STA 426 First Lecture

- survey
- course structure
- Molecular Biology lecture (Hubert)
- R survey + computing + Exercise 1

Mark D. Robinson, Statistical Bioinformatics

Today’s structure

9.00-9.45: Survey + Course Structure (Mark)

10.00-10.45: Introduction to Molecular Biology (Hubert)

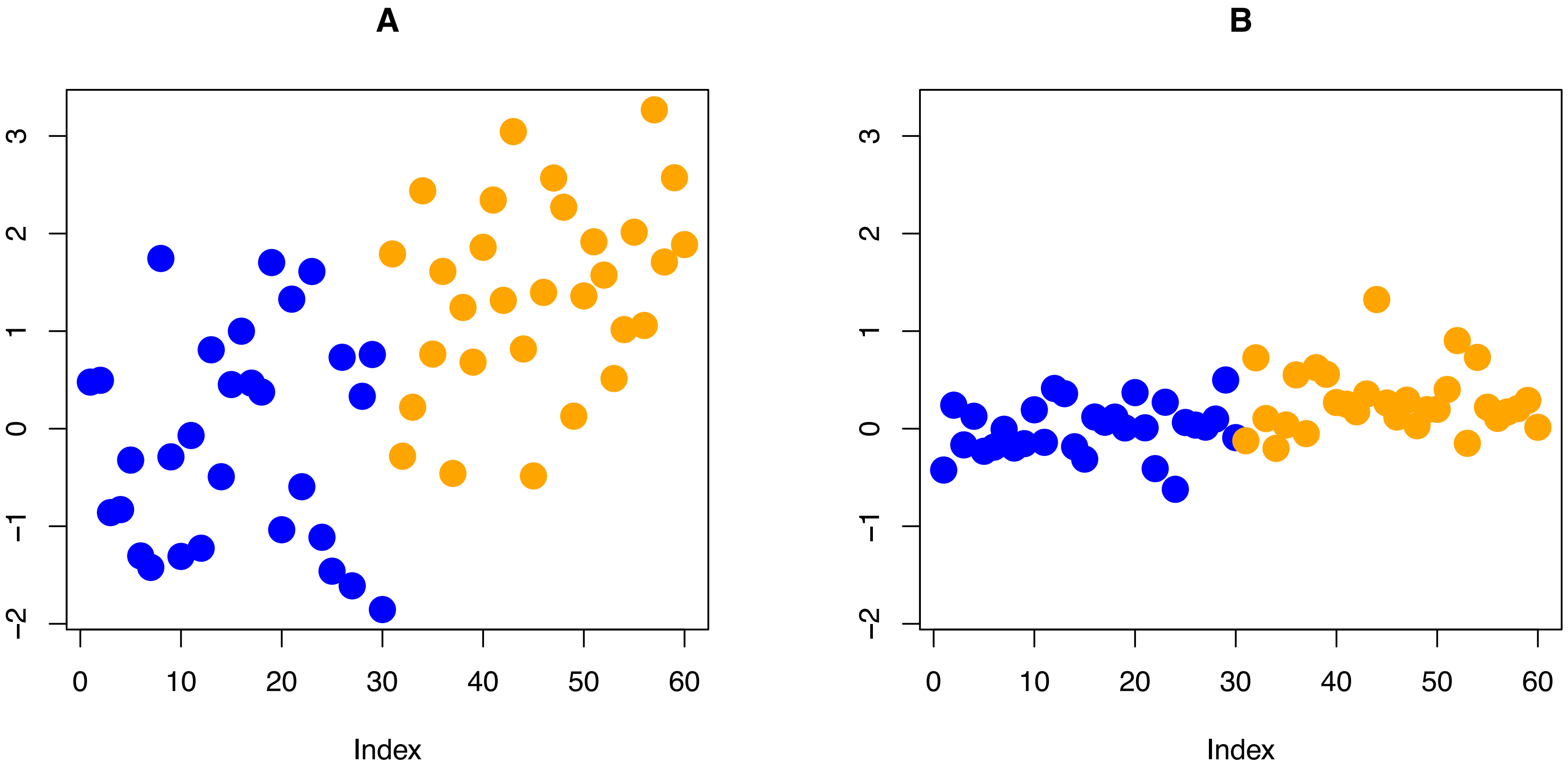
11.00-11.45: Computing + R quiz + Quarto exercise

Survey: Statistical Insight

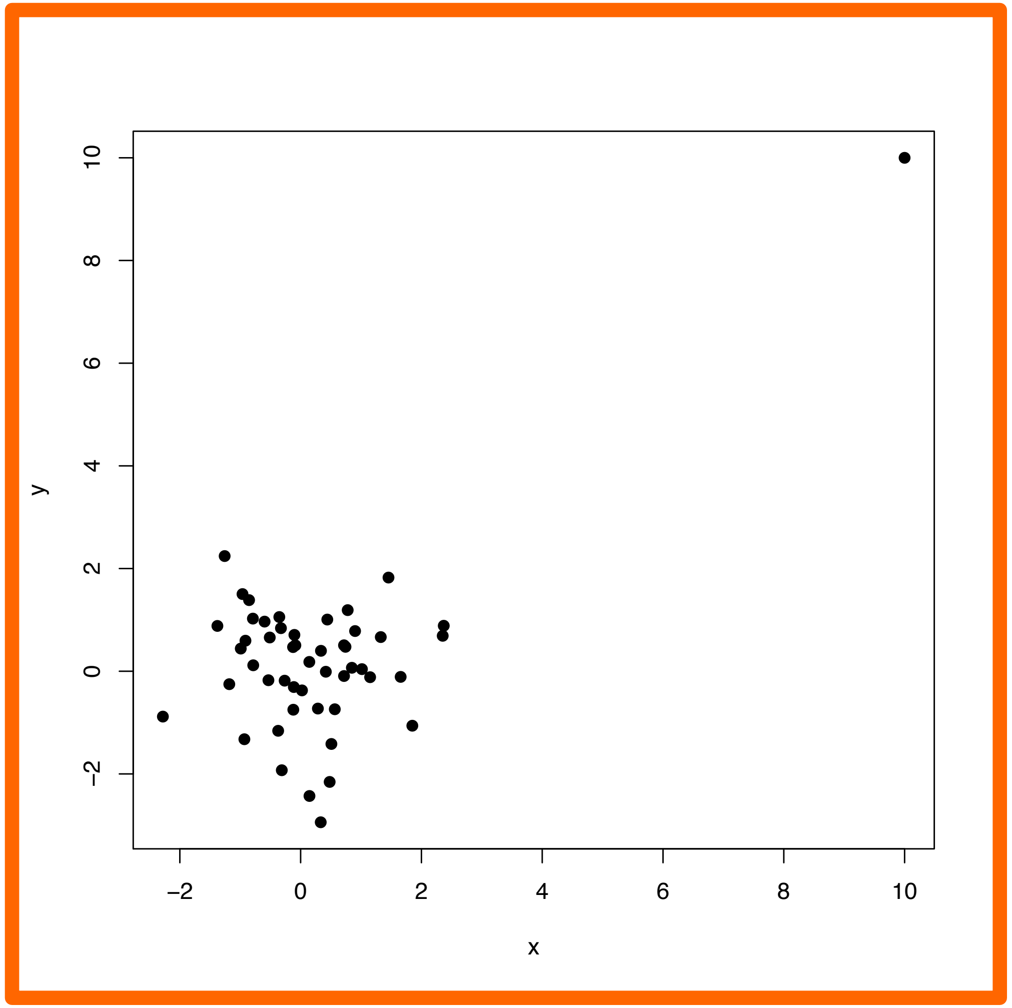
app.klicker.uzh.ch/join/marobi

Klicker UZH

Question 1: Which plot highlights more (statistical) evidence for a change in the population means (between orange and blue)?



Question 2: In your view, what best describes the associations shown in the plot of 'x' and 'y' ?



http://en.wikipedia.org/wiki/Statistical_hypothesis_testing

Question 3: Of these equations, which one resembles the standard two sample t-test ?

1

$$\frac{(\hat{p}_1 - \hat{p}_2)}{\sqrt{\hat{p}(1 - \hat{p})(\frac{1}{n_1} + \frac{1}{n_2})}}$$

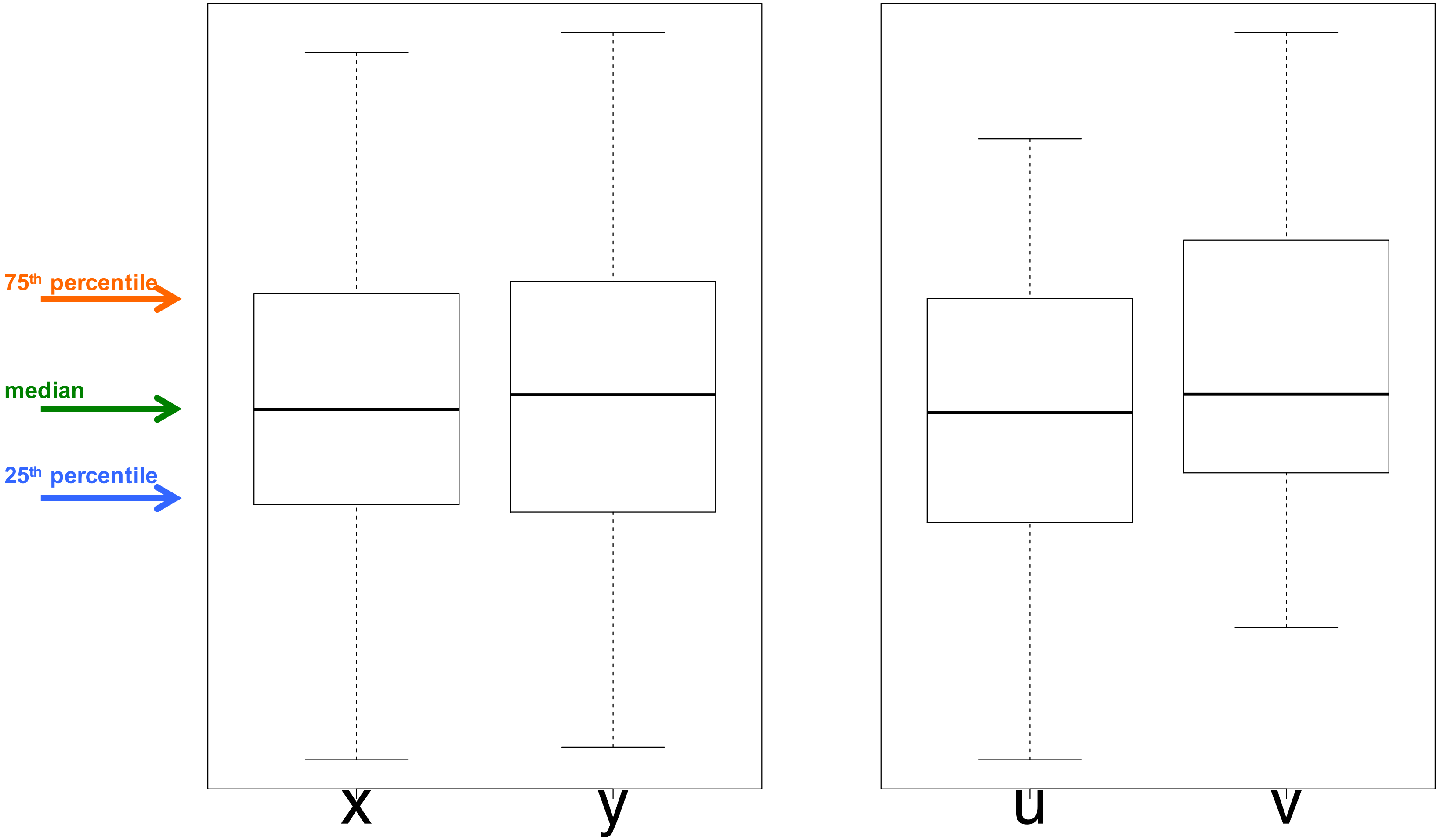
2

$$\sum^{k} \frac{(\text{observed} - \text{expected})^2}{\text{expected}}$$

3

$$\frac{(\overline{x}_1 - \overline{x}_2) - d_0}{s_p \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}},$$

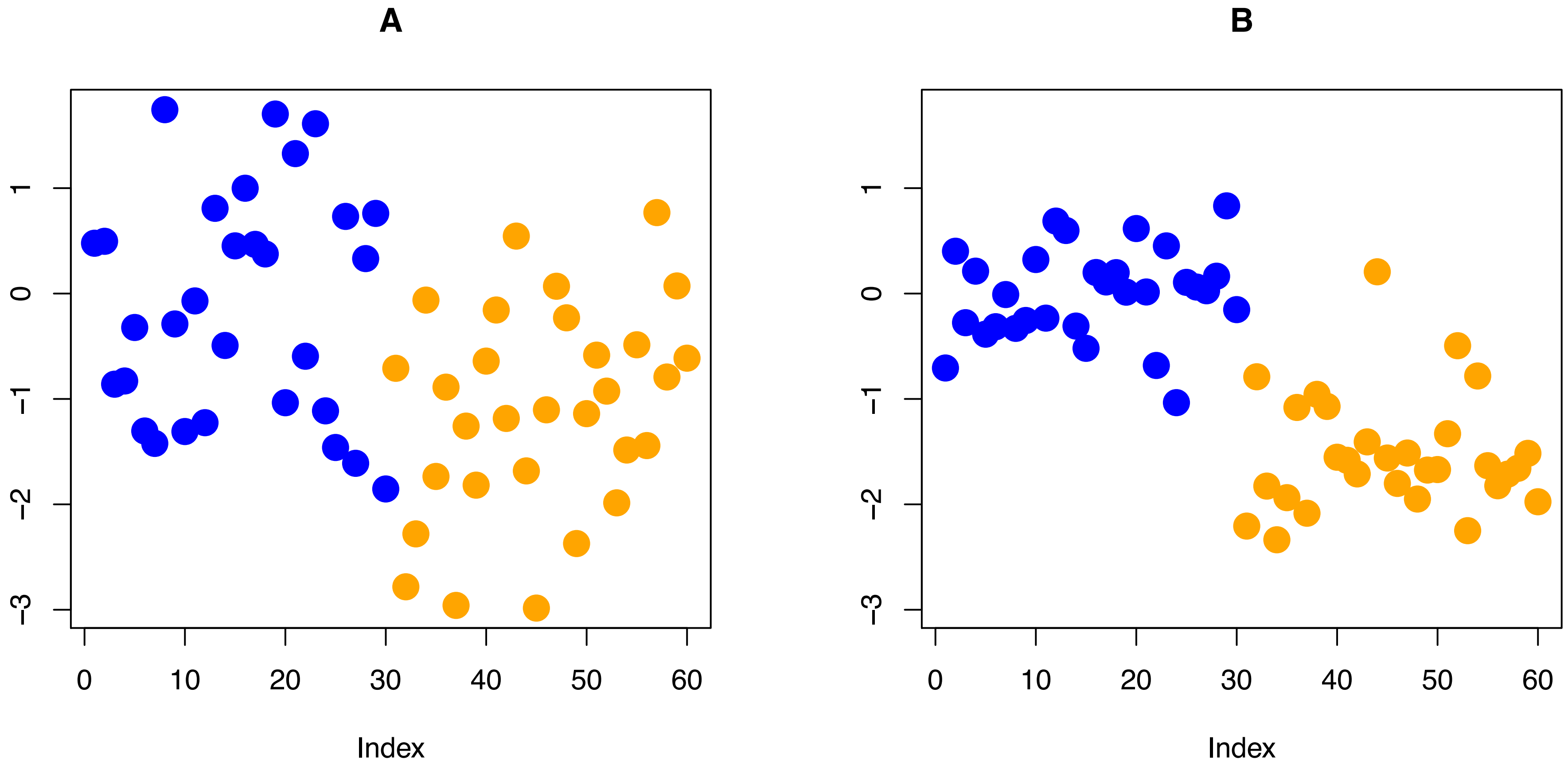
Question 4: Given these boxplots, which of two underlying distributions are more similar?



Question 6: Given this design matrix, describe the experimental design.

$$X = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 \\ 1 & 0 & 1 & 0 \\ 1 & 1 & 0 & 0 \\ 1 & 1 & 0 & 0 \\ 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 \end{bmatrix}$$

Question 8: Which plot highlights more (statistical) evidence for a change in the population means (between orange and blue)?



Course communication

- Video situation: we will have recordings, hopefully posted within 24 hours of the lecture
- Slack: vast majority of communication happens here (note: all invitations were sent to UZH email addresses)
- Except for exceptional circumstances, **no emails please**; communicate on Slack only (maybe later on GitHub)
- Slack policy: unless private, ask questions in a public channel (please note: *good questions get good answers*); use threads when relevant; good manners/behaviours are expected

Course evaluation

1. Journal club presentation	20%
2. Project	50%
3. Exercises	30%
4. Technology day (participation)	0% or -10%

Rough structure of lecture/exercise time

Monday mornings: we will run X.00-X.45; X in {9,10,11}

- Lectures and Exercises
- Lecture/journal club presentation (9.00-whenever)
- Remaining time: free (can be used to work on exercises; we are available for questions)

M.Sc. thesis projects

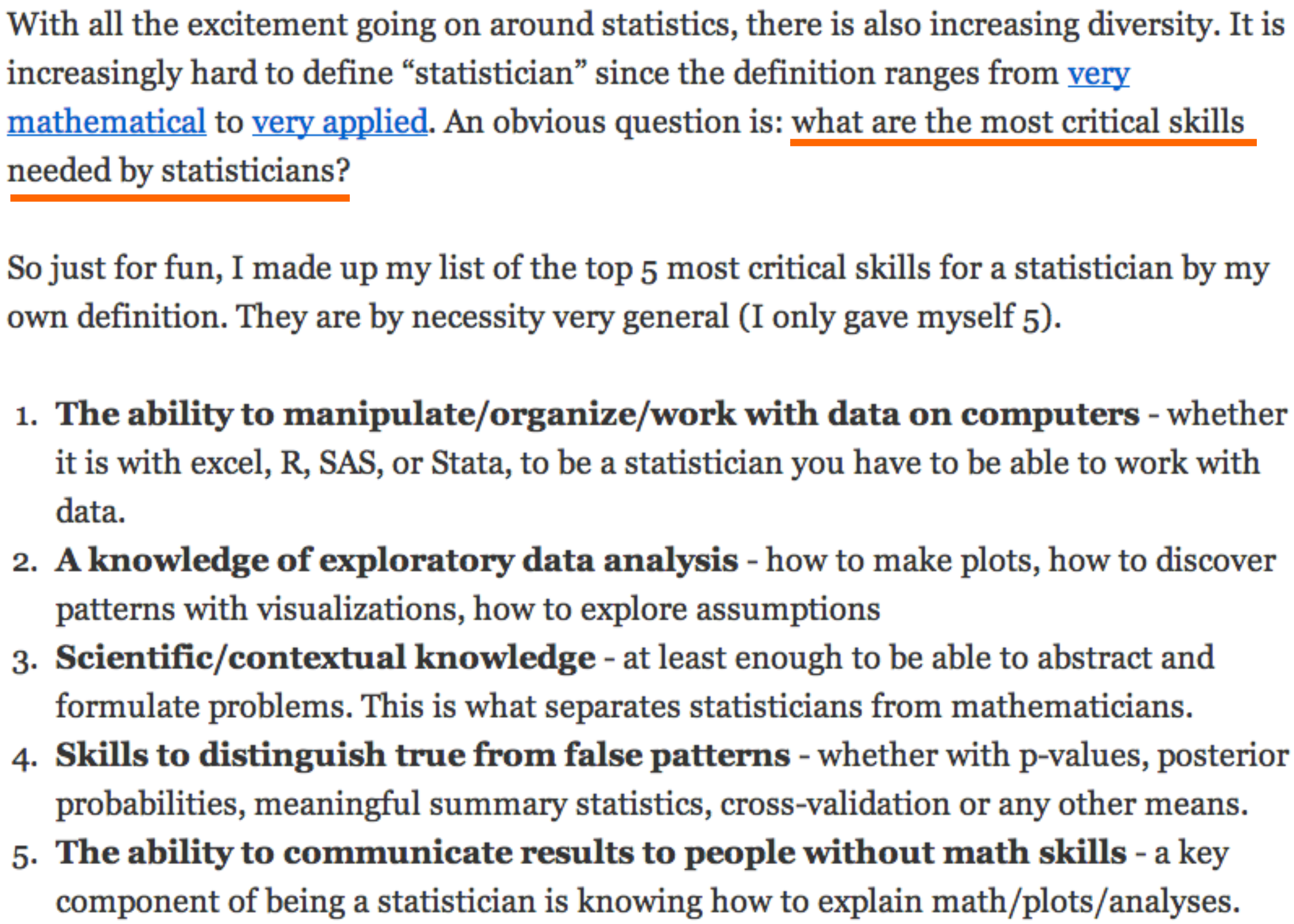
If you are:

- in a M.Sc. programme (ETHZ or UZH)
- have a solid background/experience in mathematics / statistics / computation
- have an interest in research in this field ("statistical bioinformatics")
- looking for a thesis project

→ Discuss a project in my lab

http://simplystatistics.org/2013/07/03/repost-the-5-most-critical-statistical-concepts/

Critical skills needed by statisticians (Jeffrey Leek's words):



With all the excitement going on around statistics, there is also increasing diversity. It is increasingly hard to define "statistician" since the definition ranges from very mathematical to very applied. An obvious question is: what are the most critical skills needed by statisticians?

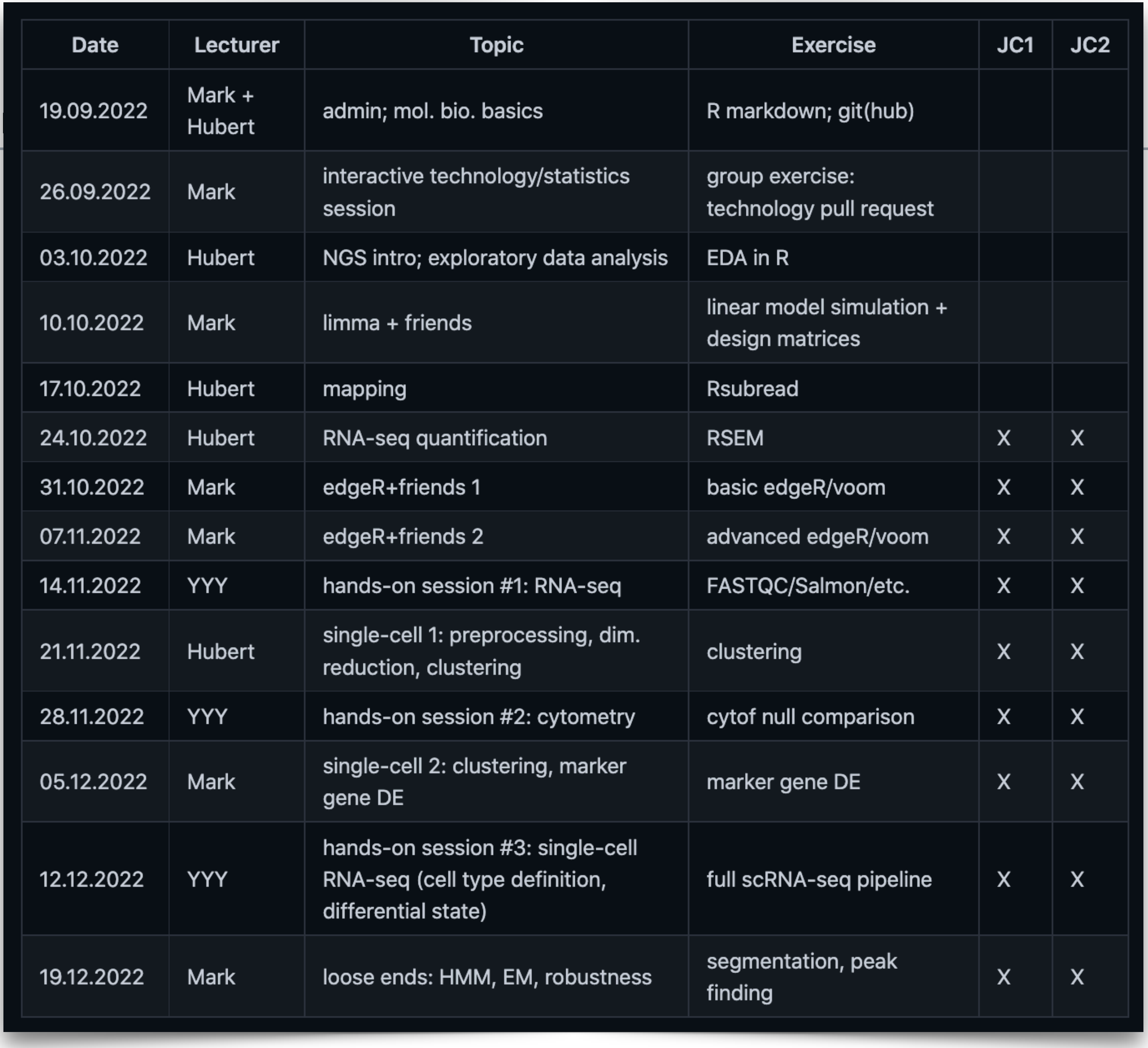
So just for fun, I made up my list of the top 5 most critical skills for a statistician by my own definition. They are by necessity very general (I only gave myself 5).

1. **The ability to manipulate/organize/work with data on computers** - whether it is with excel, R, SAS, or Stata, to be a statistician you have to be able to work with data.
2. **A knowledge of exploratory data analysis** - how to make plots, how to discover patterns with visualizations, how to explore assumptions
3. **Scientific/contextual knowledge** - at least enough to be able to abstract and formulate problems. This is what separates statisticians from mathematicians.
4. **Skills to distinguish true from false patterns** - whether with p-values, posterior probabilities, meaningful summary statistics, cross-validation or any other means.
5. **The ability to communicate results to people without math skills** - a key component of being a statistician is knowing how to explain math/plots/analyses.

Learning outcomes (in my words)

- Understand the fundamental “scientific process” in the field of Statistical Bioinformatics
- Be equipped with the skills / tools to preprocess genomic data (Unix, Bioconductor, mapping, etc.) and ensure reproducible research (R / markdown / quarto)
- Have a general knowledge of (some) **types** of data and **biological applications** encountered with high throughput genomic data
- Have the general knowledge of the range of statistical methods that get used with microarray and sequencing data
- Gain the ability to apply statistical methods / knowledge / software to a collaborative biological project
- Gain the ability to critical assess the statistical bioinformatics literature
- Write a coherent summary of a bioinformatics problem and it’s solution in statistical terms

The semester-long course structure (subject to change)



Date	Lecturer	Topic	Exercise	JC1	JC2
19.09.2022	Mark + Hubert	admin; mol. bio. basics	R markdown; git(hub)		
26.09.2022	Mark	interactive technology/statistics session	group exercise: technology pull request		
03.10.2022	Hubert	NGS intro; exploratory data analysis	EDA in R		
10.10.2022	Mark	limma + friends	linear model simulation + design matrices		
17.10.2022	Hubert	mapping	Rsubread		
24.10.2022	Hubert	RNA-seq quantification	RSEM	X	X
31.10.2022	Mark	edgeR+friends 1	basic edgeR/voom	X	X
07.11.2022	Mark	edgeR+friends 2	advanced edgeR/voom	X	X
14.11.2022	YYY	hands-on session #1: RNA-seq	FASTQC/Salmon/etc.	X	X
21.11.2022	Hubert	single-cell 1: preprocessing, dim. reduction, clustering	clustering	X	X
28.11.2022	YYY	hands-on session #2: cytometry	cytof null comparison	X	X
05.12.2022	Mark	single-cell 2: clustering, marker gene DE	marker gene DE	X	X
12.12.2022	YYY	hands-on session #3: single-cell RNA-seq (cell type definition, differential state)	full scRNA-seq pipeline	X	X
19.12.2022	Mark	loose ends: HMM, EM, robustness	segmentation, peak finding	X	X

Expectations: **journal club** presentation

- 20-25 minutes (+5 minutes discussion)
- MUST:
  - ➡ be a paper about a **statistical** method in bioinformatics
  - ➡ be approved by Mark/Hubert
- Should:
  - ➡ describe the biological context and/or data collected
  - ➡ describe the (new) model used
  - ➡ describe comparisons to existing methods
- Should not:
  - ➡ be one of the papers discussed in detail in lectures: limma, edgeR, DEXSeq, etc.
- (since 2017) feedback forms from fellow students

Expectations: **project**

- ~10-15 page report, with R code in line (e.g. **quarto**)
- Describe the biological setting, statistical analysis, exploratory analysis with publication-quality graphics embedded
- Three possibilities:
  - Comparison of statistical methods (simulation / reference data + metrics)
  - Reproduce an analysis from a paper from the raw data
  - Real collaborative project with FGCZ or a local laboratory
- Be strategic: work on something related to your interests!
- Typically due at end of first working week of January

Expectations: **exercises**

- There will be an exercise **every** week
- Across 14 weeks, the *best 9* exercises are counted towards the 30%

Soft technical skills needed (developed) in this course …

- **Data Science!**
- Use unix-like operating system to run command-line programs
- Options:
  - use your own computer (if Windows, use cygwin)
  - use renkulab.io
- R: from the command line or RStudio (https://rstudio.com/); getting help; creating workflows; how to make publication-quality graphics (ggplot2); knitr/Rmarkdown/quarto
- Bioconductor – www.bioconductor.org
- git/github
- bioconda/Docker (cloud computing)

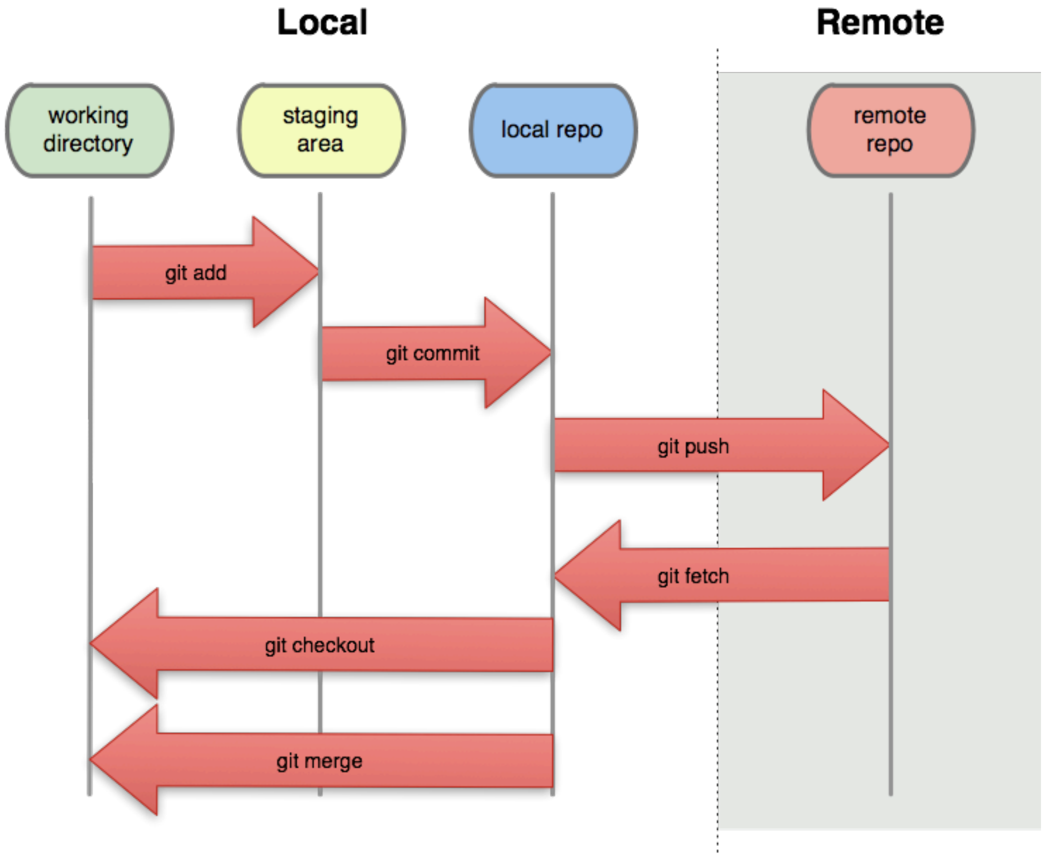
Hubert’s lecture

Demos:

- git/github
- renkulab.io (fork a project, start a session)
- quarto.org

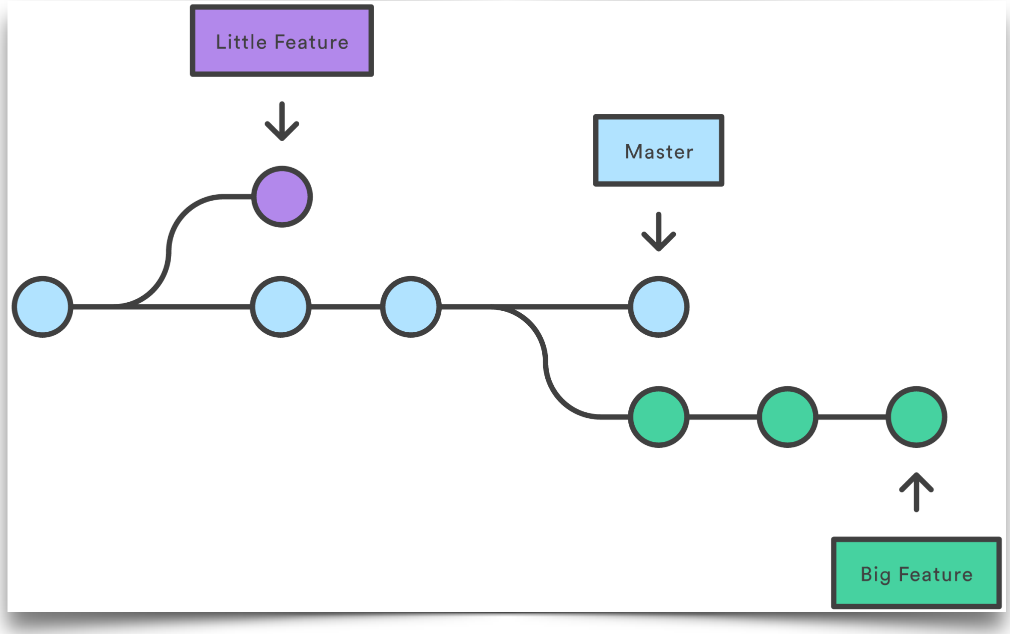
```
git clone
git pull
git status
git branch
git commit
git add
git checkout
git push
```

Quick intro to Git/Github (version control)



https://skylabcoders.github.io/bootcamp-winter2017/?full#17

Branching



https://blog.seibert-media.net/blog/2015/07/31/git-mit-branches-arbeiten-git-branch/

Exercise 1
Part a: GitHub
Part b: quarto

Note: all homework submissions occur via github

Week 1 Exercise Part A:

1. Recommend: get R 4.2.1, latest RStudio, git, quarto, etc.
2. If you haven't already, create an account at github.com/join; give GitHub username (+details about computing) to Mark via https://forms.gle/sc7ci6jPFweBE8xKA
3. Acquaint yourself with git / github (gitlab) [1]; make sure you can check in (`push`) / out (`pull/clone`) files from command line or app [2].
4. Create a new public github repository, add a README.md (using markdown [3]) and add some content; include an image; include a web link, etc.
5. Add an Issue to the 'material' repo [4] with a link to your repo (you can delete the repo after I've closed the issue, if you want)

[1] https://gist.github.com/andrewpmiller/9668225
[2] https://confluence.atlassian.com/stash/basic-git-commands-278071958.html
[3] http://markdowntutorial.com/
[4] https://github.com/sta426hs2022/material

Quarto for executable documents / reproducibility

Week 1 Exercise Part B:

1. Test your R knowledge here: https://forms.gle/FFHiFx8UHrBVGv2R9 (only 9 questions)
2. Acquaint yourself with quarto for executable documents [1].
3. Create an HTML document with R code that samples 100 values from a negative binomial distribution (say, mu=10, dispersion=2; using the parameterisation with mean=mu and variance=mu+mu^2*dispersion); create a histogram of sampled data on both the linear and log [or maybe log(x+1) due to zeros] scale; Write 1-2 sentences to describe your steps (ideally also with section headings) and report the mean and variance of the sample *in line* in the text.
4. Add the QMD and HTML files to your repo from Week 1 Exercise Part A.

[1] https://quarto.org/