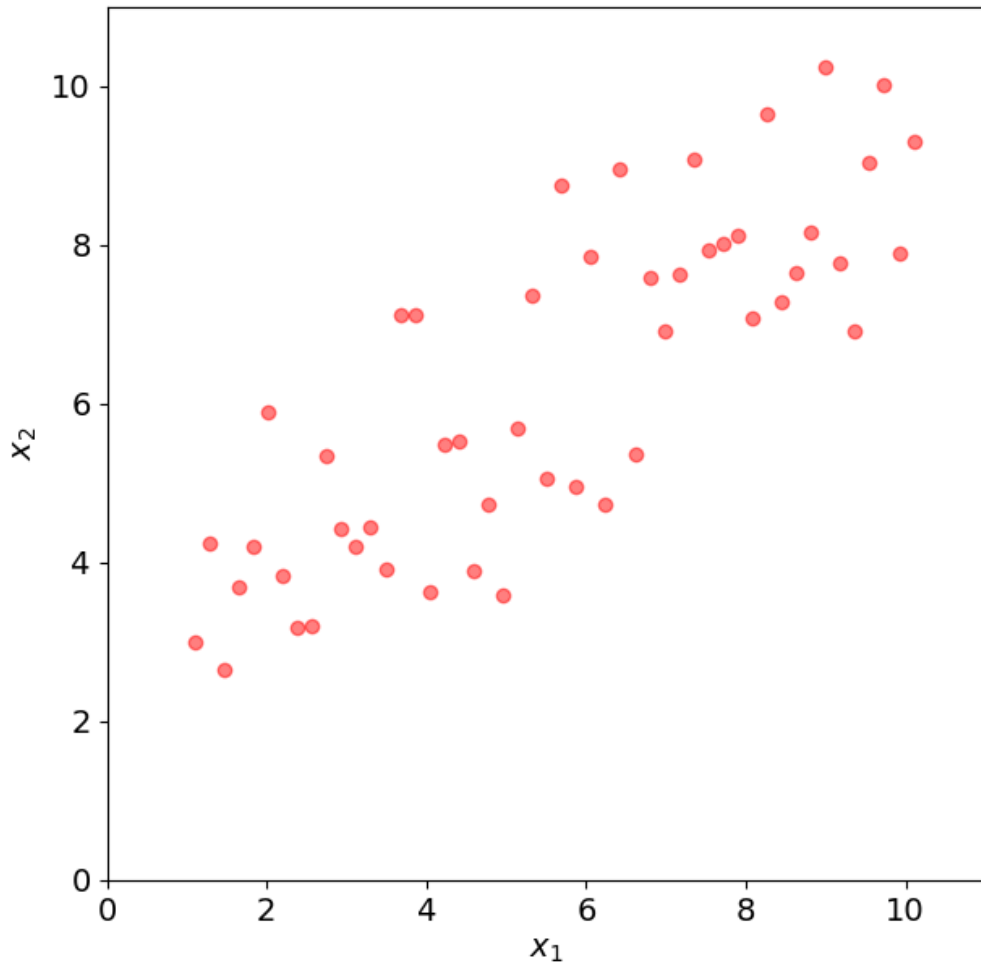
Reducing features increases data density

- Chose appropriate features [expert user]
- Remove features
- Find a lower dimensional representation E of features X



Principal Components Analysis (PCA)

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



- Center data:

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

- Compute data covariance matrix \mathbf{C} :

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

- Calculate eigenvalue decomposition:

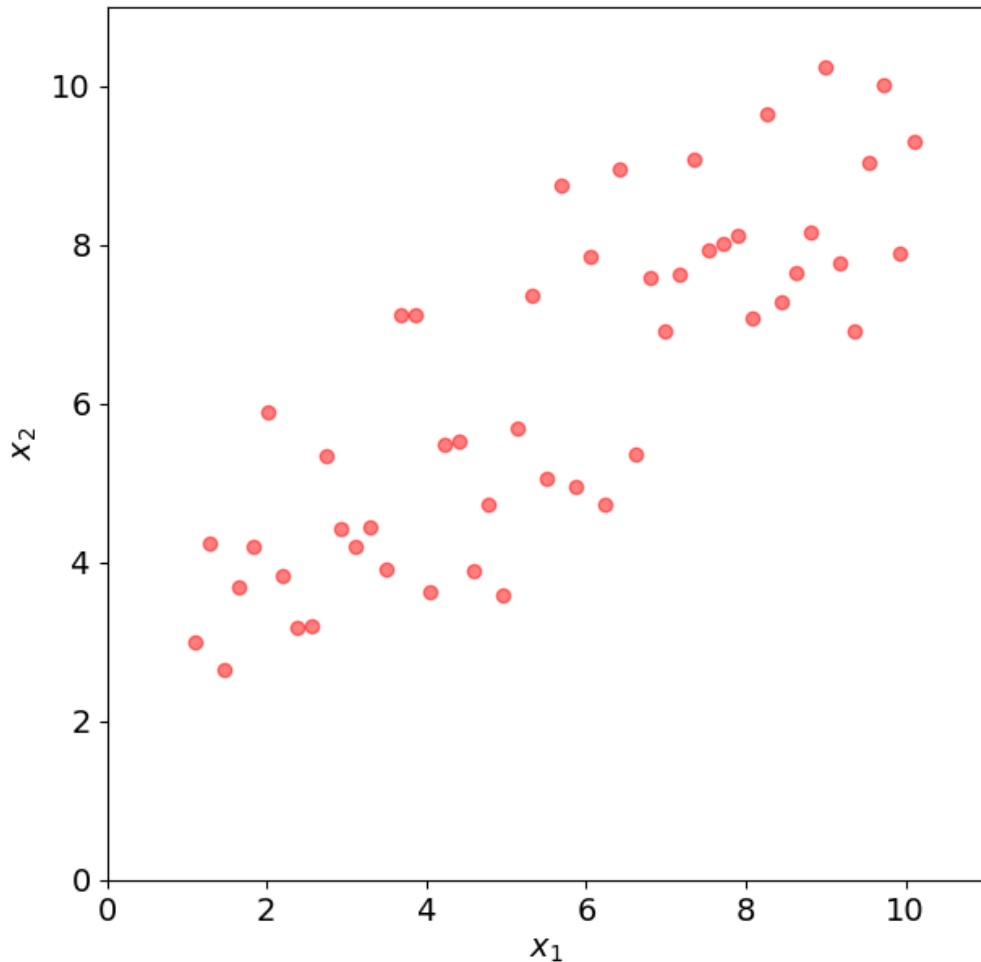
$$\mathbf{C} = \mathbf{V} \boldsymbol{\lambda} \mathbf{V}^{-1}$$

$N \times N$ matrix of
eigenvectors

$N \times N$ diagonal matrix of
eigenvalues

[Extra] Principal Components Analysis (PCA)

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



An eigenvector \mathbf{v} of \mathbf{C} respects:

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

Find eigenvalues as the roots of the characteristic polynomial:

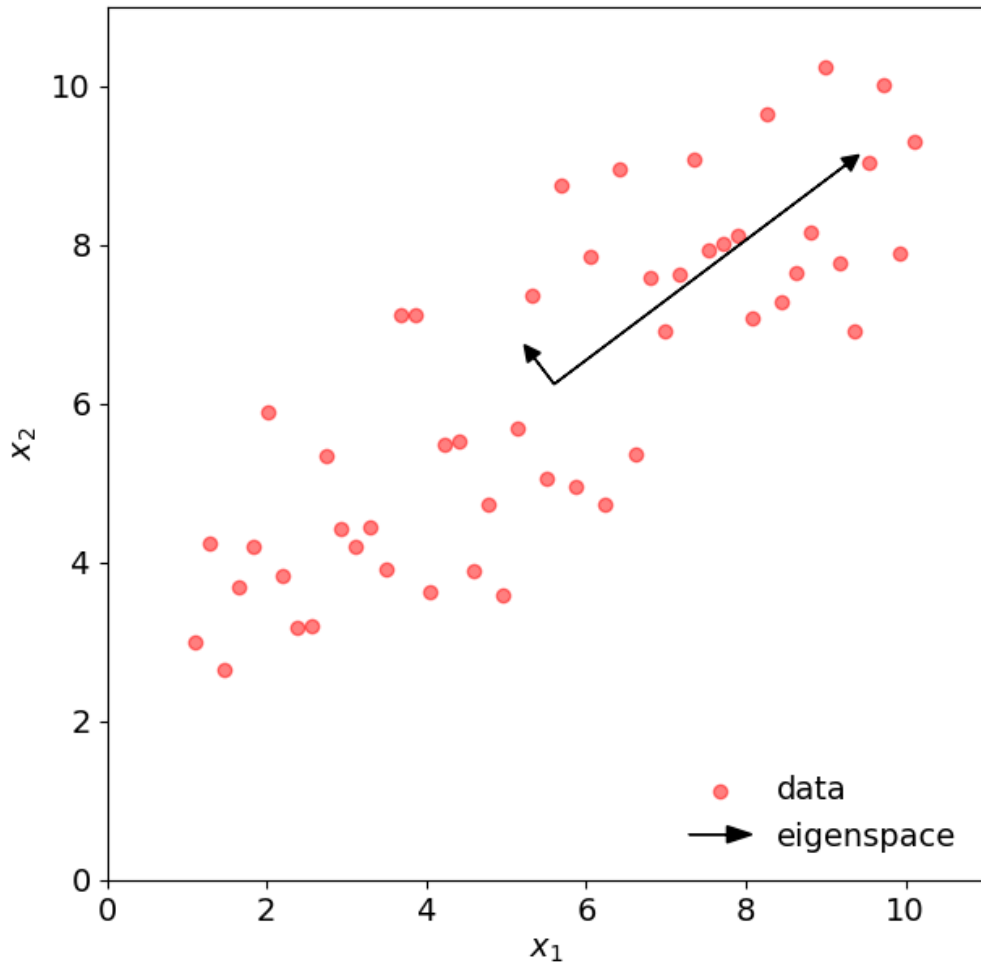
$$p(\lambda) = \det(\mathbf{C} - \lambda\mathbf{I}) = 0$$

The i -th eigenvector \mathbf{v}_i is found by solving:

$$\mathbf{C}\mathbf{v}_i = \lambda_i\mathbf{v}_i$$

Principal Components Analysis (PCA)

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



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

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

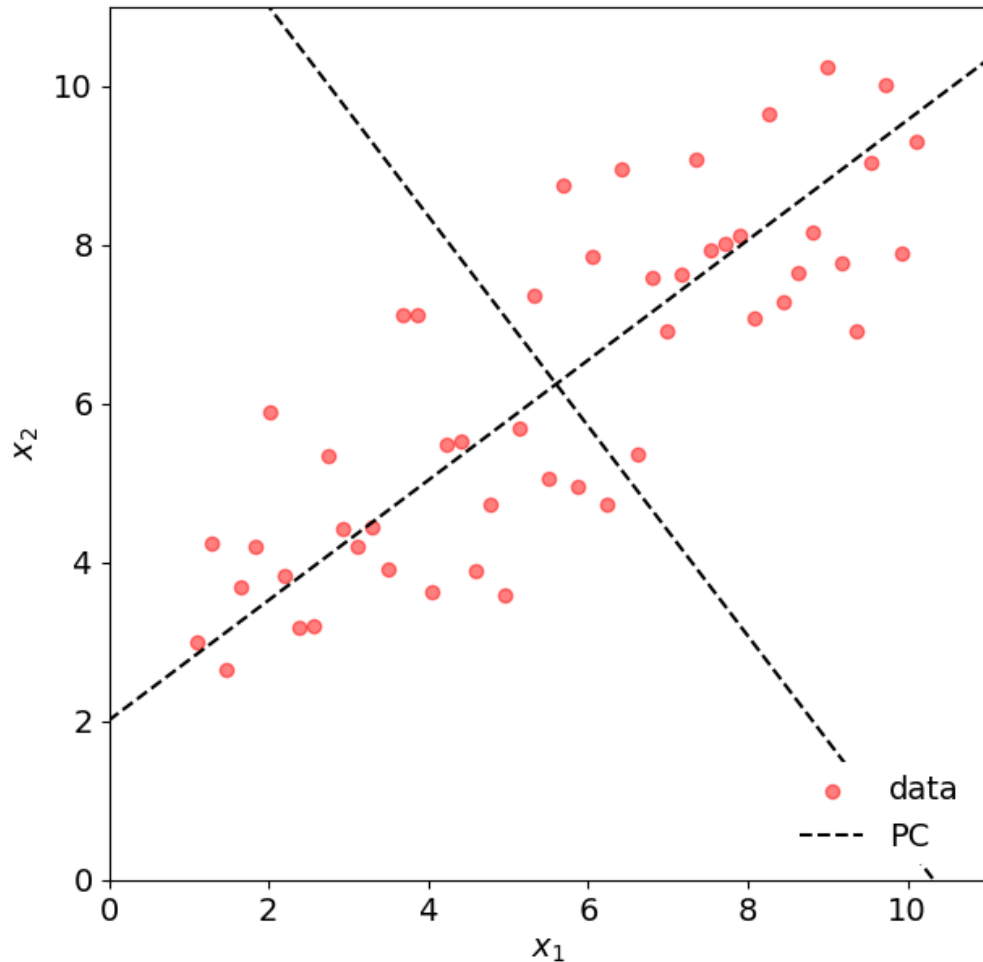
λ eigenvalues: scalars defining the
importance of each eigenvector
Importance r_i of each eigenvector \mathbf{v}_i :

$$r_i = \frac{\lambda_i}{\sum \lambda}$$

Sort \mathbf{V} and λ according to λ

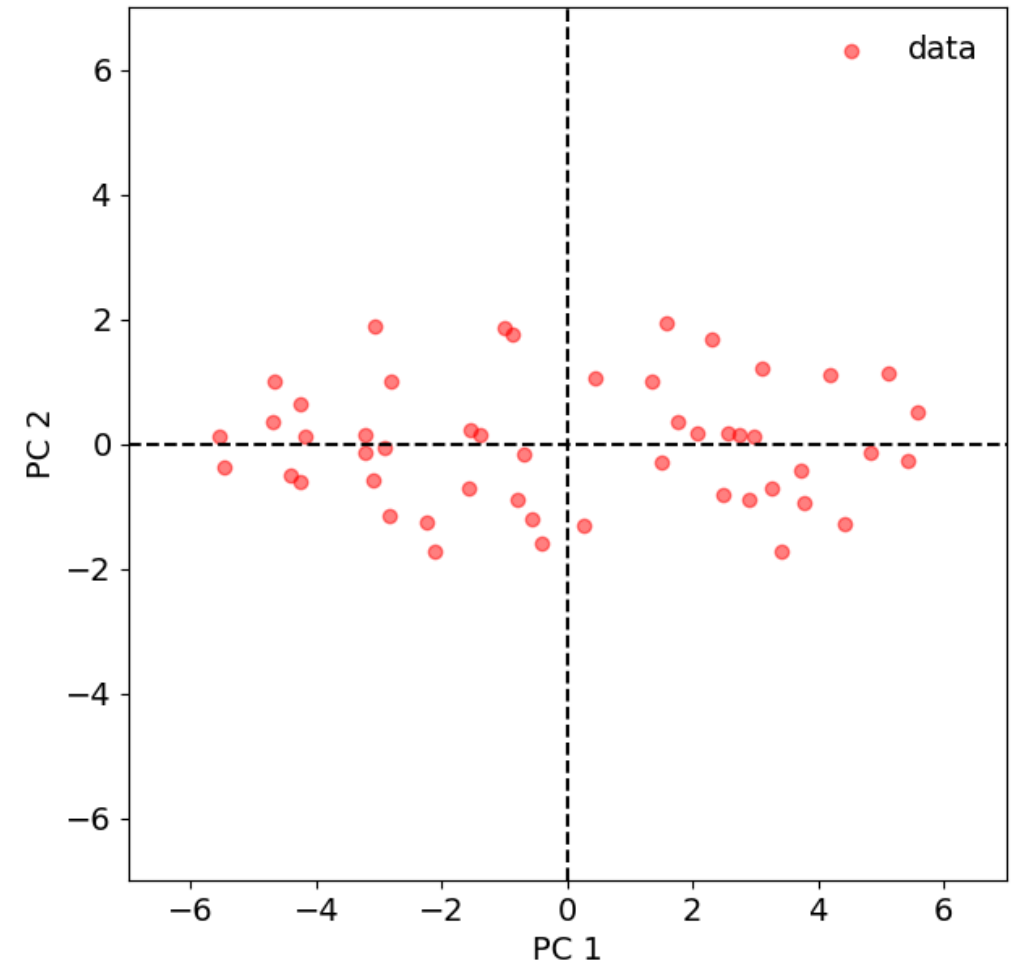
Projection into the eigenspace

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



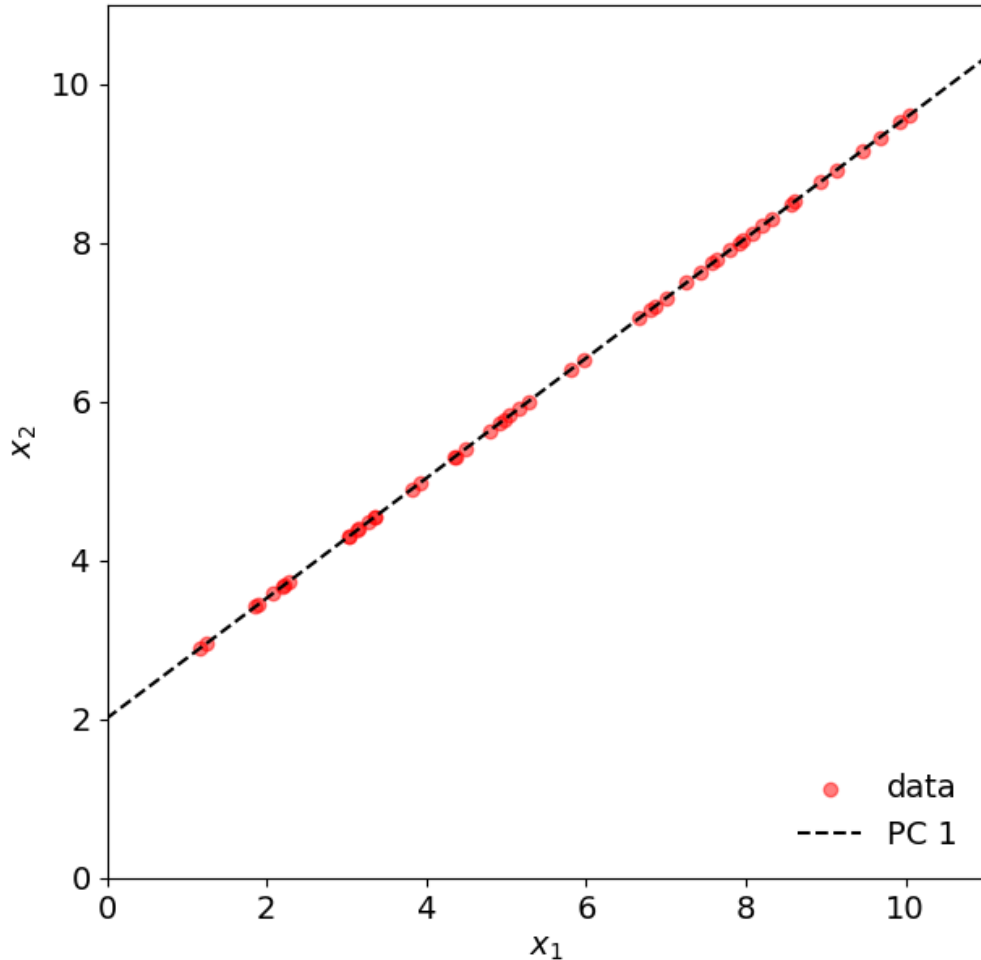
$$p = V^T(x - \mu)$$

transform



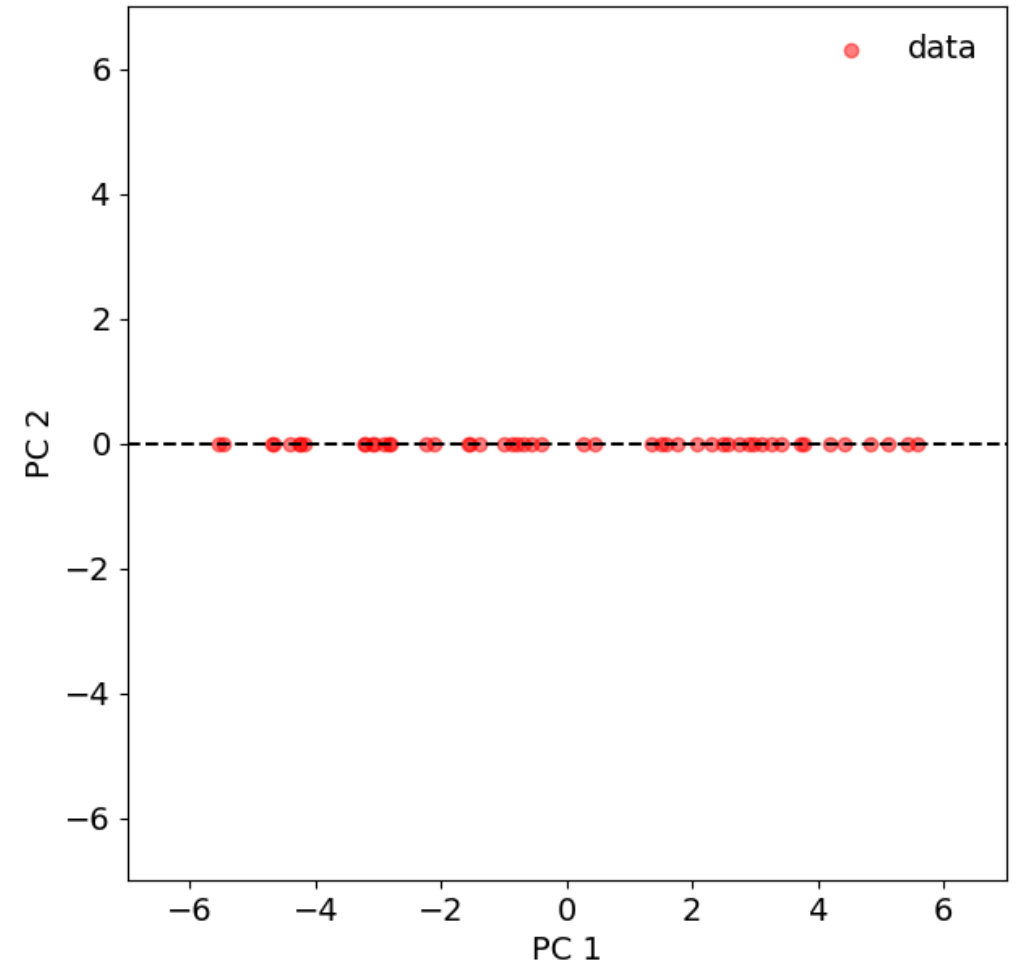
Dimensionality reduction

Remove dimensions that least contribute to data variance



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

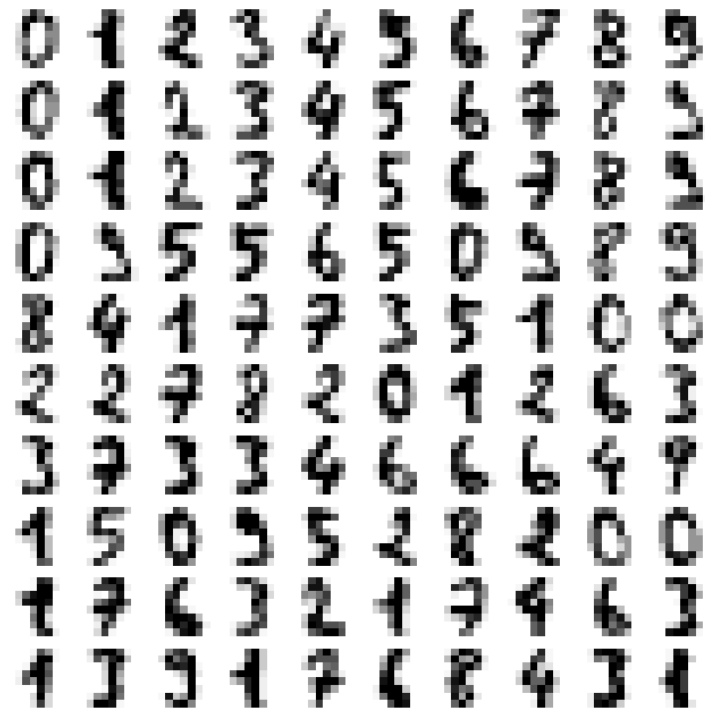
transform



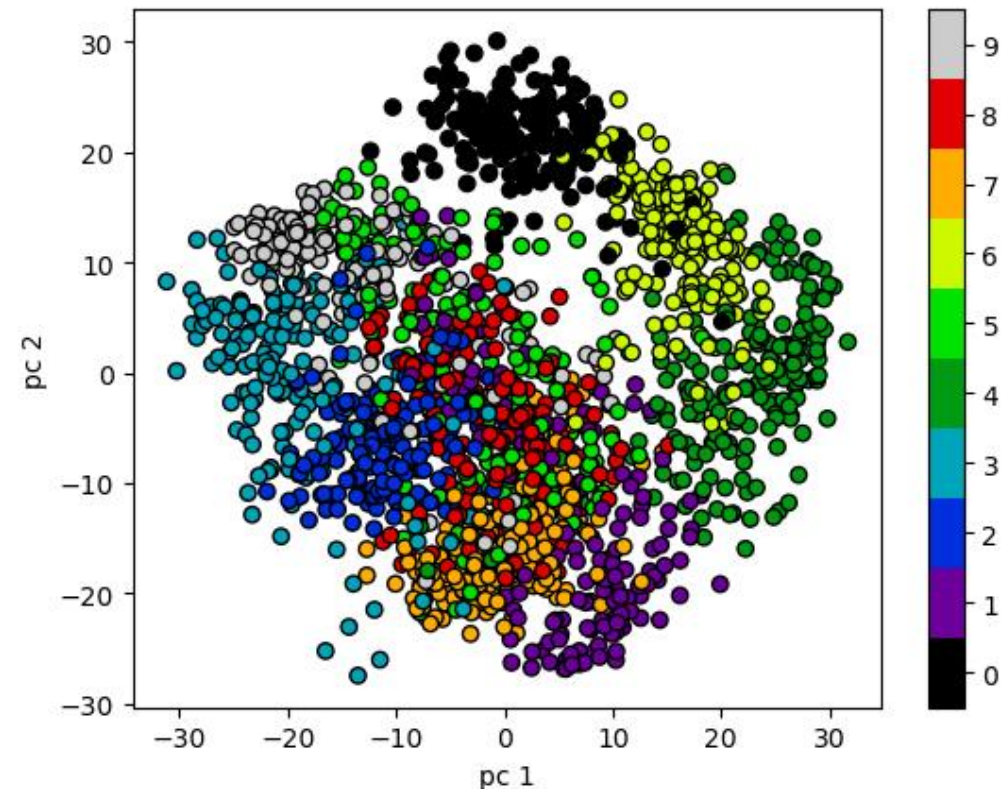
[Example 1] Representing written digits

MNIST database of written digits

Input is a vector of 64
dimensions 8x8 pixel digits

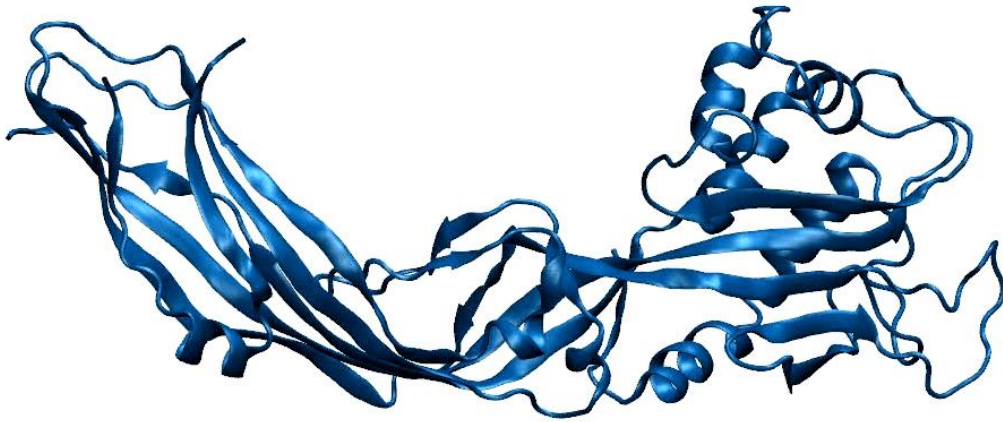


2 principal components manage
to project a few of the digits in a
similar area of space!

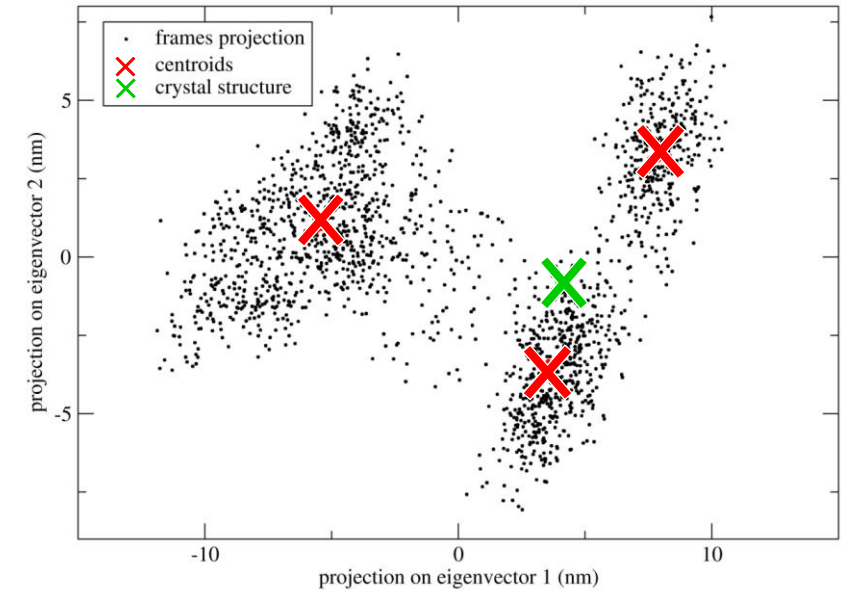


[Example 2] Identifying dominant motions in proteins

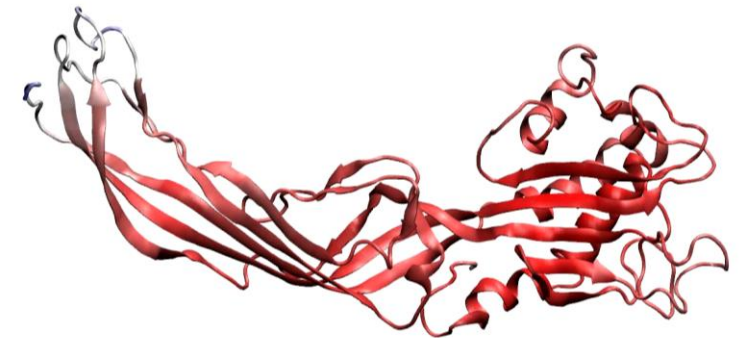
Protein MD simulation



Eigenspace of C α coordinates



- Simulations are complex and noisy
- select only first few PC (eigenvectors) to separate signal from noise

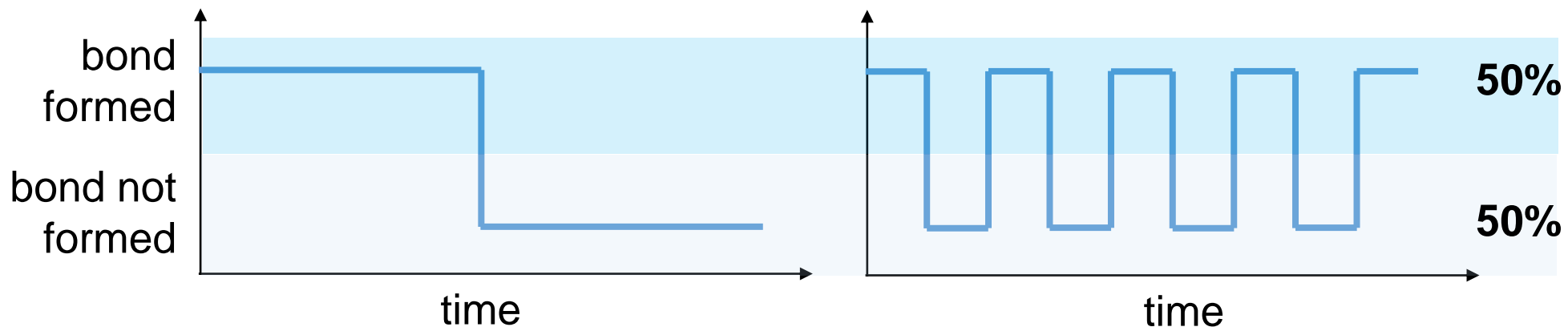


Time-lagged independent component analysis (tlICA)

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

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

Thought experiment reminder: typically hydrogen bond is considered established if donor-acceptor distance $< 2.5 \text{ \AA}$, and donor-acceptor-hydrogen angle $< 20^\circ$.



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

Time-lagged independent component analysis (tlICA)

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

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

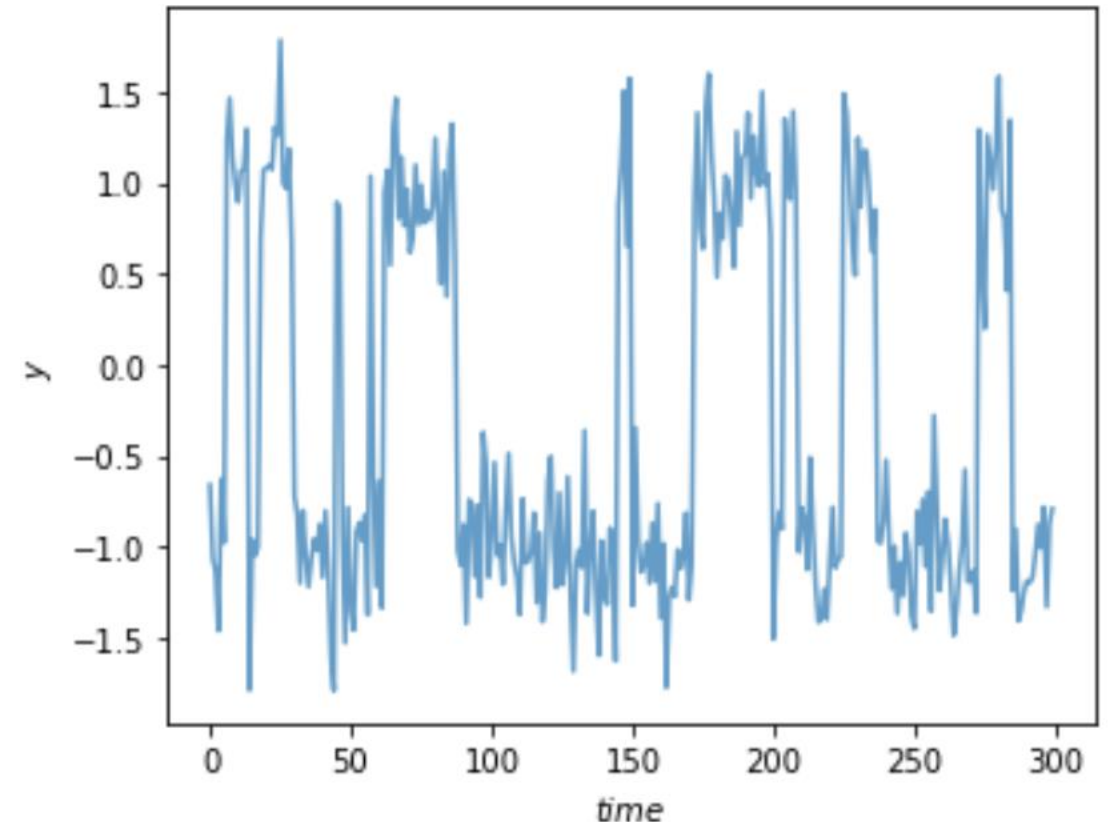
$$\mathbf{r}(t) = (r_i(t))_{i=1,\dots,D}$$

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 $\mathbf{C}(\tau)$



Time-lagged independent component analysis (tlICA)

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

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

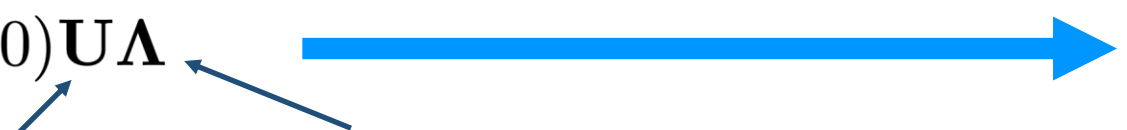
Entries of the covariance matrix can be computed as:

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

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

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

We can now solve the generalised eigenvalue problem:

$$\mathbf{C}(\tau)\mathbf{U} = \mathbf{C}(0)\mathbf{U}\mathbf{\Lambda}$$


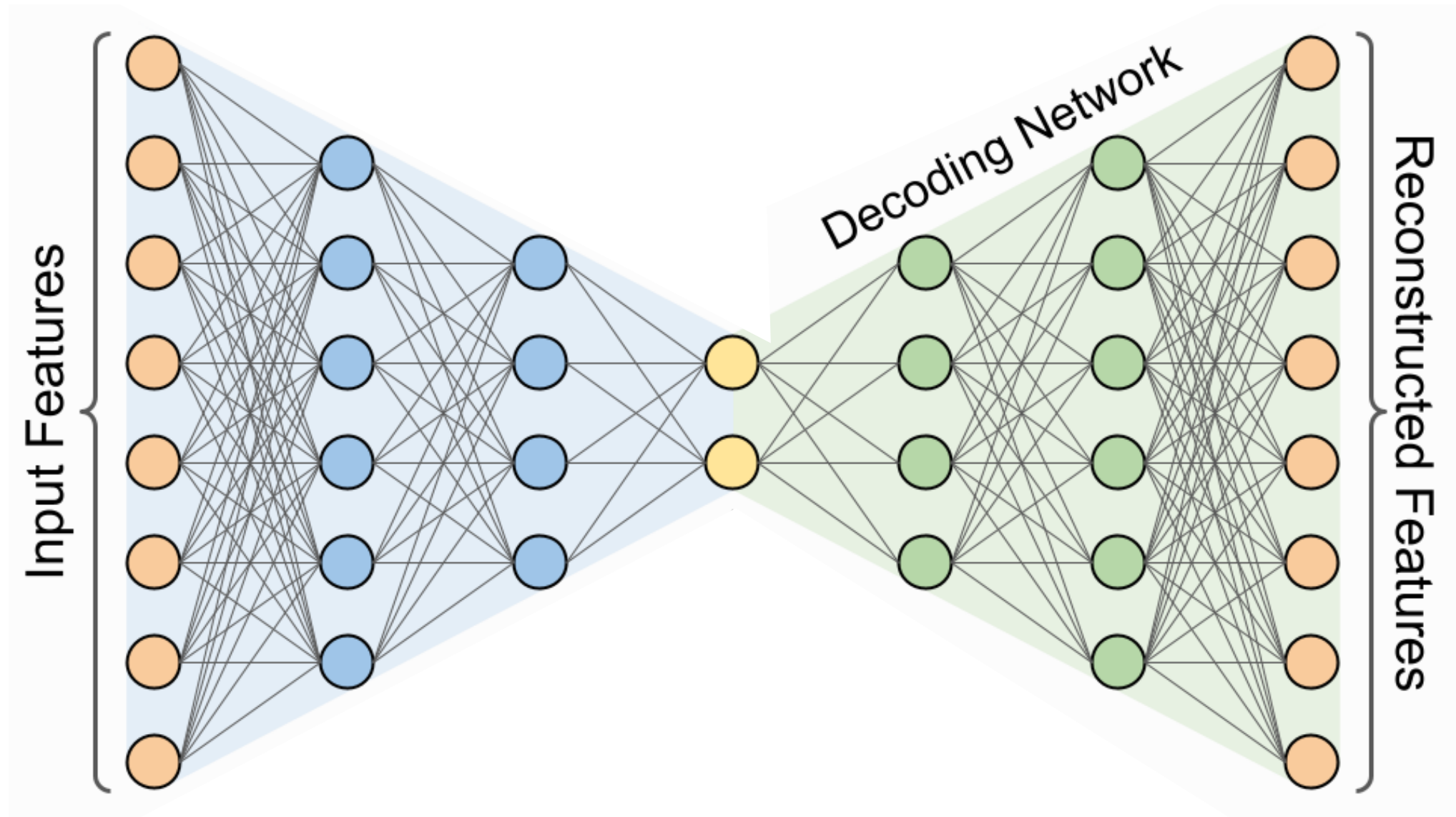
Eigenvector matrix containing ICs

Diagonal matrix with eigenvalues

$$\mathbf{z}^T(t) = \mathbf{r}^T(t)\mathbf{U}$$

M columns of full rank \mathbf{U} for DR

[Extra] Dimensionality reduction with neural networks



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