Welcome to Bioinformatics Applications 2019 Spring

Overview

Bioinformatics Applications (PLPTH813)

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Goal

PLPTH813 will cover **the basic principle** of regular bioinformatics applications and emphasize **the practice of bioinformatics**.

The ultimate goal of this course is to help you to be prepared for next-generation biological research that often generates large data and requires researchers to have the capability in data management and data mining.

Course materials are online

Course site at Github

https://github.com/liu3zhenlab/teaching/tree/master/PLPTH813Bioinformatis/2019

- Course information
- Lecture slide files
- Labs slide files

Bioinformatics

Bioinformatics is an ***interdisciplinary*** field that develops methods and software tools for understanding ***biological data***.

Sequencing technology

1980 Nobel Prize

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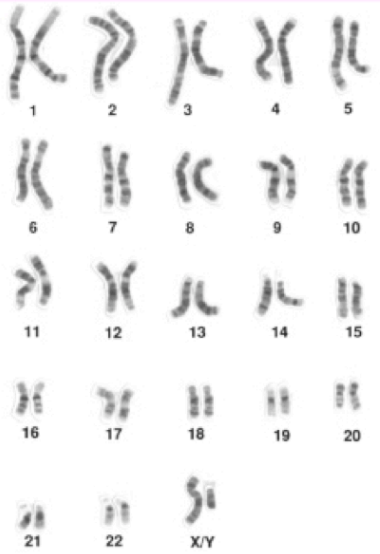
```

gene

chromosome

genome



www.ncbi.nlm.nih.gov

Human Genome Project (HGP)

1st-gen sequence (Sanger)

```
>sample
TGCCGCCTACTAACCGGTTCTGAGAGTTCTGAGATG
AGAGAATGCCTACTAACCGGTTCTGAGAATGCCTA
CTAACCGATGCCTACTAACCGGTTCTGAGAGTTCTG
AGCTGAGATGCCTACTAACCGGTTCTGAGAATGCCT
ACTAACCGATGCCTACTAACCGGTTCTGAGAGTTCT
GAGATGAGAGAATGCCTACTAACCGGTTCTGAGAA
TGCCTACTAACCGATGCCTACTAACCGGTTCTGAGA
GTTCTGAGCTATGCCTACTAACCGGTTCTGAGAATG
CCTACTAACCGATGCCTACTAACCGGTTCTGAGAGT
TCTGAGATGAGAGAATGCCTACTAACCGGTTCTGA
GAATGCCTACTAAATGCCTACTAACCGGTTCTGAGA
ATGCCTACTAACCGATGCCTACTAACCGGTTCTGAG
AGTTCTGAGATGAGAGAATGCCTACTAACCGGTTCT
GAGAATGCCTACTAACCGATGCCTACTAACCGGTTC
TGAGAGTTCTGAGCTCCGATGCCTACTAACCGGTTC
TGAGAGTTCTGAGCTAATACTAACCGGTTATGCCTA
CTAACCGGTTCTGAGAATGCCTACTAACCGGTTCTG
AGAATGCCTACTAACCGATGCCTACTAACCGGTTCT
GAGAGTTCTGAGATGAGAGAATGCCTACTAACCGG
TTCTGAGAATGCCTACTAACCGATGCCTACTAACCG
GTTCTGAGAGTTCTGAGCTGAGAA
```

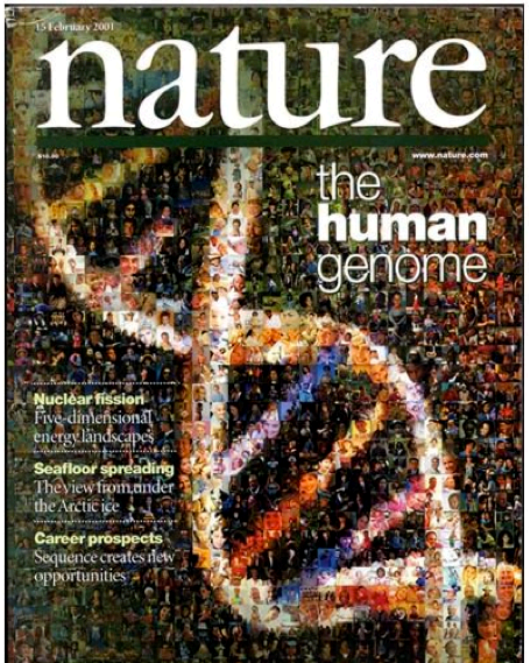
- International Human Genome Sequencing Consortium

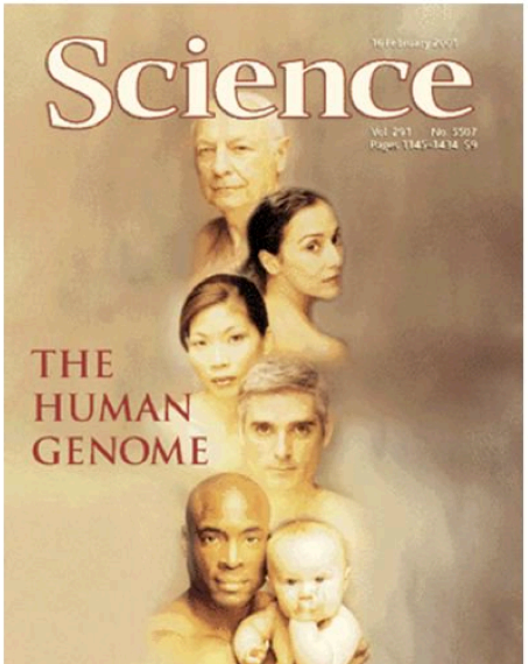
Proposed 1985, endorsed in 1988; BAC-by-BAC

- Craig Venter & Celera Genomics:

Founded 1998, finished in 3 years; whole genome shotgun

February 2001 - Publication of the first draft of the human genome





First draft

DNA sequencing technology

1st-gen sequence (Sanger)

1980 Nobel Prize

```
>sample
TGCCGCCTACTAACCGGTTCTGAGAGTTCTGAGATG
AGAGAATGCCTACTAACCGGTTCTGAGAATGCCTA
CTAACCGATGCCTACTAACCGGTTCTGAGAGTTCTG
AGCTGAGATGCCTACTAACCGGTTCTGAGAATGCCT
ACTAACCGATGCCTACTAACCGGTTCTGAGAGTTCT
GAGATGAGAGAATGCCTACTAACCGGTTCTGAGAA
TGCCTACTAACCGATGCCTACTAACCGGTTCTGAGA
GTTCTGAGCTATGCCTACTAACCGGTTCTGAGAATG
CCTACTAACCGATGCCTACTAACCGGTTCTGAGAGT
TCTGAGATGAGAGAATGCCTACTAACCGGTTCTGA
GAATGCCTACTAAATGCCTACTAACCGGTTCTGAGA
ATGCCTACTAACCGATGCCTACTAACCGGTTCTGAG
AGTTCTGAGATGAGAGAATGCCTACTAACCGGTTCT
GAGAATGCCTACTAACCGATGCCTACTAACCGGTTC
TGAGAGTTCTGAGCTCCGATGCCTACTAACCGGTTC
TGAGAGTTCTGAGCTAATACTAACCGGTTATGCCTA
CTAACCGGTTCTGAGAATGCCTACTAACCGGTTCTG
AGAATGCCTACTAACCGATGCCTACTAACCGGTTCT
GAGAGTTCTGAGATGAGAGAATGCCTACTAACCGG
TTCTGAGAATGCCTACTAACCGATGCCTACTAACCG
GTTCTGAGAGTTCTGAGCTGAGAA
```

800 letters

next-gen sequence (NGS)

billions of letters

1970's Sanger sequencing

Sequencing cost

cost per megabase

$5,000

Roche 454

$1000

$100

Illumina

$10

$1

Illumina

$0.1

$0.05

Illumina

$0.02

cost

Sep-01 Mar-02 Sep-02 Mar-03 Oct-03 Jan-04 Apr-04 Jul-04 Oct-04 Jan-05 Apr-05 Jul-05 Oct-05 Jan-06 Apr-06 Jul-06 Oct-06 Jan-07 Apr-07 Jul-07 Oct-07 Jan-08 Apr-08 Jul-08 Oct-08 Jan-09 Apr-09 Jul-09 Oct-09 Jan-10 Apr-10 Jul-10 Oct-10 Jan-11 Apr-11 Jul-11 Oct-11 Jan-12 Apr-12 Jul-12 Oct-12 Jan-13 Apr-13 Jul-13 Oct-13 Jan-14 Apr-14 Jul-14 Oct-14 Jan-15 Apr-15 Jul-15 Oct-15

time

Data source: genome.gov/sequencingcosts

Sequence genomes of model species

2000

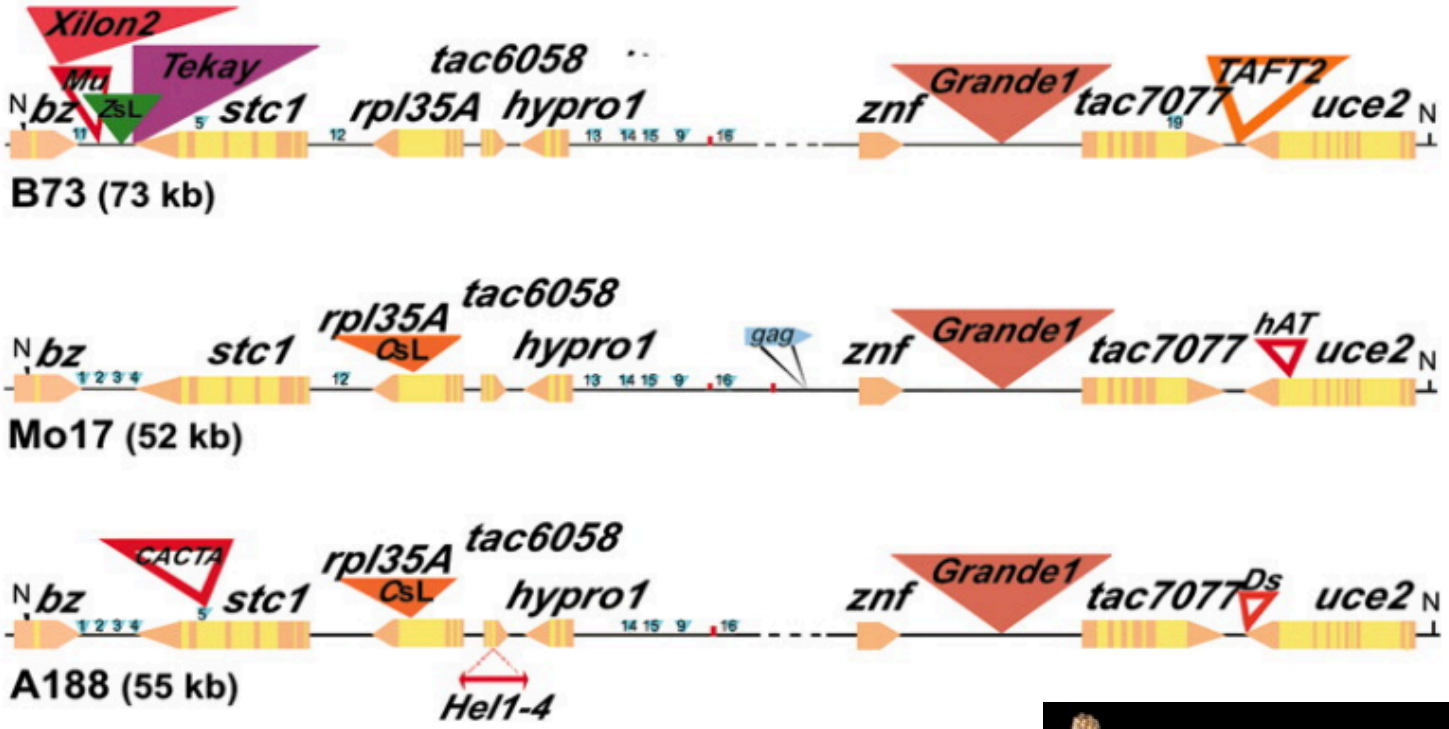
2002

2009

2018

Sequence EVERY species

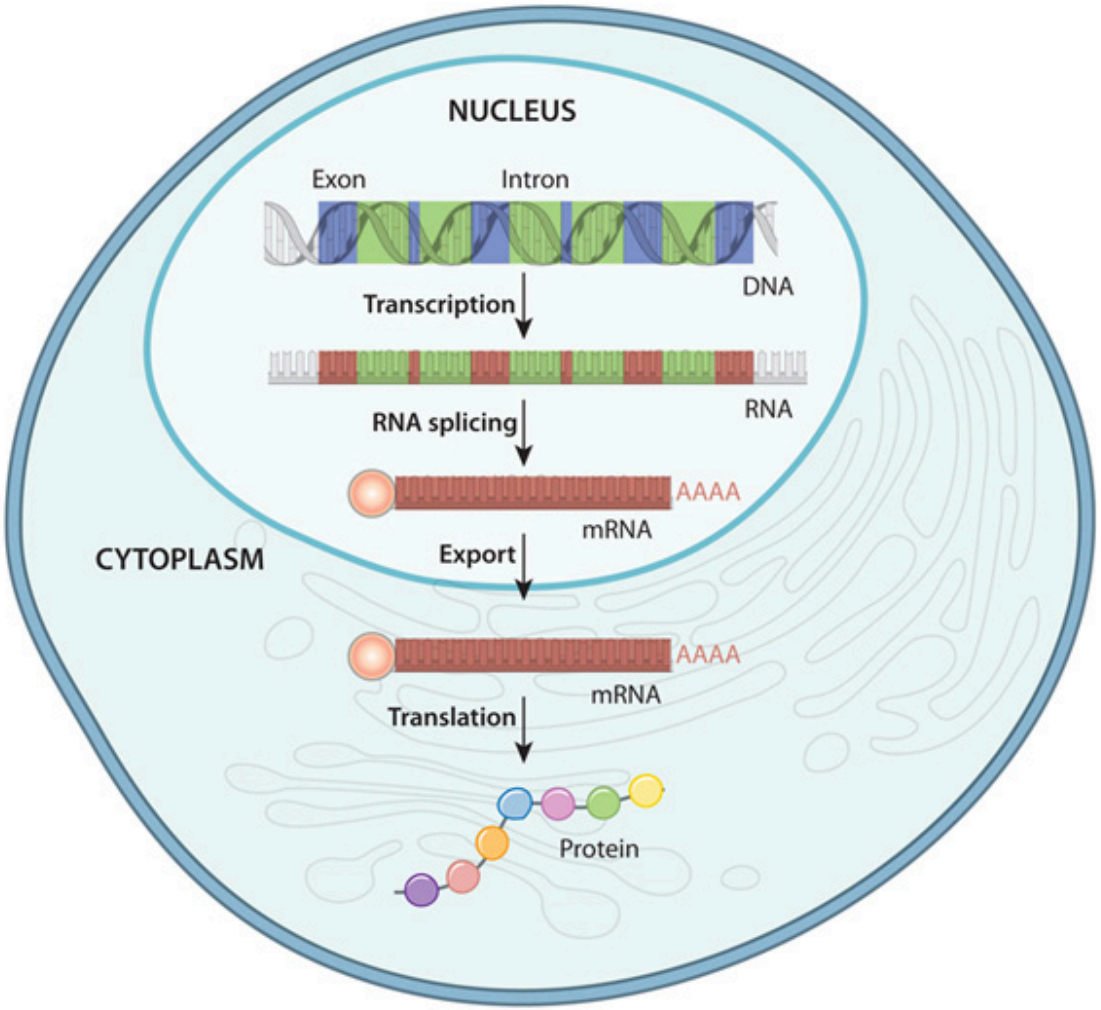
Comparative genomics



Remarkable variation in maize genome structure at the *bz* locus

PNAS, 2006, 103:17644-49

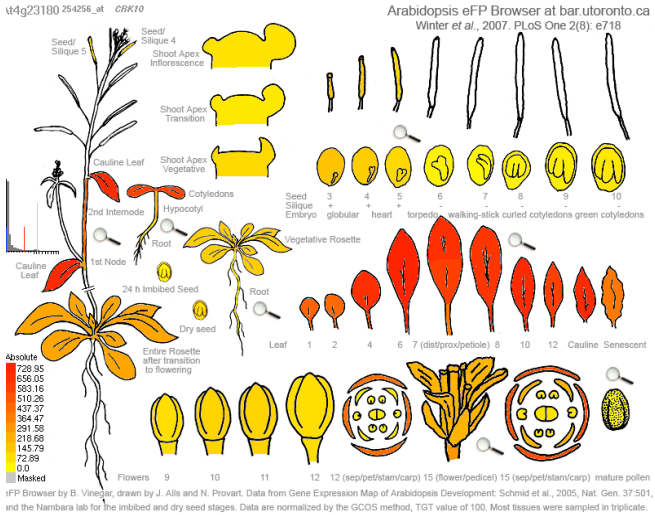
Complexity of transcriptome



DNA to protein in eukaryote

nature.com/scitable/topicpage/gene-expression-14121669

Transcriptome analysis



Expression profiles in different tissues

Response to biotic stress

1. What are sequences of transcripts?
2. What is the expression level of each transcript?

RNA-Seq addresses both questions pretty well

NGS is changing the way to discover genetic variants

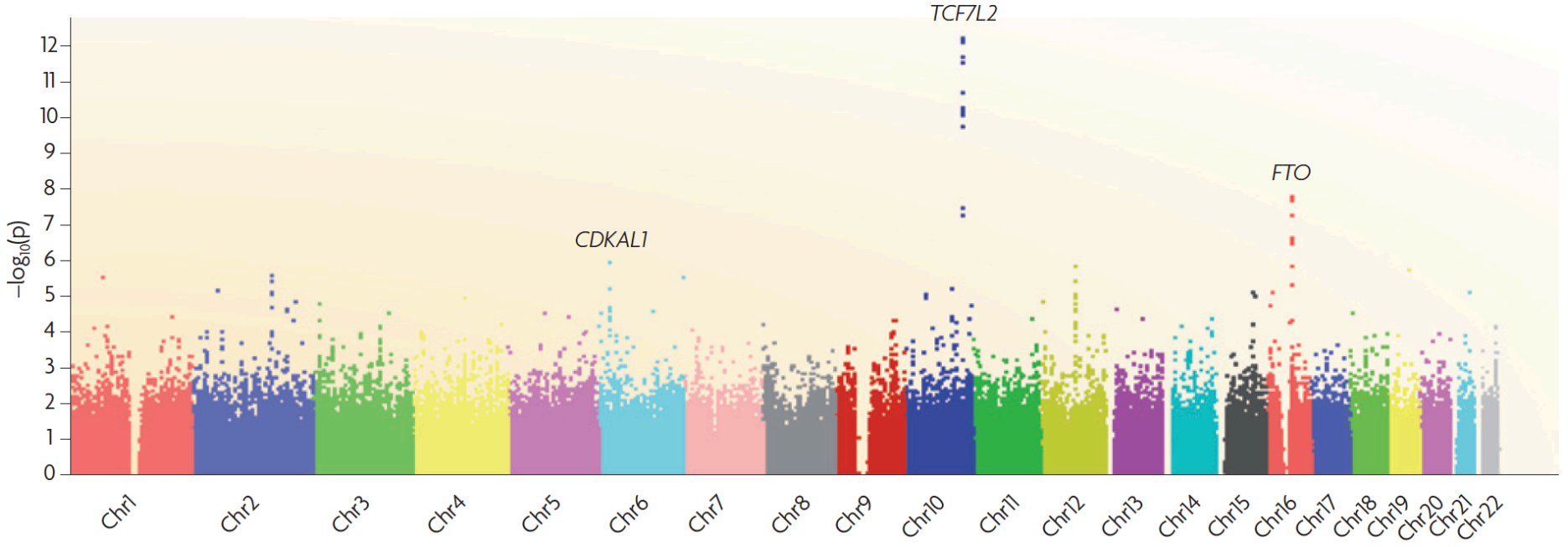
Reference ATCGCTGCCGATCTGCGTCATACGGAATCGTCGGCTTCAG

Sequences

ATCGCTGCCGATCTGCGTCATACGGAATCGTCGGCTTCAG
ATCGCTGCCGATCTGCGTGATACGGAATCGTCGGCTTCAG
ATCGCTGCCGATCTGCGTCATACGGAATCGTCGGCTTCAG
ATCGCTGCCGATCTGCGTGATACGGAATCGTCGGCTTCAG
ATCGCTGCCGATCTGCGTGATACGGAATCGTCGGCTTCAG
ATCGCTGCCGATCTGCGTGATACGGAATCGTCGGCTTCAG
ATCGCTGCCGATCTGCGTCATACGGAATCGTCGGCTTCAG
ATCGCTGCCGATCTGCGTCATACGGAATCGTCGGCTTCAG
ATCGCTGCCGATCTGCGTGATACGGAATCGTCGGCTTCAG
ATCGCTGCCGATCTGCGTCATACGGAATCGTCGGCTTCAG

Genotype ----------C/G----------

Genome-wide association mapping



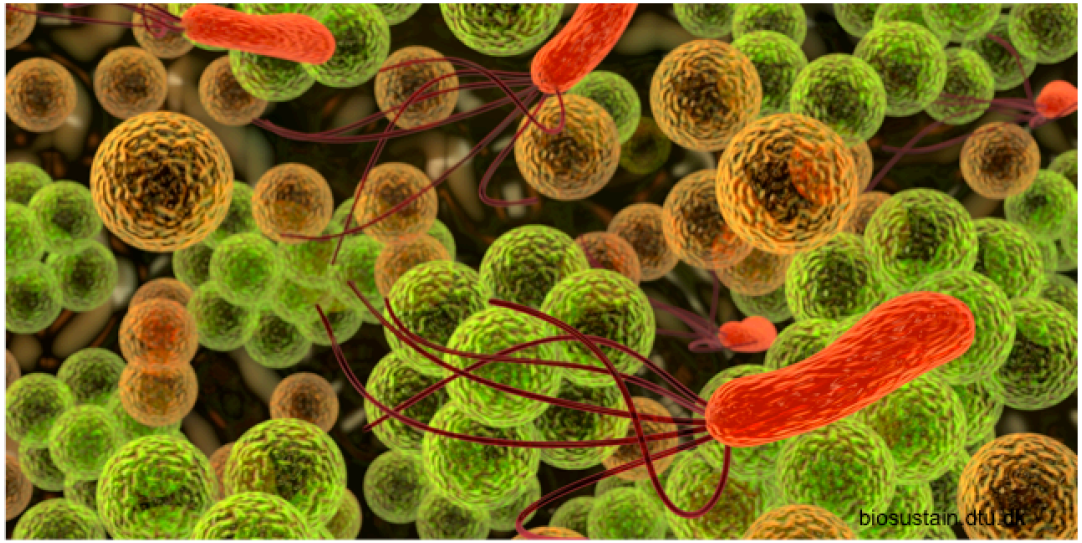
McCarthy et al., Nature Review Genetics, 2008: 9:356-369

Environmental microbiomes

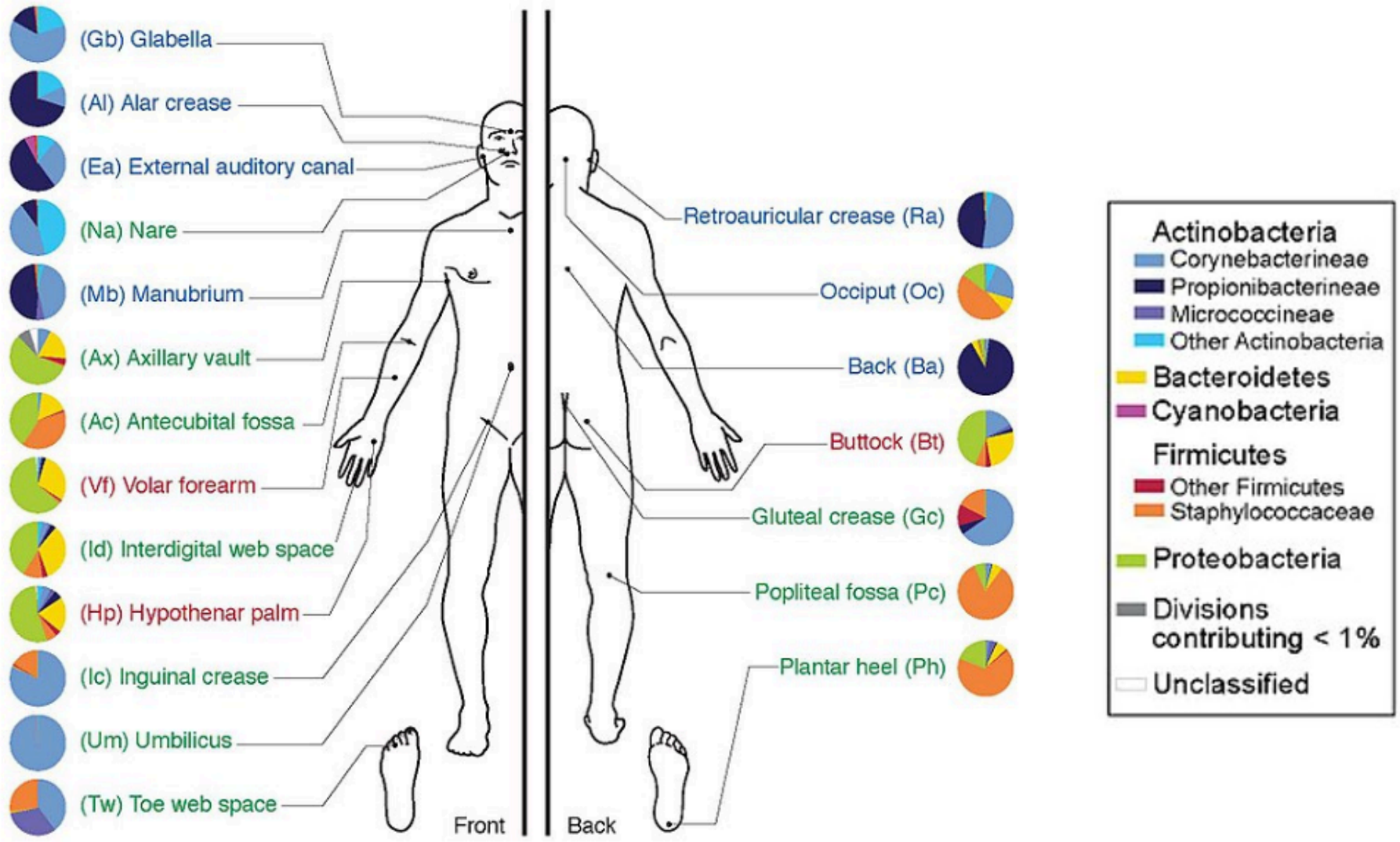
Water

Plants

Soils



Human microbiomes



The human ***skin*** microbiota (wikipedia)

Reason for command-lines analyses

- To perform **efficient** and **reproducible** data analyses
- To use advanced tools in research projects (most genomic software software packages are run in the Unix system)
- To access to powerful computer servers (e.g., beocat)

Lecture topics

1. Basic Unix
2. Basic R
3. Introduction of NGS and NGS bioinformatics tools
4. DNA sequence alignment
5. Genome variants
6. Phylogeny
7. Construction of a genetic map
8. QTL and GWAS
9. Genome assembly
10. Comparative genomics
11. Metagenomics
12. RNA-Seq

Grading and schedule

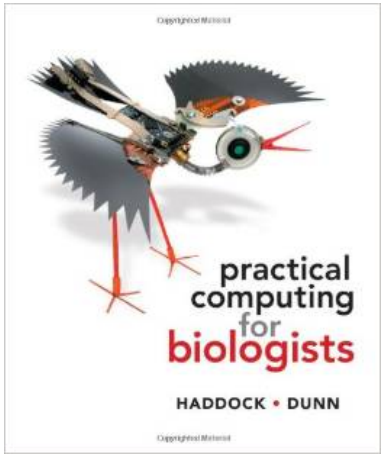
- **Grading**

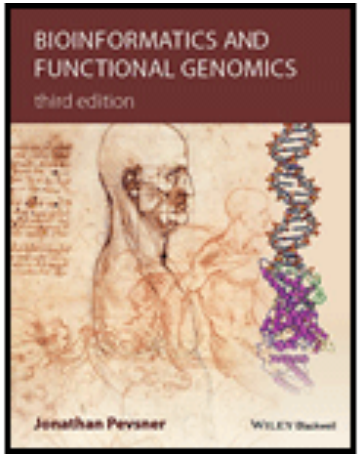
Class participation 10%, Homework 35%, Midterm Exam 20%, Oral presentation 10%, Final Exam 25%

- Homework: 6+ times
- Oral presentation
  1. Genome assembly and annotation
  2. Comparative genomics and pan-genomics
  3. Genetic mapping (QTL, GWAS, and post-GWAS)
  4. RNA-Seq (analysis methods, small RNA, non-coding RNA, circle RNA)
  5. metagenomics
  6. new genome technologies and new bioinformatics tools
- Two exams (midterm and final)

References

- Papers
- Online resources (e.g., Wikipedia)
- Practical computing for biologists, Haddock and Dunn, 2010
- Bioinformatics and Functional Genomics, Pevsner, 2015





Schedule

- Lecture: 11:00am-11:50pm, Tuesday, Thursday
- Lab: 1:00-2:30pm, Thursday

(typically each lab finished in 1:30 hours)

- Office hours: 12:00-1:00pm Tuesday