# Course Overview & Short Introduction

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MED3007
Statistical Principles in Genomics: an Introduction with Rstudio
15.01.2024

1. Course Overview
   - Course summary & schedule
   - Take-home Exam

2. Short Introduction to the Topic
   - Common statistical tasks with large-scale biological data
   - Group Work

# Course Content

## Motivations

- molecular (genomic) data increasingly important in medical research & clinical practice
- such data are *very high-dimensional* $\rightarrow$ challenges

## Aims

- **general:** learn the challenges & solutions when analysing genomic data, both in **theory** and **practice**
- **theory:** focus on three main tasks; screening, visualisation, clustering
- **practice:** introduction to RStudio, many examples

# Course Structure

## General structure

- afternoon:
  - lecture on a topic + Q & A session
  - some free time for reflection / group work
- morning after: practical lab session on the same topic

| | Monday | Tuesday | Wednesday | Thursday | Friday |
|---|---|---|---|---|---|
| 9:00 - 9:45 | Intro Course | Intro Lab 1 | Lab 2 | Lab 3 | |
| 10:00 - 11:30 | Intro RStudio | Lab 1 | Exercises | Exercises | |
| 11:30 - 13:00 | lunch | lunch | lunch | lunch | Exam |
| 13:00 - 14:00 | Lecture 1 | Lecture 2 | Lecture 3 | Exam Sim | |
| 14:00 - 16:00 | Group Work | Group Work | Group Work | Wrap-up | |

## Special Sessions

Thursday is quite interactive. Used to fix concepts from the course, to ask questions, and to see a take-home exam simulation.

# Practical Info

## Website

More interactive website we will use for teaching materials:
`https://ocbe-uio.github.io/course_med3007/`

## Canvas

- Course webpage on Canvas:
  `https://www.uio.no/studier/emner/medisin/med/MED3007`
- `https://uio.instructure.com` and Mobile App Canvas Student (for iOS and Android)
- All course material (lecture notes, computer labs, data sets, reading material) will be ALSO made available via Canvas
- If you have problems logging in, send me email asap!

# Info on the course Take-home Exam

## Idea

- The purpose of the exam is to **replicate** one of the analyses we will see in class
- **Any proposal will be accepted.** The focus is not on right/wrong answers, but on showing independence in managing high-dimensional data analysis: choosing a method for a given purpose

## Details

- Starting point is a **data set,** which will be provided via **Inspera** on **Thursday at 15:00**
- You have time until **Monday** same time
- You can provide your analysis as a .pdf or .doc file, or as a .R (or .Rmd) file. Important is to report what you think is relevant for me to understand *what* you did and *why* you did what you did

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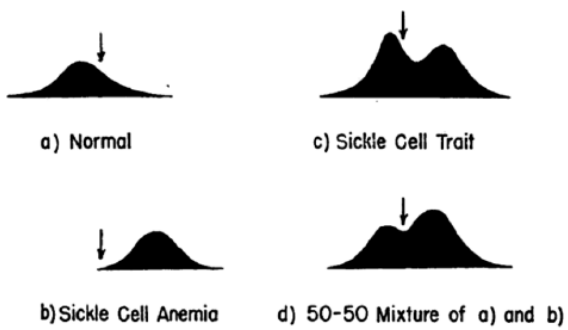
# Sickle cell anemia, a molecular disease (Pauling et al, 1949)

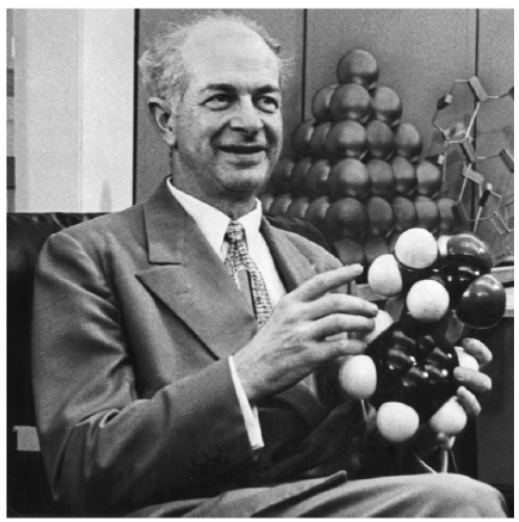
November 25, 1949, Vol. 110 SCIENCE 543

## Sickle Cell Anemia, a Molecular Disease[1]

Linus Pauling, Harvey A. Itano,[2] S. J. Singer,[2] and Ibert C. Wells[3]

*Gates and Crellin Laboratories of Chemistry,*
*California Institute of Technology, Pasadena, California*[4]



# Sickle cell anemia, a molecular disease (Pauling et al, 1949)

- Pauling et al. showed that hemoglobin from patients suffering from sickle cell anemia had a different electrical charge than that from healthy individuals.
- This report had a powerful impact on both the biomedical community and the general public for two reasons:
  1. It showed that the cause of a disease could be traced to an alteration in the molecular structure of a protein.
  2. As this disease was known to be inherited, the paper argued that genes determine the structure of proteins.

# Biomarkers / molecular markers

## Biomarker

We refer to a biomarker as a biological quantitative measure associated with a clinical outcome. It may be a single trait, or a grouping (signature) of traits that separates different populations with respect to an outcome of interest." (Sargent *et al.*, 2005)[a].

**Examples:** classic laboratory parameters (blood pressure, cholesterol level, blood glucose) and molecular markers.

[a] Sargent, D. J., Conley, B. A., Allegra, C., & Collette, L. (2005). Clinical trial designs for predictive marker validation in cancer treatment trials. *Journal of Clinical Oncology*, 23(9), 2020-2027.

## Molecular marker

A molecular marker is a biomarker that can be detected using genomics and/or proteomics technologies.

**Examples:** gene mutations, gene expression, protein expression, methylation patterns.

# Molecular diagnostics

It means **to identify molecular markers in the genome by applying molecular biology to medical testing.** The technique is used to diagnose and monitor disease, detect risk, and decide which therapies will work best for individuals.

**Examples:**

- **Prenatal tests** for chromosomal abnormalities (e.g. Trisomy 21)
- **Infectious diseases:** test for infectious diseases such as chlamydia, influenza virus and tuberculosis; or for specific strains such as the **H1N1 virus** (pathogenomics).
- **Cancer screening:** for example testing for mutations in BRCA1 or BRCA2 for familial form of breast cancer (about 5% of all breast & ovarian cancers) $\rightarrow$ "Angelina Jolie" effect

# Statistical Principles in Genomics

- The main difference to "classical statistics" is the **high-dimensionality of the data**: in genomic data we have tens of thousands or millions of input variables/ features.
- Most of those features will not be of interest in the specific context of the experiment. $\rightarrow$ The main task is the **identification of important features** (genes, SNP's, etc).
- We have to deal with the curse of dimensionality.

References:


1. James et al. (2013) An Introduction to Statistical Learning with Applications in R, `https://www.statlearning.com/`, Chapters: 1, 2, 12, 13
2. Holmes, Huber (2019). Modern Statistics for Modern Biology, `http://web.stanford.edu/class/bios221/book/` Chapters: 3, 5, 6, 7

# Statistical Principles in Genomics

1. Screening and multiple testing
   (to determine lists of differentially expressed genes)
2. Exploratory analysis and unsupervised learning
   - Exploratory analysis: Dimension reduction and visualisation
     (ex. principal components analysis)
   - Unsupervised learning: Clustering and heatmaps
     (ex. to find subgroups of similarly regulated genes)

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# Info on the course Group Work

## Idea

- The purpose of the group work is to **find practical examples** of the analyses we will see in class
- Aim: **Get the discussion going.** The focus is not on right/wrong answers, but on discussing issues seen in class in a practical setting

## Details

- Starting point: **two papers**, paper 1 and paper 2 (see next slides)
- Paper 1 is related to Lecture 1 and 2; Paper 2 to Lecture 3
- **Group Work: what are you supposed to do?** Read the paper, and try to answer in groups to the following questions
  1. Which was the main research question addressed in the paper?
  2. Where do results of methods seen in class are reported in the paper? (which figures/tables)

# Paper 1 (focus for Lectures 1 & 2)

Cappelletti *et al. Clinical Proteomics* (2022) 19:23
https://doi.org/10.1186/s12014-022-09361-1

Clinical Proteomics

RESEARCH Open Access

## Quantitative proteomics reveals protein dysregulation during T cell activation in multiple sclerosis patients compared to healthy controls

Chiara Cappelletti[1], Anna Eriksson[3], Ina Skaara Brorson[3,4], Ingvild S. Leikfoss[3,4], Oda Kråbøl[2], Einar August Høgestøl[3,4,5], Valeria Vitelli[6], Olav Mjaavatten[7], Hanne F. Harbo[3,4], Frode Berven[7], Steffan D. Bos[4] and Tone Berge[1,2*]

# Paper 2 (focus for Lecture 3)

*Published online 24 March 2022*

*NAR Cancer, 2022, Vol. 4, No. 1* **1**
*https://doi.org/10.1093/narcan/zcac008*

## Epigenetic alterations at distal enhancers are linked to proliferation in human breast cancer

**Jørgen Ankill [1,2], Miriam Ragle Aure [3], Sunniva Bjørklund [3], Severin Langberg [4], Oslo Breast Cancer Consortium (OSBREAC), Vessela N. Kristensen [3], Valeria Vitelli [5], Xavier Tekpli [3] and Thomas Fleischer [1,*]**

[1]Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital, Oslo, Norway, [2]Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway, [3]Department of Medical Genetics, Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway, [4]Cancer Registry of Norway, Oslo, Norway and [5]Oslo Centre for Biostatistics and Epidemiology, Department of Biostatistics, Faculty of Medicine, University of Oslo, Oslo, Norway