Exploratory Data Analysis and visualisation (cont-d)

Kaspar Märtens

4 December 2018

Last time:

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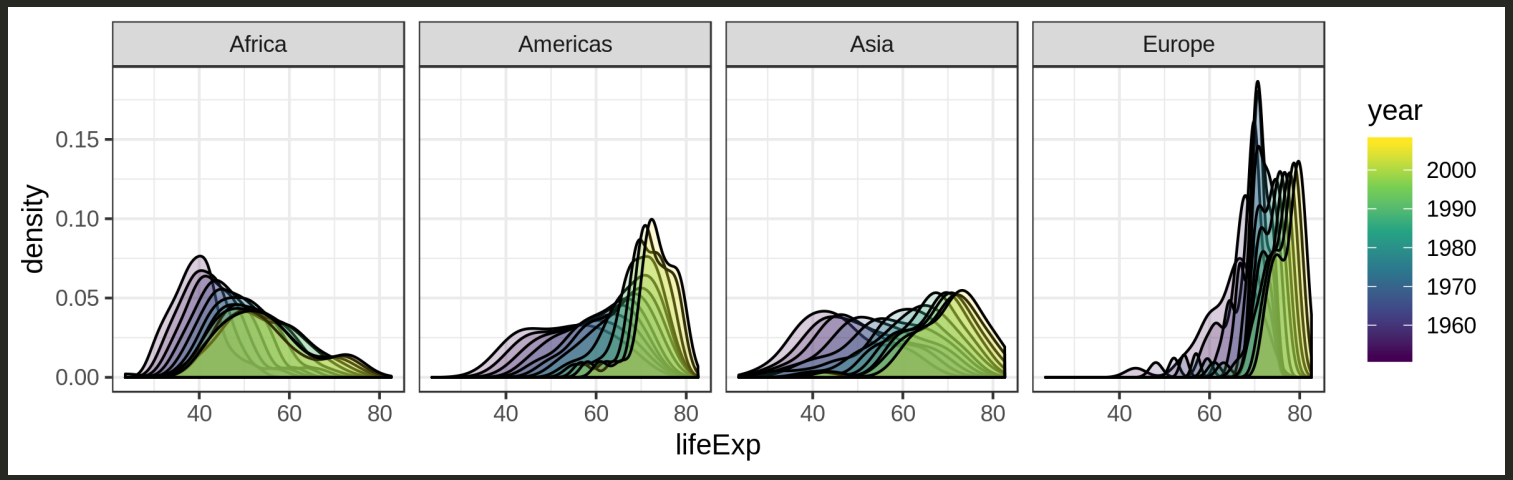
Data visualisation and ggplot2 (with examples based on gapminder data)



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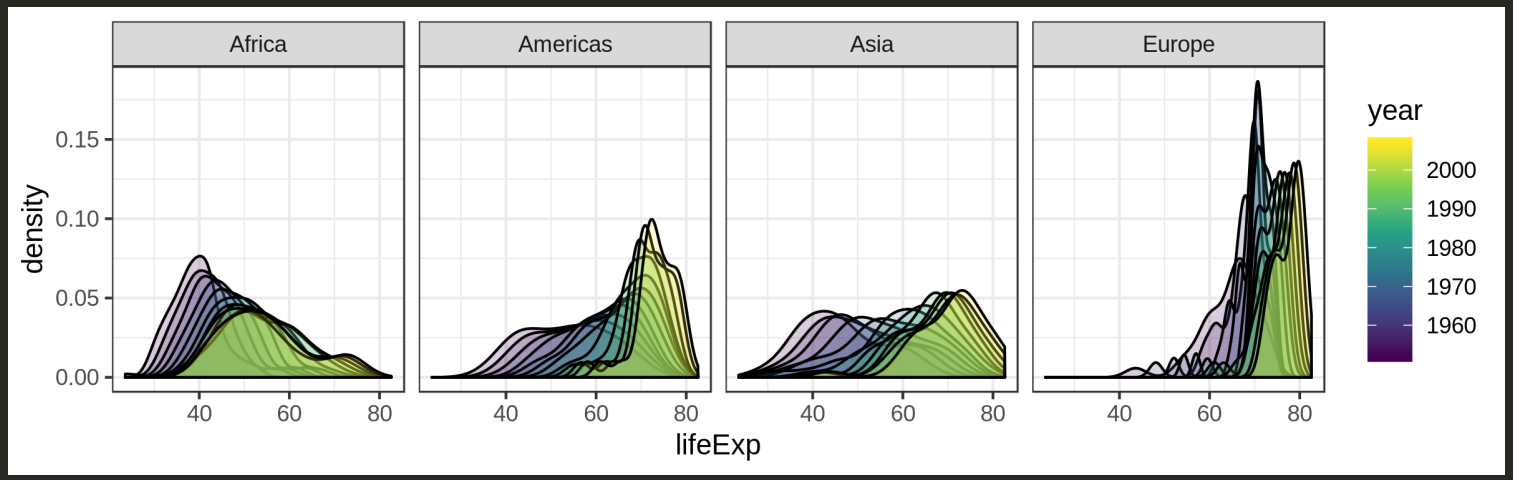

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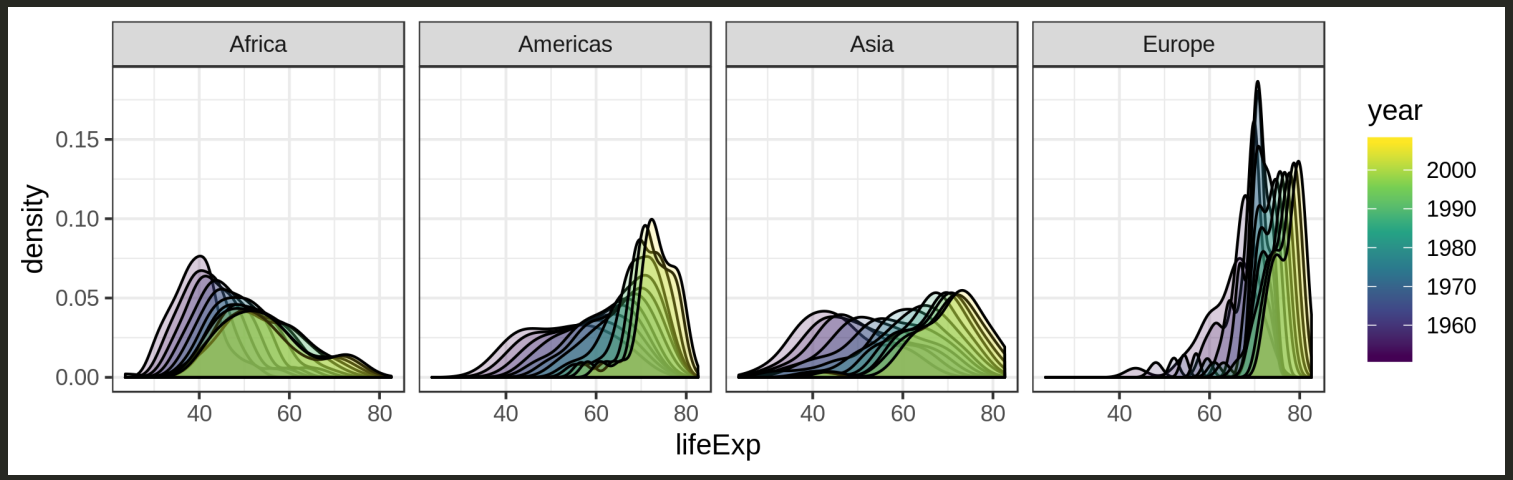


Today:

Exploratory data analysis (using tidyverse) in practice:

Let's try out some real data analysis on TCGA breast cancer data

If there is time, we might take a look at the gganimate package

TCGA breast cancer data set

- Phenotypes:
  - age at diagnosis
  - ER status (estrogen-receptor-positive or negative)
  - PAM50 cancer subtype
  - etc
- Gene expression data:
  - `log(x+1)` transformed expression for all genes

Find data and notebook in https://github.com/kasparmartens/2018_12_bham

```r
df_clinical <- readRDS("data/TCGA_clinical.rds")
head(df_clinical)
```

```
##             id stage PAM50 age_at_diagnosis ER_status PR_status pathology
## 1 TCGA-3C-AAAU                           55  Positive  Positive      <NA>
## 2 TCGA-3C-AALI                           50  Positive  Positive      <NA>
## 3 TCGA-3C-AALJ                           62  Positive  Positive      <NA>
## 4 TCGA-3C-AALK                           52  Positive  Positive      <NA>
## 5 TCGA-4H-AAAK                           50  Positive  Positive      <NA>
## 6 TCGA-5L-AAT0                           42  Positive  Positive      <NA>
```

```r
df_exprs <- readRDS("data/TCGA_exprs.rds")
head(df_exprs[, 1:5])
```

```
##             id SLC7A2_ENSG00000003989 HSPB6_ENSG00000004776
## 1 TCGA-3C-AAAU                8.605850                2.086391
## 2 TCGA-3C-AALI                3.017706                2.884330
## 3 TCGA-3C-AALJ                4.342539                3.086235
## 4 TCGA-3C-AALK                4.861960                2.754787
## 5 TCGA-4H-AAAK                4.298637                2.873187
## 6 TCGA-5L-AAT0                2.595548                2.472016
##   PDK4_ENSG00000004799 ZMYND10_ENSG00000004838
## 1             3.467477                3.891913
## 2             2.749256                2.385003
## 3             5.311276                2.766632
## 4             3.407671                4.407235
## 5             4.594217                4.634472
```

Differences between groups, focusing on a particular gene

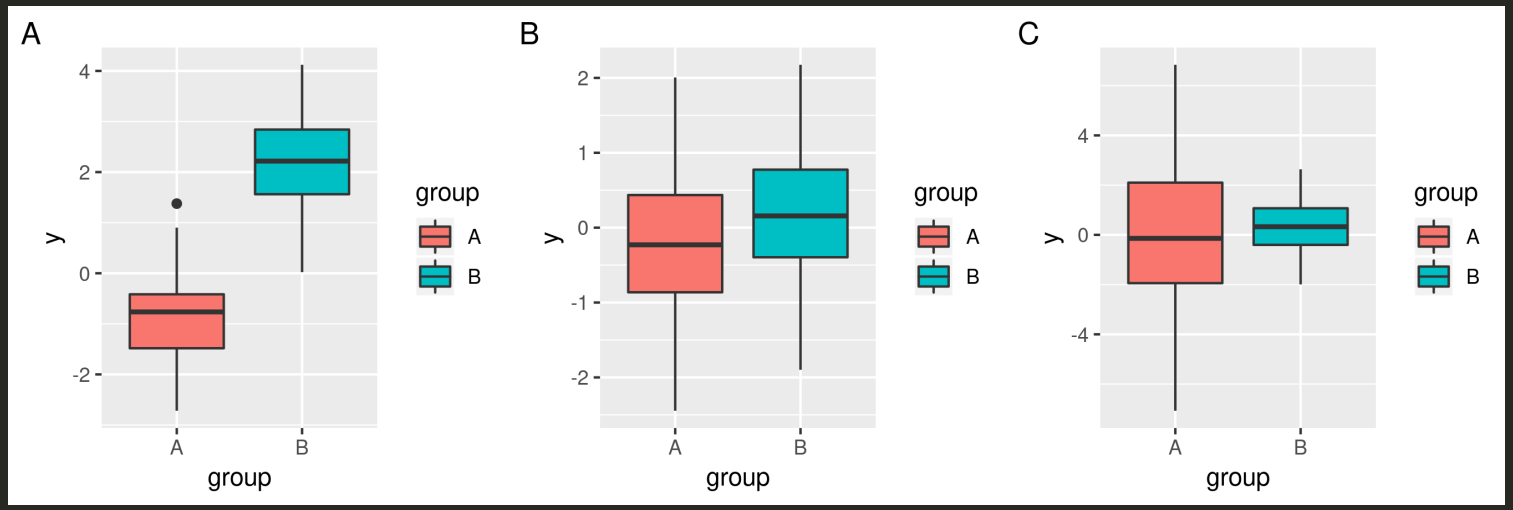
Q1: Do ER+ and ER- patients exhibit differences in the expression of a particular gene of interest (ESR1)?

Q2: Same question about PAM50 subtypes.

- How would you answer these questions
  - Using numerical quantification -- which model or test would you use?
  - Visually -- what type of plots would you consider?

Boxplot quiz

Is there a significant difference between the groups?



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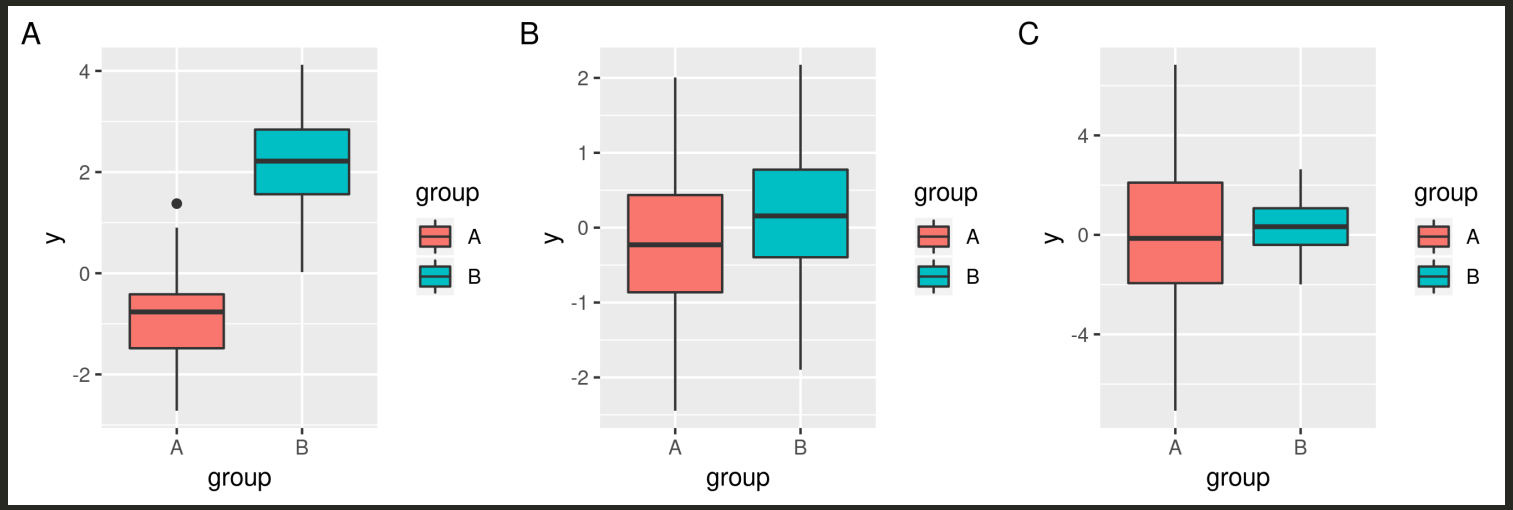


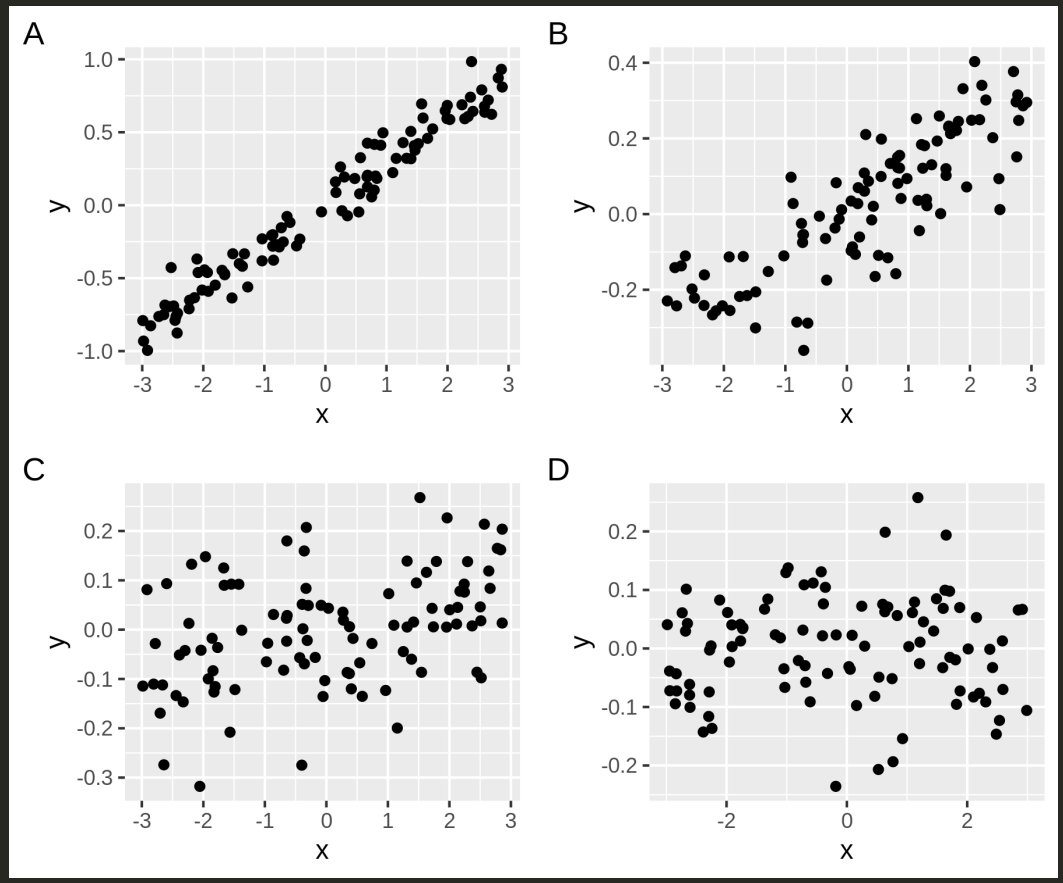
Do you think

- Yes, `p < 0.05` (i.e. group means are significantly different)
- Not enough information to decide
- No, `p > 0.05`

If you choose "cannot decide", what additional information would you need?

Correlation quiz

How strong is the correlation between the two variables? Is it significant?



Correlation quiz

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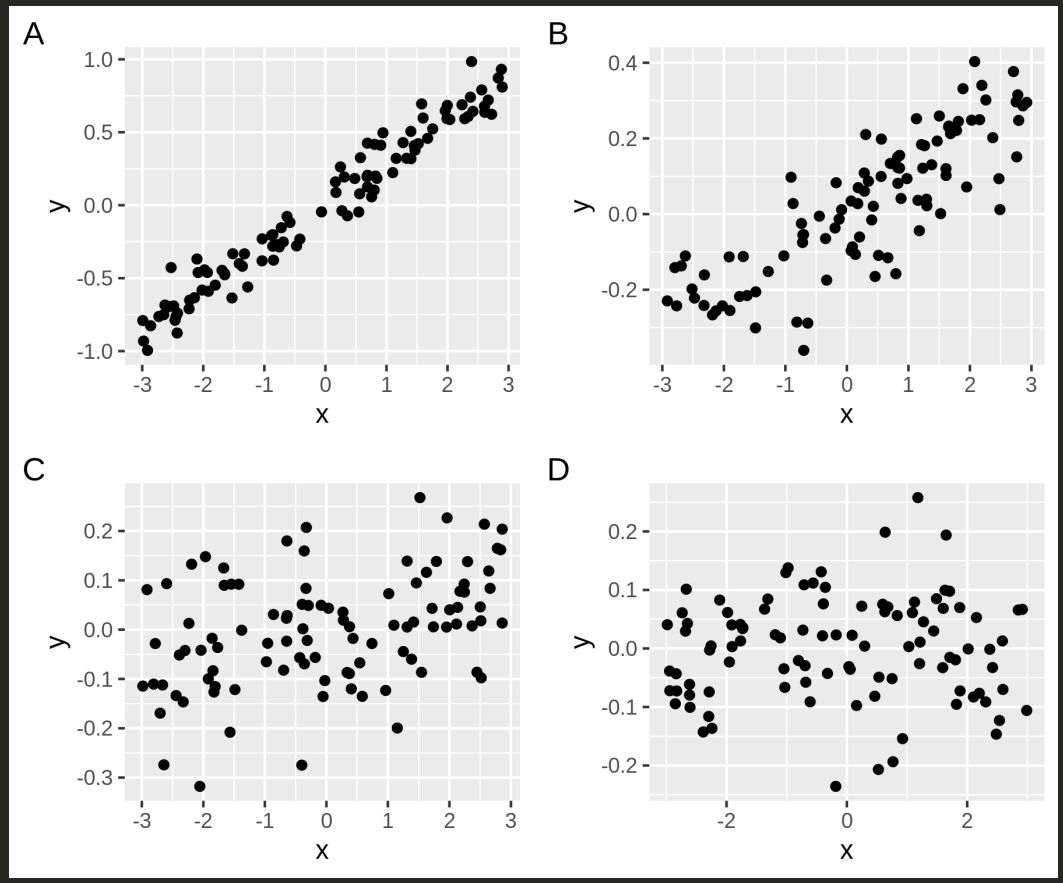

Also, see http://guessthecorrelation.com/

So far, we focused on a single gene

Now let's consider the expression of all genes

Before going further: a detour on tidy data (idea underlying the tidyverse)

Tidy data

> “Tidy datasets are all alike, but every messy dataset is messy in its own way.” — Hadley Wickham

1. Each variable must have its own column.
2. Each observation must have its own row.
3. Each value must have its own cell.

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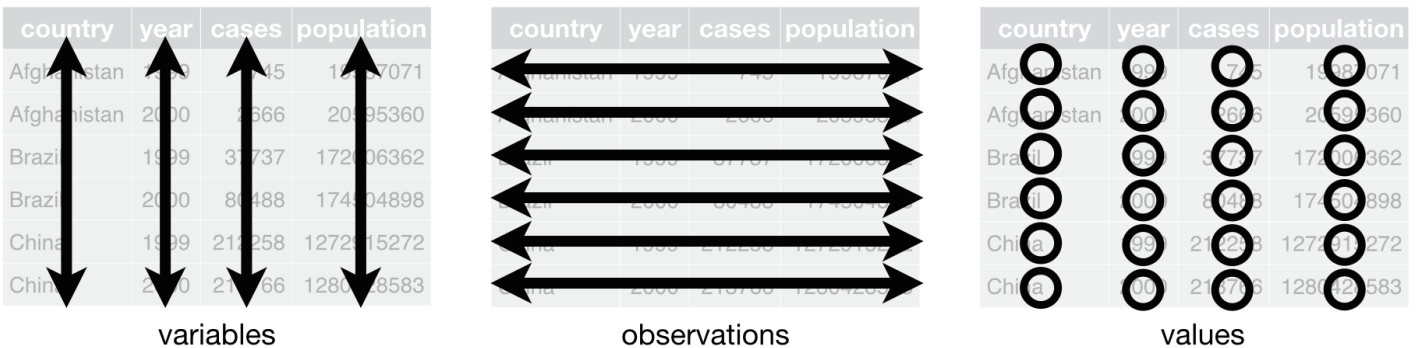


When unsure, we should ask ourselves: Is our data trapped in column names? Column headers should be variable names (but not values).

Tidy vs untidy data

Wide-format

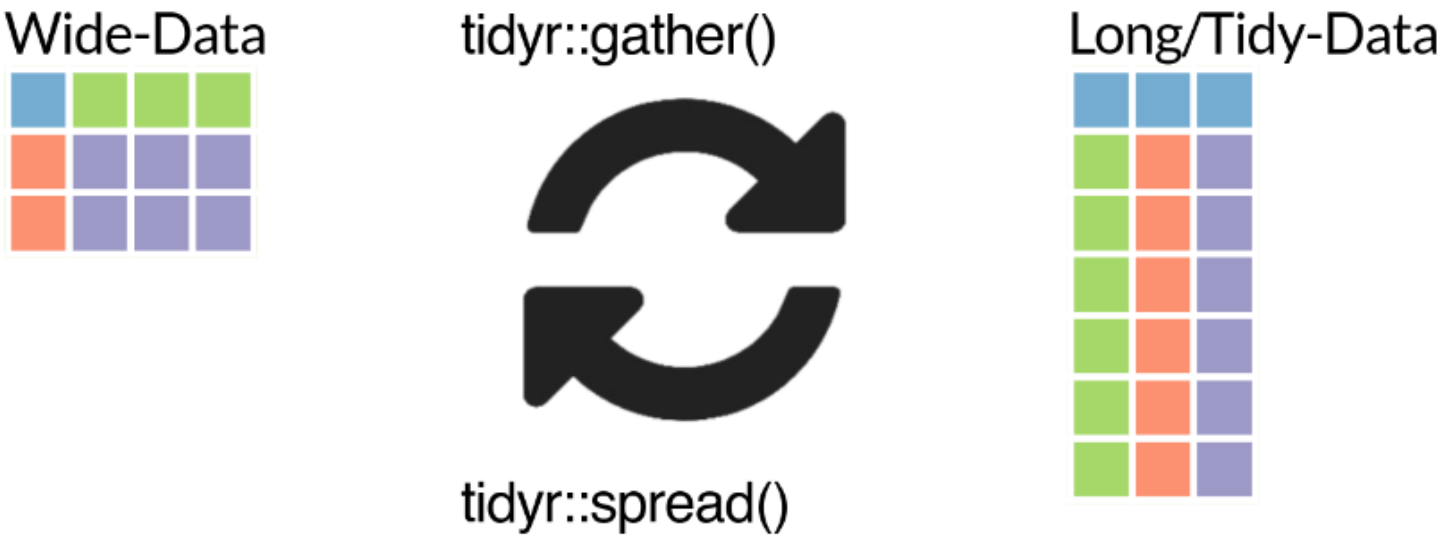
Year	Alice	Bob	Charlie
2010	105	100	90
2011	110	97	95

Long/Tidy-Data

Name	Year	Sales
Alice	2010	105
Alice	2011	110
Bob	2010	100
Bob	2011	97
Charlie	2010	90
Charlie	2011	95

Source: slides by David Zimmermann

tidyr for converting between the two formats



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Converting from wide format to tidy

```
data %>%
  gather(key = "Name", value = "Sales", -year)
```

Your turn

Is gene expression matrix in a tidy format?

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```
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```

id	SLC7A2_ENSG00000003989	HSPB6_ENSG00000004776	PDK4_ENSG00000004799	ZMYND10_ENSG00000004838
TCGA-3C-AAAU	8.6058498	2.0863915	3.4674773	3.8919134
TCGA-3C-AALI	3.0177057	2.8843299	2.7492562	2.3850030
TCGA-3C-AALJ	4.3425394	3.0862352	5.3112761	2.7666318
TCGA-3C-AALK	4.8619597	2.7547870	3.4076714	4.4072346
TCGA-4H-AAAK	4.2986373	2.8731872	4.5942167	4.6344716
TCGA-5L-AAT0	2.5955476	2.4720156	3.1656451	3.4055321

Convert this gene expression data into a tidy format using `tidyr::gather()`.

dplyr for joining data frames

Joining data frames

Source: slides by David Zimmermann

inner_join()

inner_join(df_a, df_b,
by = "id")

Output Data

full_join()

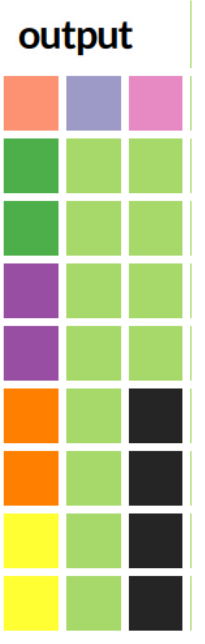

```
full_join(df_a, df_b,
          by = "id")
```

Output Data

left_join()


```
left_join(df_a, df_b,
by = "id")
```

Output Data



Getting insights into high-dimensional data

Now considering *all genes*.

Q1: Do ER+ and ER- patients have generally quite different expression profiles, or are they quite similar?

Q2: Same question about PAM50 subtypes.

How would you answer these questions?

Briefly discussed last time:

How to visually explore data if there are more than two or three variables?

That is, how to visualise high-dimensional data?

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How to visually explore data if there are more than two or three variables?

That is, how to visualise high-dimensional data?

Options include:

- visualise a subset of variables,
    - randomly selected
    - selection based on summary statistics
- compute summary statistics and visualise those instead
- apply a dimensionality reduction method such as PCA

Why you should first visualise your data before launching your favourite ML model

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You should have a rough idea about:

- Data quality
  - Are there any batch effects?
  - Are there possible sample mislabellings?
  - Outliers?
- Distributions - should you apply a transformation?
- Is there a feature which explains majority of variation in the data (e.g. gender, age, batch)

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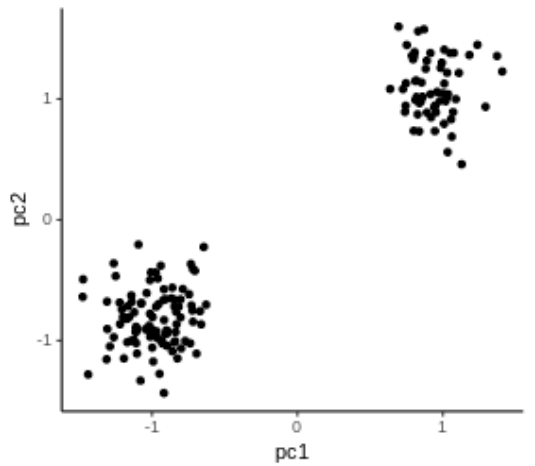
Before fitting a fancy complicated model, you should consider starting with a simple one, to have a rough idea about:

- Expected model fit:
  - Is there strong (linear) signal?
  - Your expected prediction accuracy (will it be close to random or close to 100%)

Why you should first visualise your data before launching an ML algorithm



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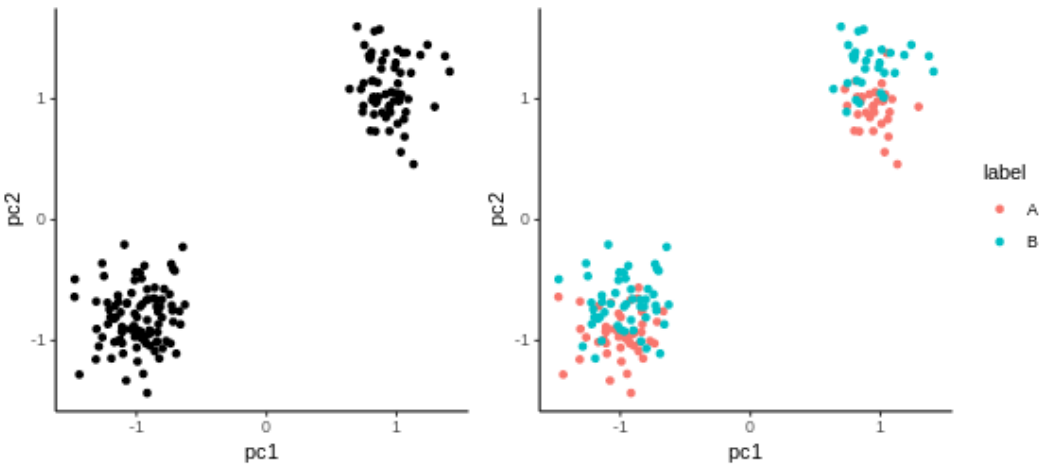

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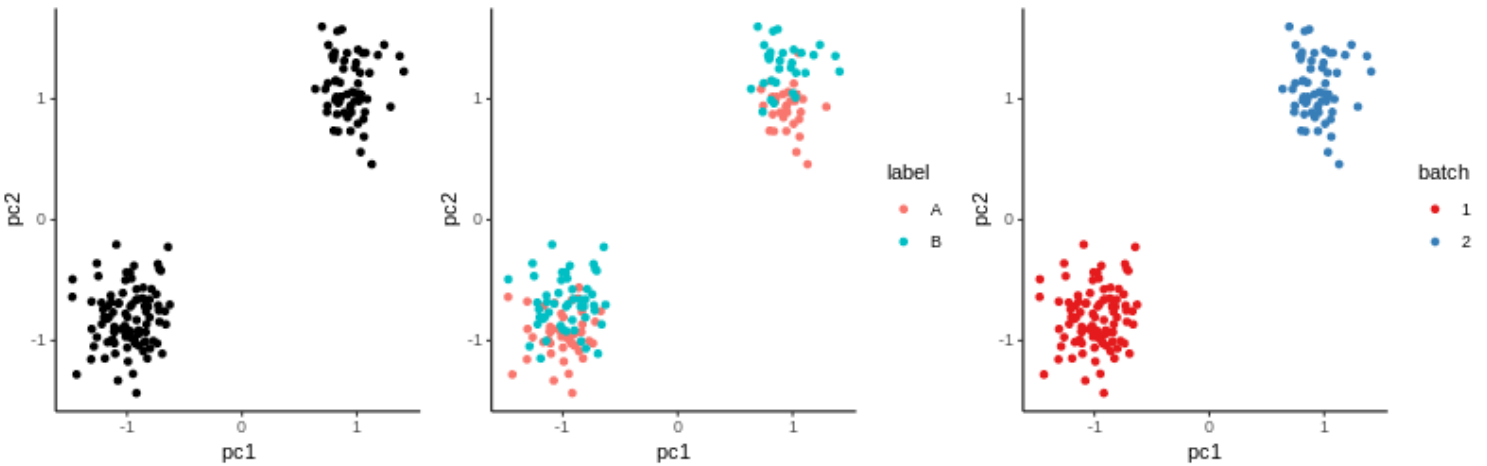

Data science workflow within tidyverse