GL Applied Data Science Program

Data Collection and Visualization for Exploratory Data Analysis

January 31, 2022

Introduction

http://www.carolineuhler.com

Overview

Overview of this week / module:

- Data collection and visualization for exploratory data analysis
- Network analysis
- Unsupervised learning - clustering

Overview of this lecture:

- Data collection: Mammography case study
- Hypothesis testing
- Visualizing high-dimensional data for exploratory data analysis

Case study: Mammography and breast cancer

- Breast cancer is one of the most common malignancies among women in the United States
- Mammography: screening women for breast cancer by X-rays

✶ Does mammography speed up detection by enough to matter?

✶ How would you approach this problem? What is important when setting up a study / experiment?

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✶ How would you approach this problem? What is important when setting up a study / experiment?

$\Rightarrow$ Perform a **controlled, randomized, double-blind experiment** to minimize the problem of **confounding**

HIP study: First large-scale randomized controlled experiment on mammography performed in 1960s

Table 1. HIP data. Group sizes (rounded), deaths in 5 years of followup, and death rates per 1000 women randomized.

	Group size	Breast cancer No.	Breast cancer Rate	All other No.	All other Rate
Treatment					
Screened	20,200	23	1.1	428	21
Refused	10,800	16	1.5	409	38
Total	31,000	39	1.3	837	27
Control	31,000	63	2.0	879	28

Reference: D. A. Freedman. *Statistical Models: Theory and Practice*, 2009.

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HIP study

Which rates should be compared to show the efficacy of treatment?

- Seems natural to compare those who accepted screening to those who refused or the control group
- But this is an **observational** comparison!
- Becomes clear when comparing the death rates from all other causes
- Instead compare the whole treatment group against the whole control group

✶ **Intention-to-treat analysis**

Hypothesis testing

- Death rate from breast cancer in control group: 0.0020 ($= \frac{63}{31000}$)
- Death rate from breast cancer in treatment group: 0.0013 ($= \frac{39}{31000}$)

Is the difference in death rates between the treatment and control group sufficient to establish that mammography reduces the risk of death from breast cancer?

$\Rightarrow$ Perform a **hypothesis test**

Hypothesis testing

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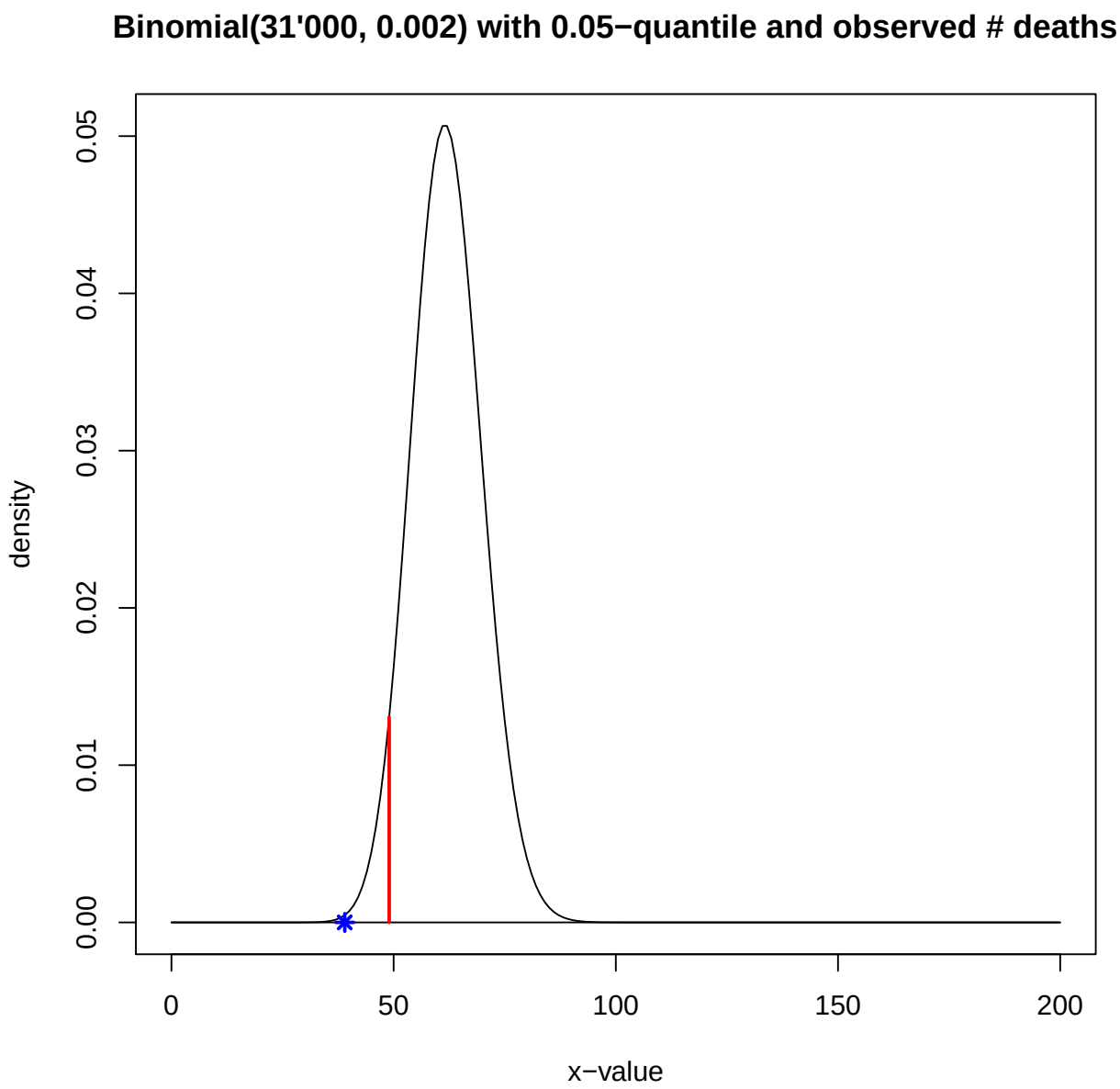
4. Determine a **significance level** (α), i.e. the probability of rejecting H_0 when H_0 is true: $\alpha = 0.05$

Binomial distribution



P-value

- Probability under H_0 to obtain the observed value or a more extreme value of the test statistic

  $\Rightarrow$ p-value is always between 0 and 1!

  For mammography study: p-value is 0.0012

- Can be used for hypothesis testing: Reject H_0 if p-value $\leq \alpha$

- Quantifies significance of alternative

Hypothesis testing applications outside of healthcare

Hypothesis testing applications outside of healthcare

- Quality management in manufacturing environments: deciding whether new process, technique, method is likely to change number of defective products
- Finance: deciding which investment / instrument is likely to provide satisfactory return
- Business: make informed decisions on which initiatives help grow your business
- Advertising: deciding whether an advertising campaign, marketing technique, etc. is likely to increase sales

Example research findings

Giovannucci et al., Journal of the National Cancer Institute 87 (1995):

Intake of tomato sauce (p-value of 0.001), tomatoes (p-value of 0.03), and pizza (p-value of 0.05) reduce the risk of prostate cancer;

But for example tomato juice (p-value of 0.67), or cooked spinach (p-value of 0.51), and many other vegetables are not significant.

Wonder-pill

- randomized group of 1000 people
- measure 100 variables before and after taking the pill: weight, blood pressure, etc.
- perform a hypothesis test with a significance level of 5%

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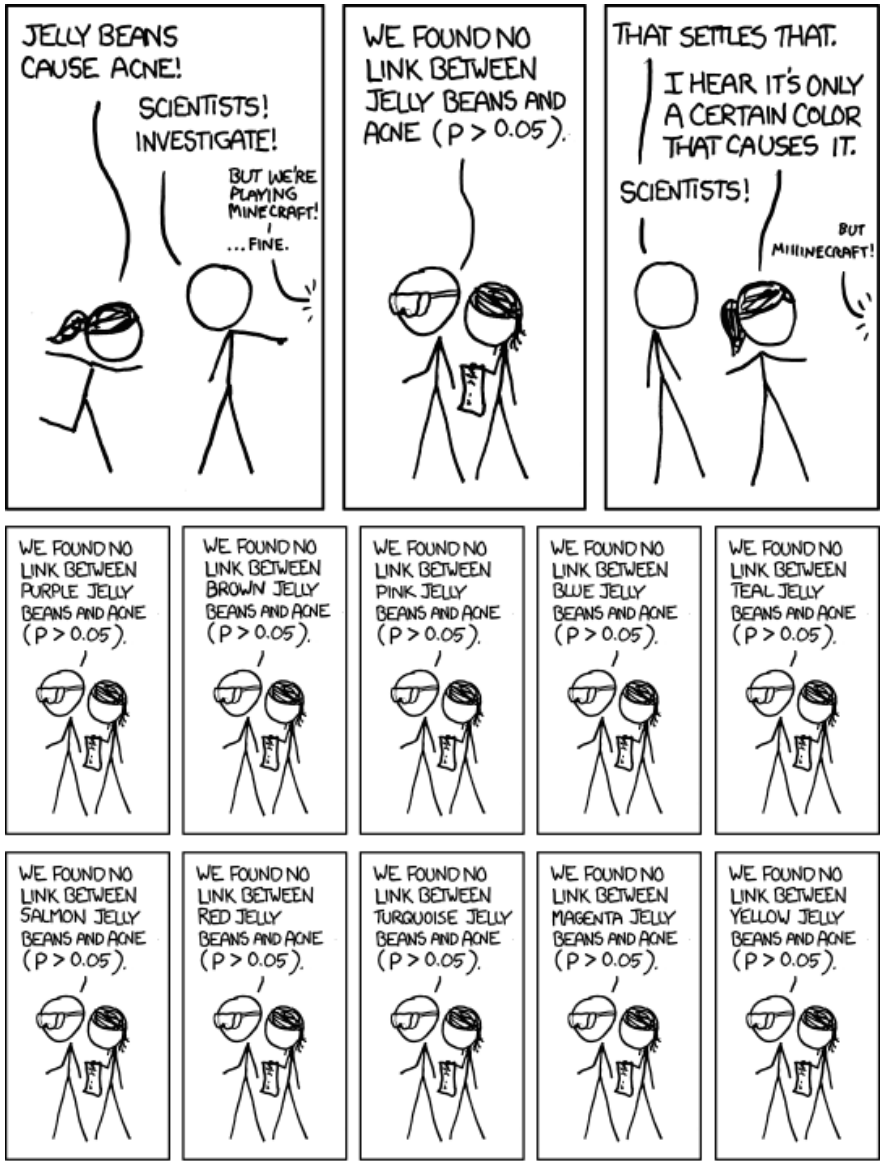
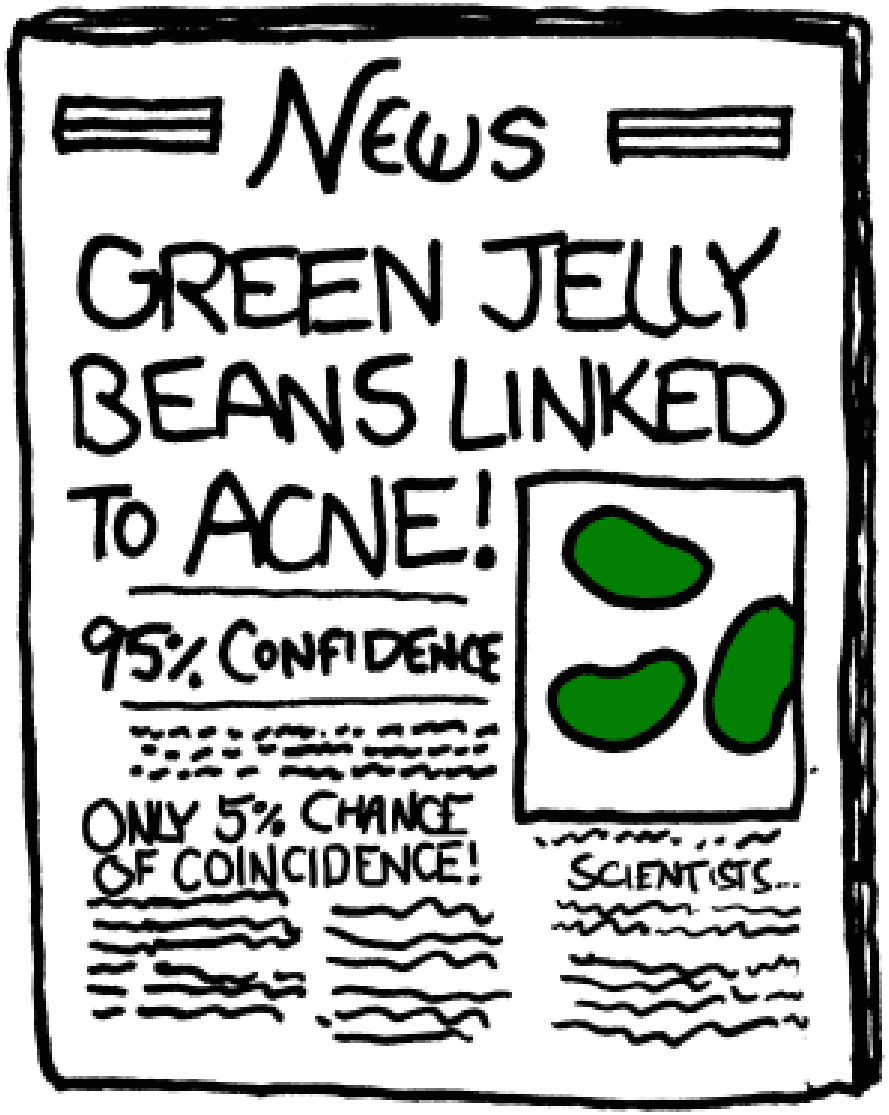
- randomized group of 1000 people
- measure 100 variables before and after taking the pill: weight, blood pressure, etc.
- perform a hypothesis test with a significance level of 5%
- $V := \#$ false significant tests: $\quad V \sim \mathrm{Binomial}(100, 0.05)$

  $\Rightarrow$ in average 5 out of 100 variables show a significant effect!

Jelly Beans and Acne



Problematic of selective inference



http://imgs.xkcd.com/comics/significant.png

Different protection levels

Compute p-values using methods that control:

- family-wise error rate (FWER) $\leq \alpha$, where

$$\text{FWER} = \mathbb{P}(\text{at least one false significant result})$$

- false discovery rate (FDR) $\leq \alpha$, where

$$\begin{aligned}\text{FDR} &= \text{expected fraction of false significant results} \\ &\quad \text{among all significant results}\end{aligned}$$

Corrections for multiple testing

Bonferroni correction:

- Reject H_0 when: $m \cdot p\text{-value} \leq \alpha$
  where m is the total number of hypothesis tests performed
- Bonferroni correction implies $\mathrm{FWER} \leq \alpha$

Holm-Bonferroni correction:

- Sort p-values in increasing order: $p_{(1)} \leq \cdots \leq p_{(m)}$
- Reject H_0 when: $(m - i + 1)p_{(i)} \leq \alpha$ (more power than Bonferroni)
- Holm-Bonferroni correction implies $\mathrm{FWER} \leq \alpha$

Benjamini-Hochberg correction:

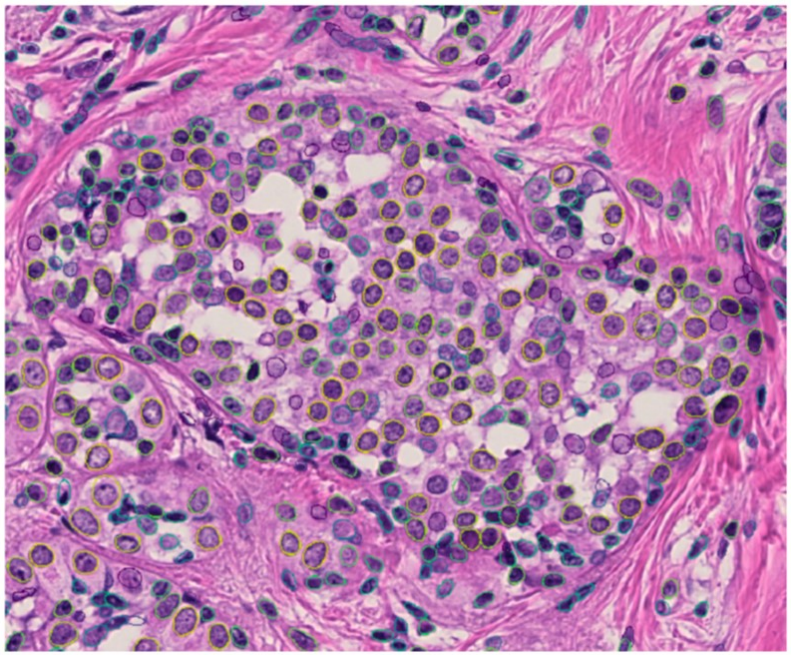
- Sort p-values in increasing order: $p_{(1)} \leq \cdots \leq p_{(m)}$
- Reject H_0 when: $mp_{(i)}/i \leq \alpha$
- Benjamini-Hochberg correction implies $\mathrm{FDR} \leq \alpha$

Commonly accepted practice

- No correction for multiple testing when generating hypotheses (but report number of tests performed)
- $\mathrm{FDR} \leq 10\%$ in exploratory analysis or screening
  - balance between high power and low # of false significant results
- $\mathrm{FWER} \leq 5\%$ in confirmatory analysis
  - food and drug administration (FDA)

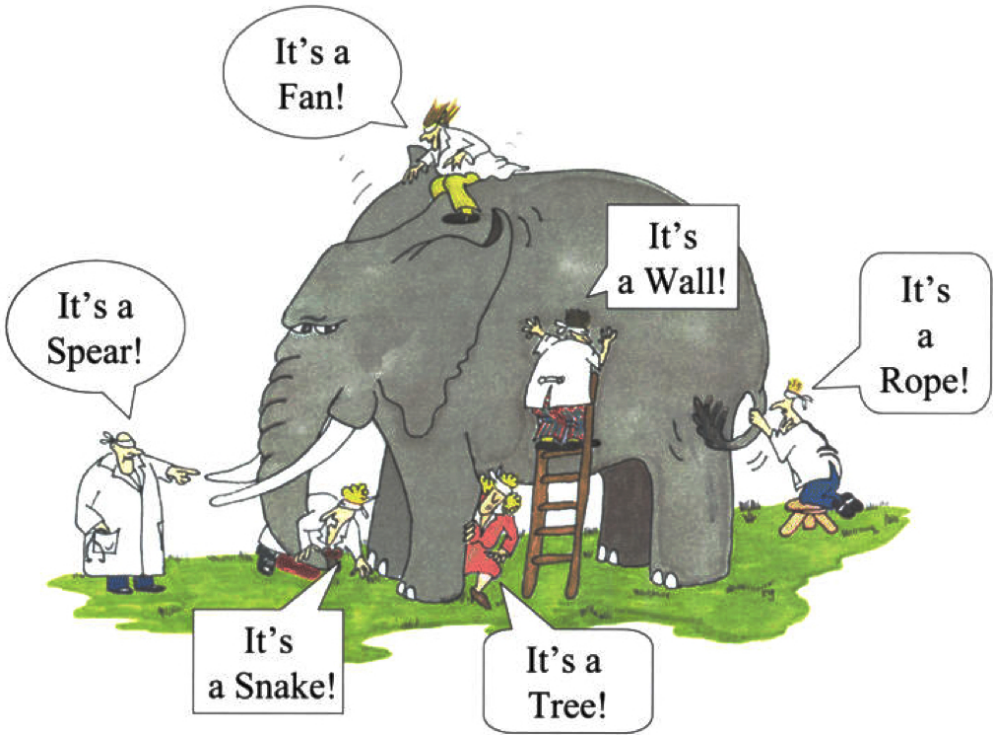
Application: Microscopy Images

- Microscopy images of human tissue slices
- Crop cells (n cells) and summarize each cell by 100 different texture features (i.e., $D = 100$)
- How can we visualize this data set to find clusters or abnormal cells?
- **Input:** $x_1, \ldots, x_n \in \mathbb{R}^D$, **Output:** $y_1, \ldots, y_n \in \mathbb{R}^d$, where $d << D$



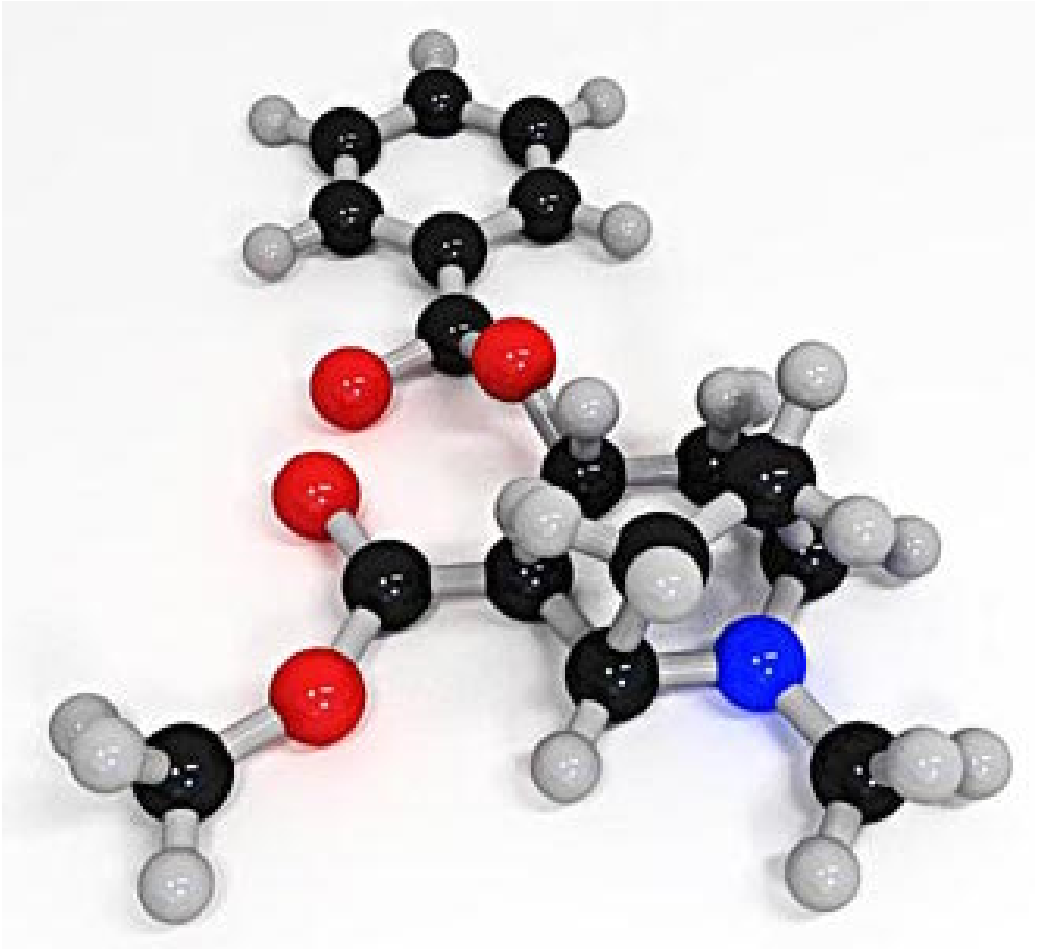
2 different approaches

- Principle component analysis: projection that spreads data as much as possible
- Stochastic neighbor embedding: non-linear embedding that tries to keep close-by points close

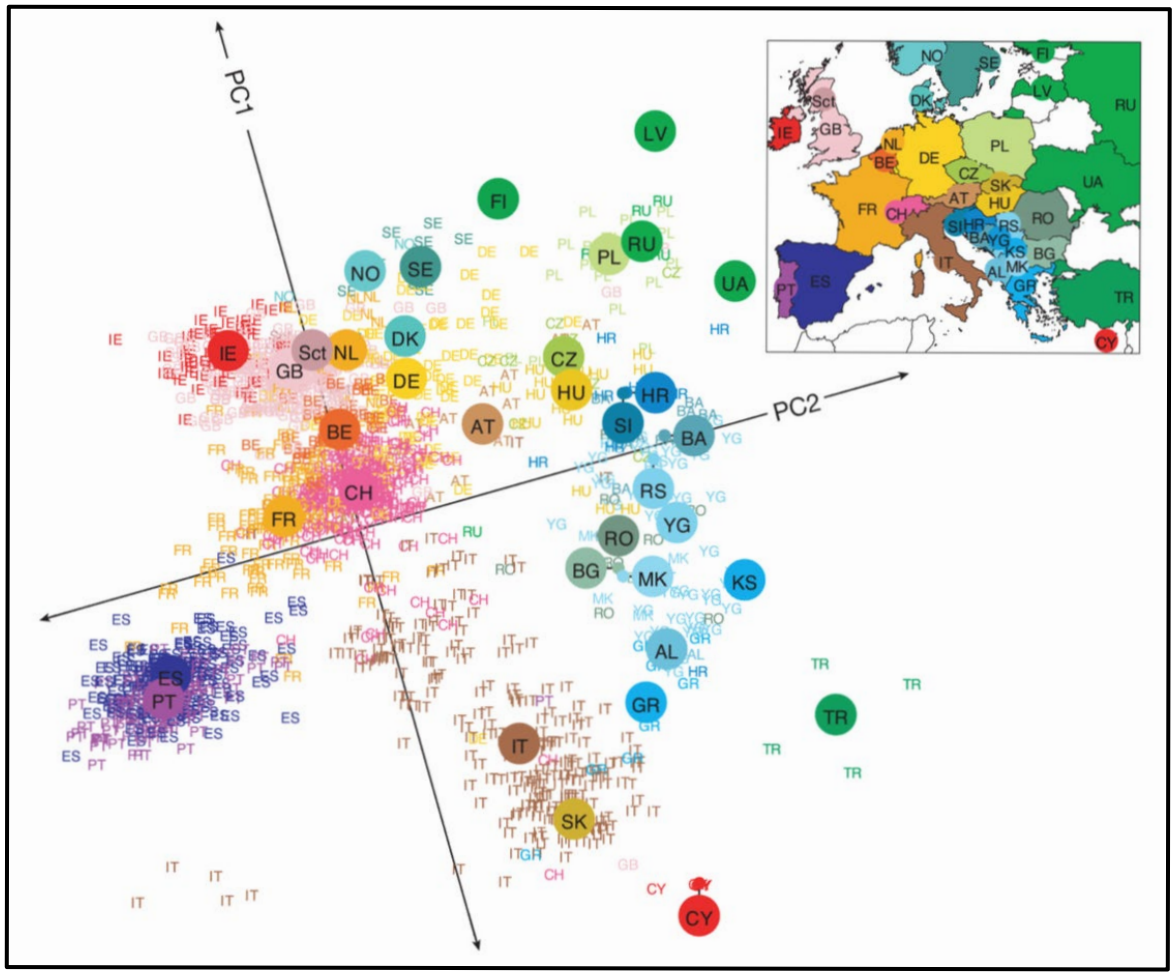


Principle Component Analysis

- **Goal:** Dimension reduction to a few dimensions
- **Intuition:** Find low-dimensional projection with largest spread



PCA application

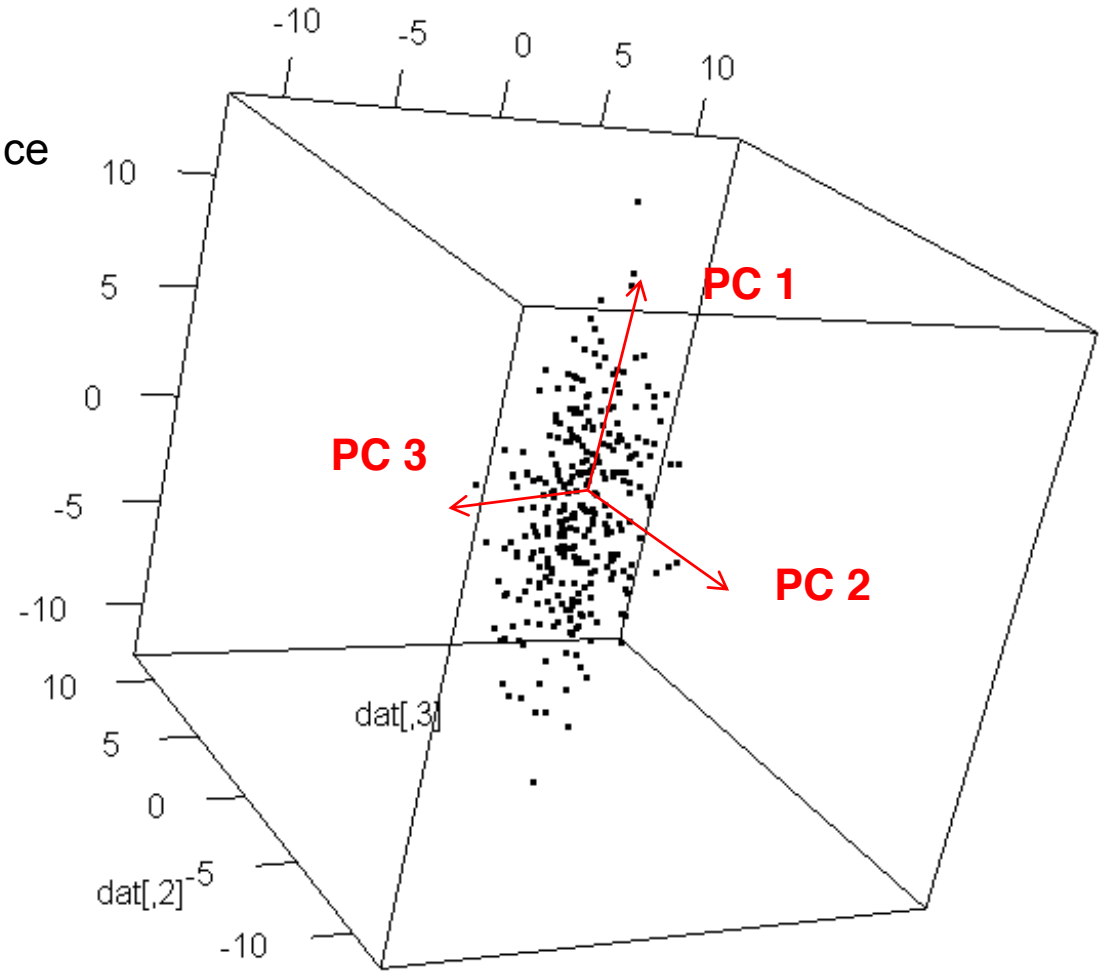


Reference: J. Novembre et al., *Genes mirror geography within Europe*, Nature 456 (2008).

Definition 1: Maximize projection variance

Start with centered data $X \in \mathbb{R}^{n \times p}$

- PC 1 is direction of largest variance
- PC 2 is
  - perpendicular to PC 1
  - again largest variance
- PC 3 is
  - perpendicular to PC 1, PC 2
  - again largest variance
- etc.



Definition 2: Minimize projection residuals

- PC 1: Straight line with smallest orthogonal distance to all points
- PC 1 & PC 2: Plane with with smallest orthogonal distance to all points
- etc.

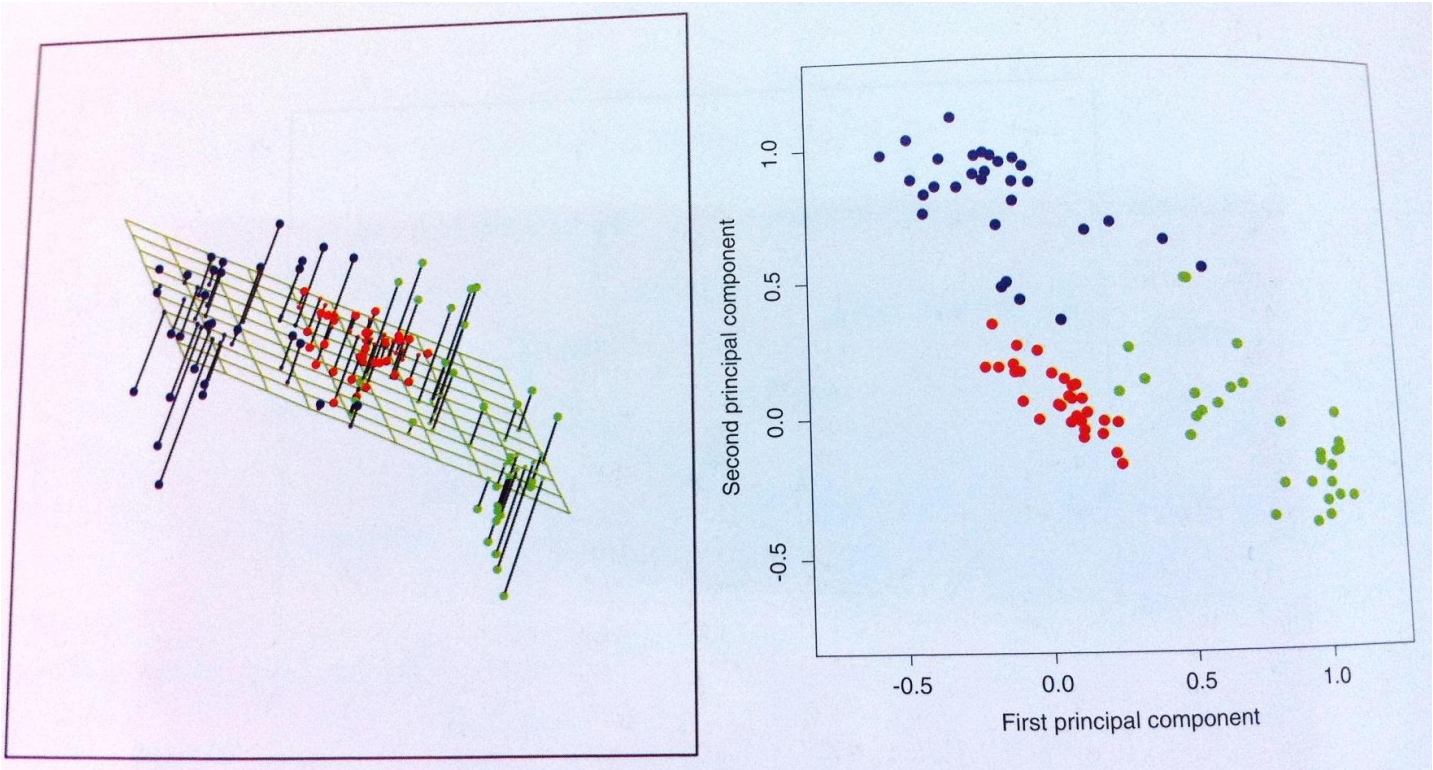


Figure from *Elements of Statistical Learning*by Hastie and Tibshirani

Definition 3: Spectral decomposition

- Covariance matrix (or correlation matrix) $R = \frac{1}{n} X^T X$ is symmetric and positive semidefinite
- **Spectral Decomposition Theorem:** Every real symmetric matrix R can be decomposed as

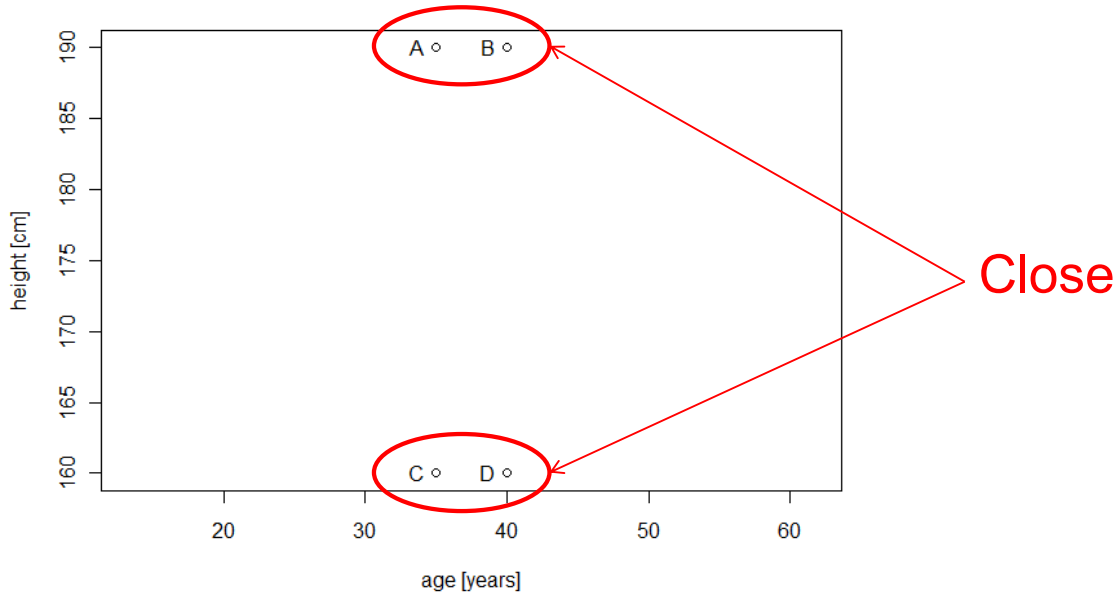
$$R = V \Lambda V^T,$$

  where Λ is diagonal and V is orthogonal
- Columns of V (= eigenvectors of R) are the PCs
- Diagonal entries of Λ (= eigenvalues of R) are variances along PCs

Covariance versus correlation - to scale or not to scale

- Using covariance will find the variable with largest spread as 1. PC
- Use correlation, if different units are compared

Person	Age (years)	Height (cm)
A	35	190
B	40	190
C	35	160
D	40	160



Covariance versus correlation - to scale or not to scale

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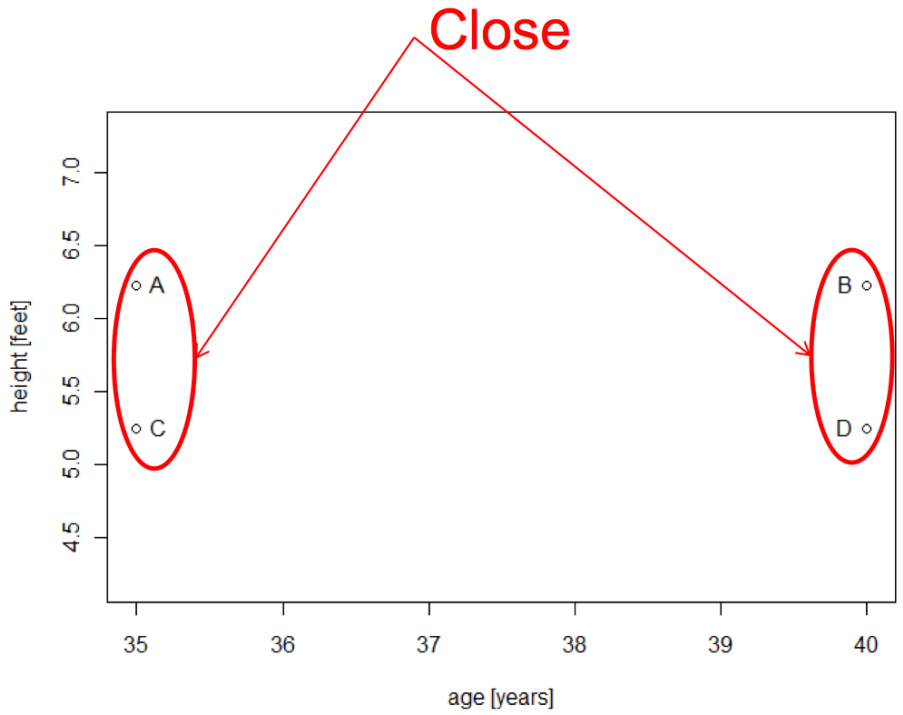
Person	Age (years)	Height (feet)
A	35	6.232
B	40	6.232
C	35	5.248
D	40	5.248



Covariance versus correlation - to scale or not to scale

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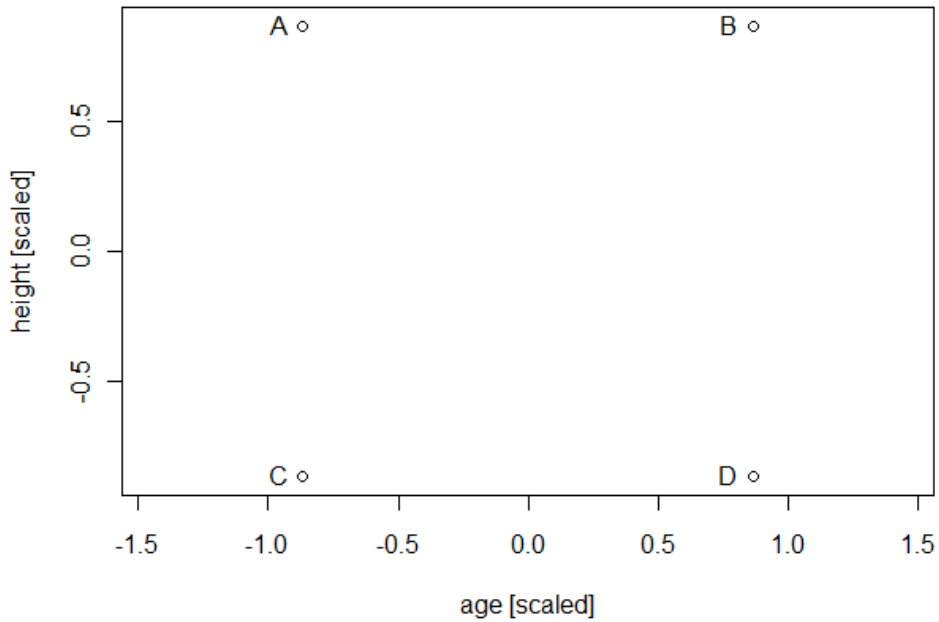
Person	Age (years)	Height (feet)
A	-0.87	0.87
B	0.87	0.87
C	-0.87	-0.87
D	0.87	-0.87



Stochastic neighbor embedding (SNE)

- probabilistic approach to place objects from high-dimensional space into low-dimensional space so as to preserve the identity of neighbors
- center a Gaussian on each object in high-dimensional space
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- center a Gaussian on each object in high-dimensional space
- find embedding so that resulting high-dimensional distribution is approximated well by resulting low-dimensional distribution
- determine low-dimensional distribution by minimizing Kullback-Leibler divergence
- allows ambiguous objects like "bank", to be close to "river" and "finance" without forcing all outdoor concepts to be located close to corporate concepts

Optional: (Symmetric) SNE

- given dissimilarity matrix D, for each object i compute probability of picking j as neighbor:

$$p_{ij} = \frac{\exp(-D_{ij}^2)}{\sum_{k \neq \ell} \exp(-D_{k\ell}^2)}$$

- in low-dimensional space, for each point y_i compute probability of picking y_j as neighbor:

$$q_{ij} = \frac{\exp(-\|y_i - y_j\|_2^2)}{\sum_{k \neq \ell} \exp(-\|y_k - y_\ell\|_2^2)}$$

- Minimize the KL-divergence

$$\mathrm{KL}(P||Q) = \sum_{i \neq j} p_{ij} \log \frac{p_{ij}}{q_{ij}}$$

- by modeling p_{ij} by $q_{ij} = p_{ij} + x$ you gain less than you lose by choosing $q_{ij} = p_{ij} - x$
- keeps nearby objects nearby and separated objects relatively far

t-SNE

- SNE (non-convex) is optimized using gradient descent from an initial configuration

t-SNE

- SNE (non-convex) is optimized using gradient descent from an initial configuration
- problem with many embedding methods: points often get crowded in the middle
- t-SNE reduces this by using t-distribution with 1 degree of freedom for y's:

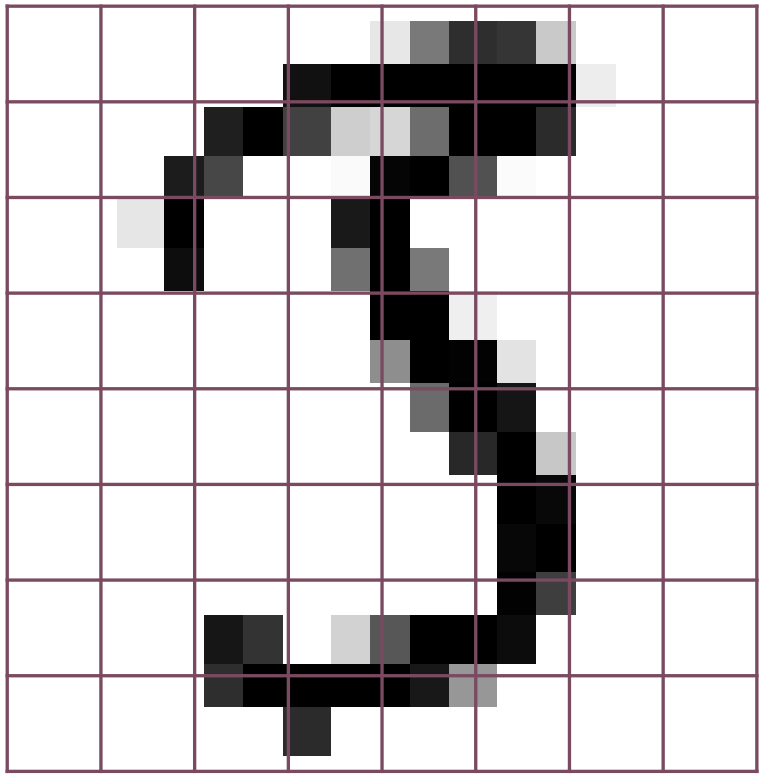
$$q_{ij} = \frac{(1 + \|y_i - y_j\|_2^2)^{-1}}{\sum_{k \neq \ell}(1 + \|y_i - y_j\|_2^2)^{-1}}$$

- reduces crowding: moderate distance in high-dim. space can be faithfully modeled by much larger distance in low-dim. space

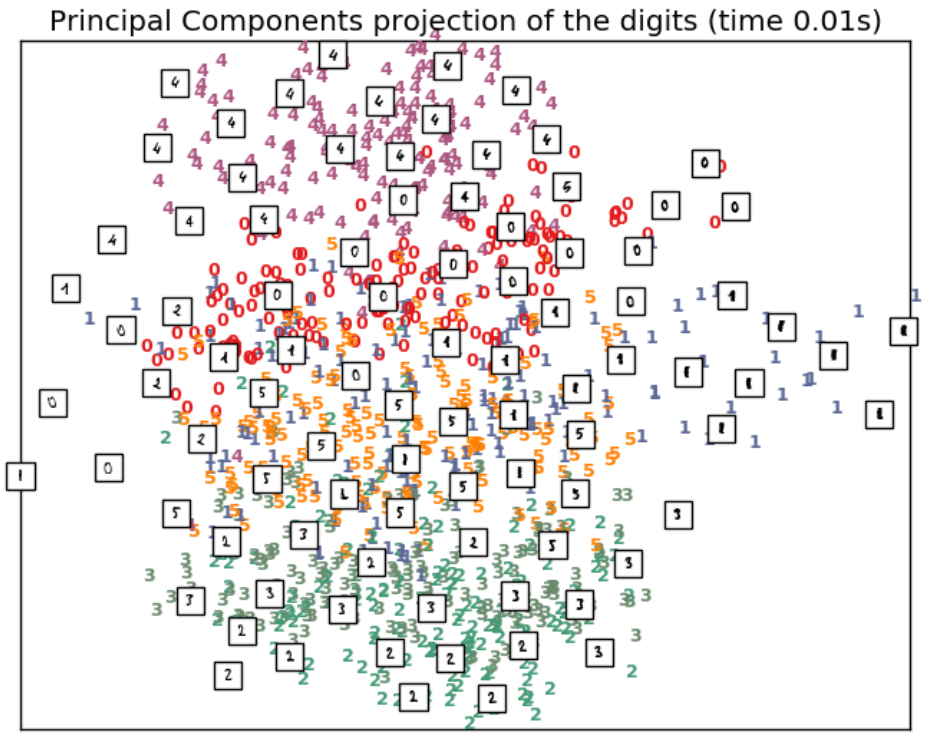
Case study: Digit recognition

- $\sim$ 1800 hand-written digits (i.e., $n \approx 180$ for each number)
- each (centered) digit was put in a 8×8-grid (i.e., $D = 64$)
- measure grey value in each part of the grid, i.e. 64 grey values
- **Input:** $x_1, \ldots, x_n \in \mathbb{R}^D$, **Output:** $y_1, \ldots, y_n \in \mathbb{R}^d$, where $d << D$

A selection from the 64-dimensional digits dataset



Case study: Digit recognition



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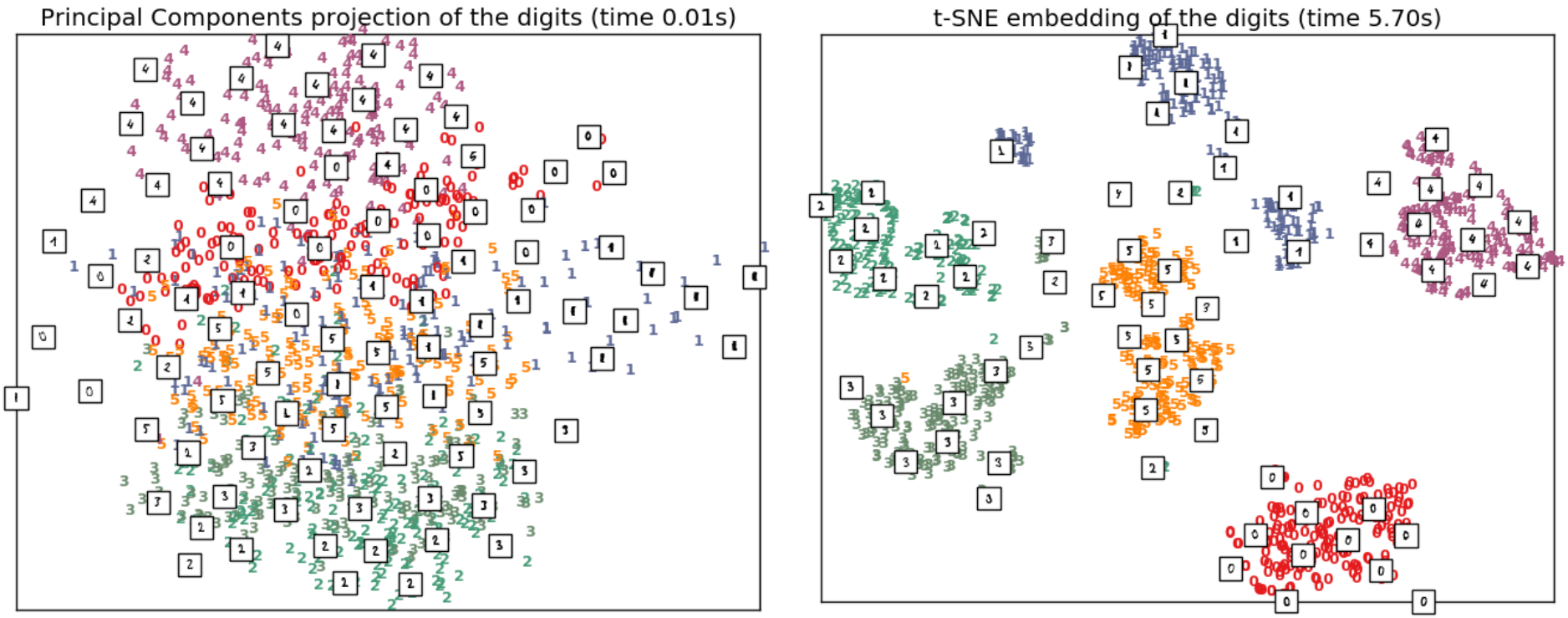

- tSNE seems to find meaningful clusters
- Note: tSNE embedding is result of non-convex optimization problem: depends on starting configuration; also: axes have NO meaning

For code and figures see

`http:scikit-learn.orgstableauto_examplesmanifoldplot_lle_digits.html`

References for data collection and hypothesis testing

- For a statistics textbook, including controlled experiments and observational studies (chapters 1 and 2) and hypothesis testing (chapter 26-29):

  D. Freedman, R. Pisani, R. Purves. *Statistics*. 2007.

- For how to perform hypothesis testing in `R`: Chapter 4 in

  P. Dalgaard. *Introductory Statistics with R*. 2002.

- For observational studies and experiments, including the HIP study Chapter 1 in

  D. Freedman. *Statistical Models: Theory and Practice*. 2009.

- For selective inference and correcting for multiple hypothesis testing:

  Lecture by Yoav Benjamini, THE expert for multiple testing issues:

  `http://simons.berkeley.edu/talks/yoav-benjamini-2013-12-11a`

References for PCA and tSNE

- For PCA and other projection methods:
  - B. Everitt & T. Hothorn. *An Introduction to Applied Multivariate Analysis with R*. Springer, 2011.
  - T. Hastie, R. Tibshirani & J. Friedman. *The Elements of Statistical Learning: Data Mining, Inference, and Prediction*. Springer, 2009.
- For tSNE:
  - L. van der Maaten & G. E. Hinton. *Visualizing Data using t-SNE*. JMLR, 2008.
  - G. E. Hinton & S. T. Roweis. *Stochastic Neighbor Embedding*. NIPS, 2002.