Method comparison and Bland-Altman plots

Robert Haase, Myers lab, MPI CBG

Based on material by Martin J. Bland
and Douglas G. Altman

June 2021

@haesleinhuepf

Method comparison studies

- Scenario
  - You work in a lab and try to improve procedures
    - Chemical protocols
    - Sample preparation
    - Analysis protocols
      - Physical measurements
      - Image analysis

Unpaired data
- Analyze independent sample sets
- Conclude about their similarity or relationship

Inferential statistics

Paired data
- The same dataset analyzed twice with different methods
- The same dataset analyzed twice with the same method

Direct method comparison; descriptive statistics

Method comparison studies

Martin Bland and Douglas Altman work on Method Comparison (excerpt)

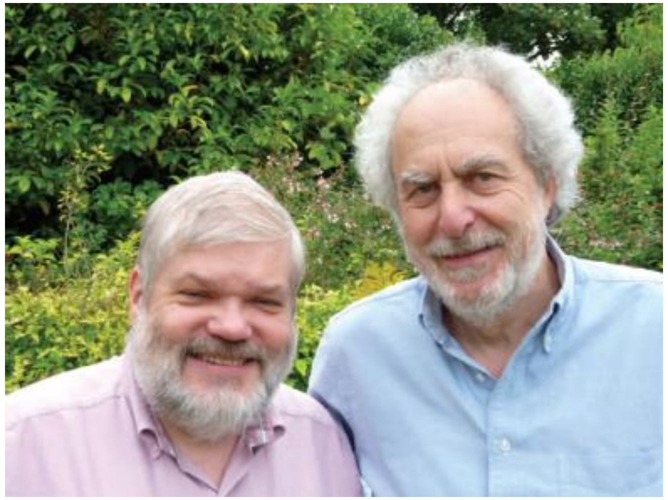
- https://www-users.york.ac.uk/~mb55/meas/ab83.pdf (Open Access)
- https://www.sciencedirect.com/science/article/pii/S0140673686908378

The Statistician 32 (1
© 1983 Institute of St

Measurem
Compariso

D. G. ALTMAN

Division of Com
Research Centre
‡ Department of
St George's Hospital Medical School, Cranmer Terrace, London SW17



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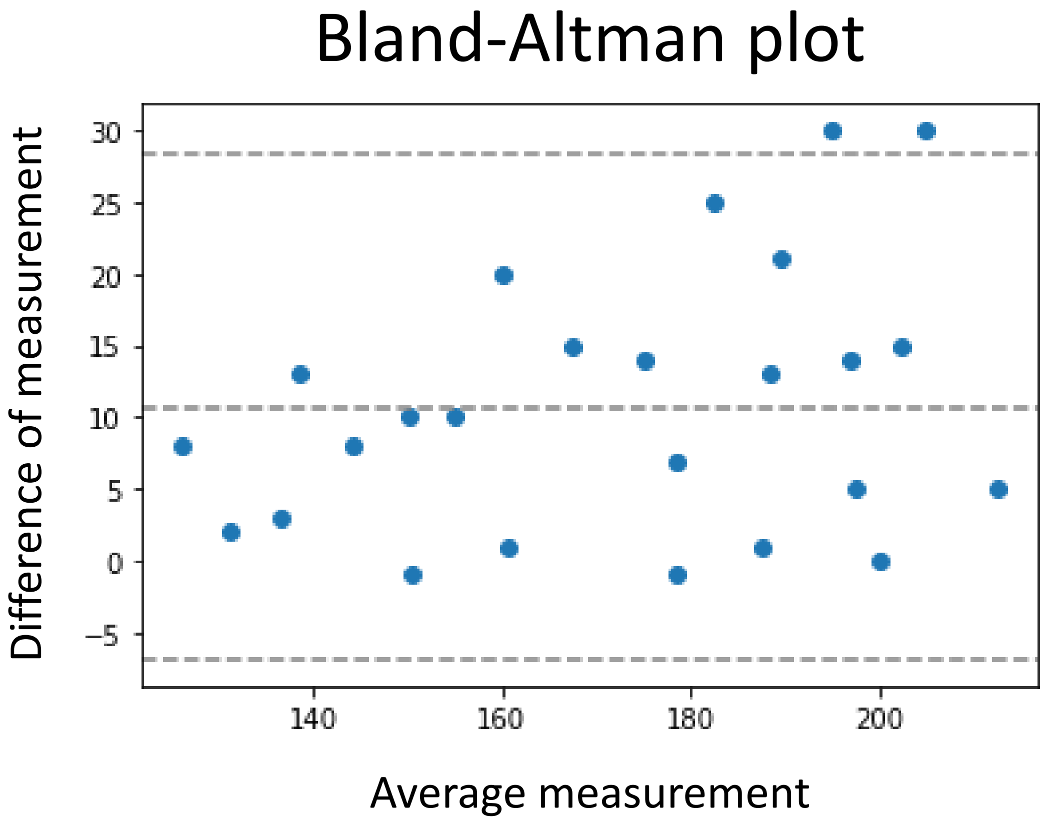
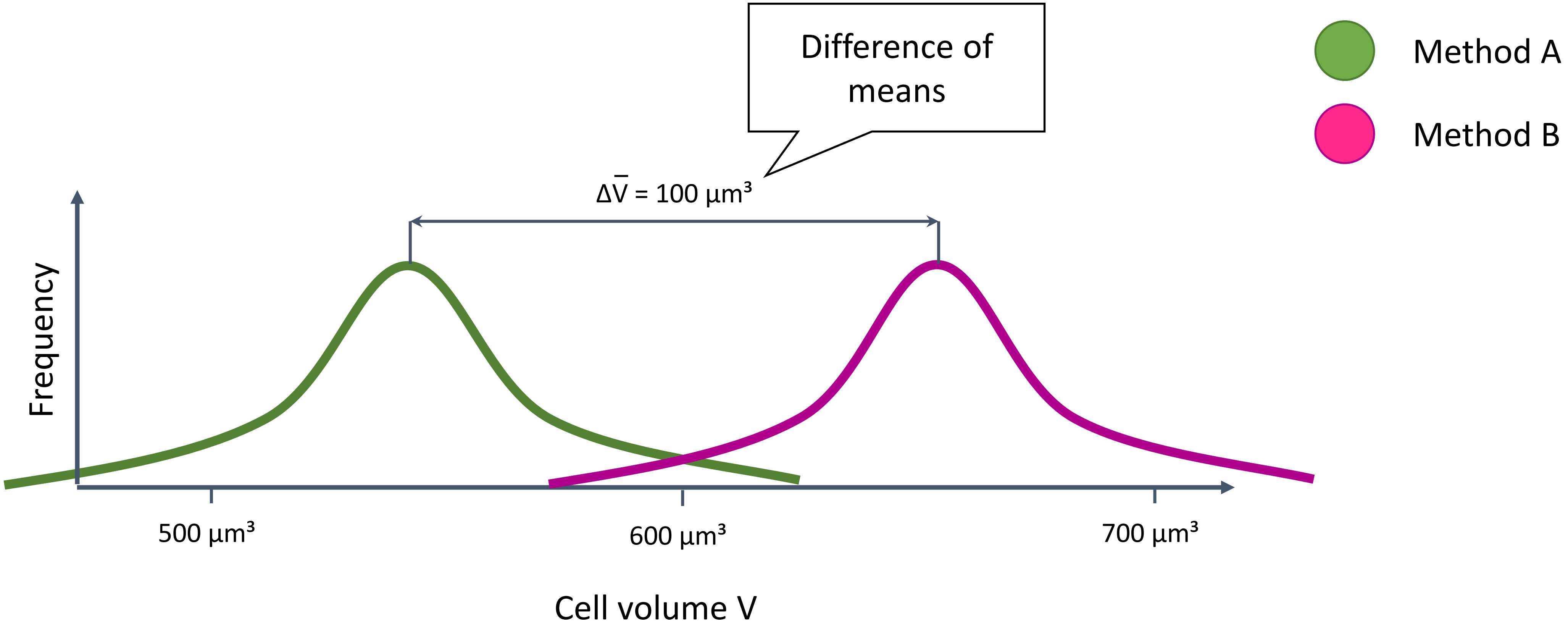
Bland-Altman plots

- Visualized method comparison



Comparison of means

- Comparing mean measurements appears reasonable on the first view.



Comparison of means

- Are two methods doing the same if their mean measurement is similar?

A	B
1	4
9	5
7	5
1	7
2	4
8	5
9	4
2	6
1	6
7	5
8	4

```
Mean(A) = 5.0
Mean(B) = 5.0
```

What if means were "very" different?

Yes

Method B cannot replace method A

No

Similar means is a necessary condition, but is it sufficient?

Comparison of means

- Are two methods doing the same if their mean measurement is similar?

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Mean(A) = 5.0
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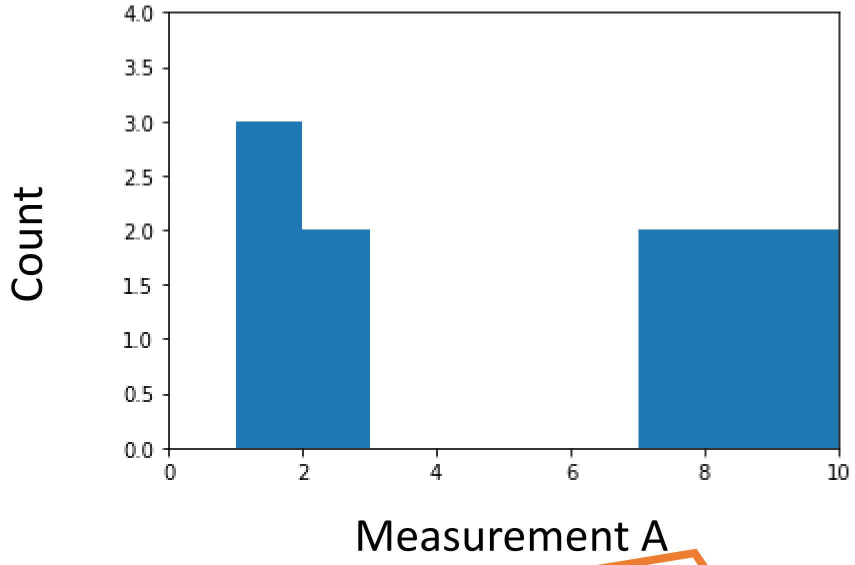
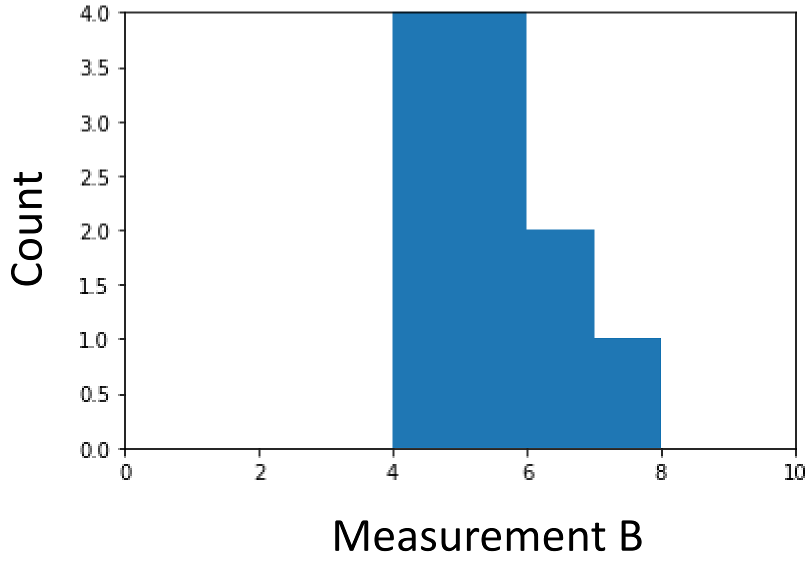
```

- Draw histograms! How can two methods do the same if histograms from their measurements are different?





Similar means is a necessary condition, but it is NOT sufficient!

The scientific method: Show that a method doesn't work with *just one* example. And you have *proven* that the method doesn't work in general.

Comparison of means

- Are two methods doing the same if their mean measurement is similar?

A	B
1	4
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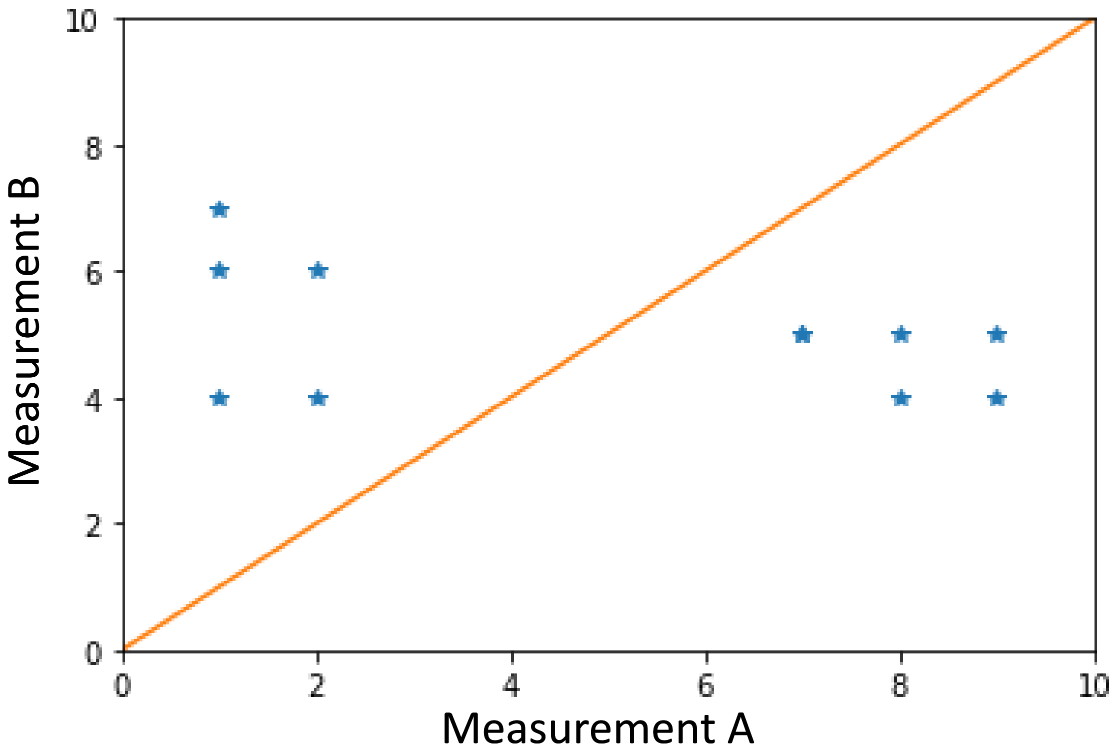
9	4
2	6
1	6
7	5
8	4

```
Mean(A) = 5.0
Mean(B) = 5.0
```

- Plot the measurements against each other. What does it mean if they lie on a straight line? What if not?



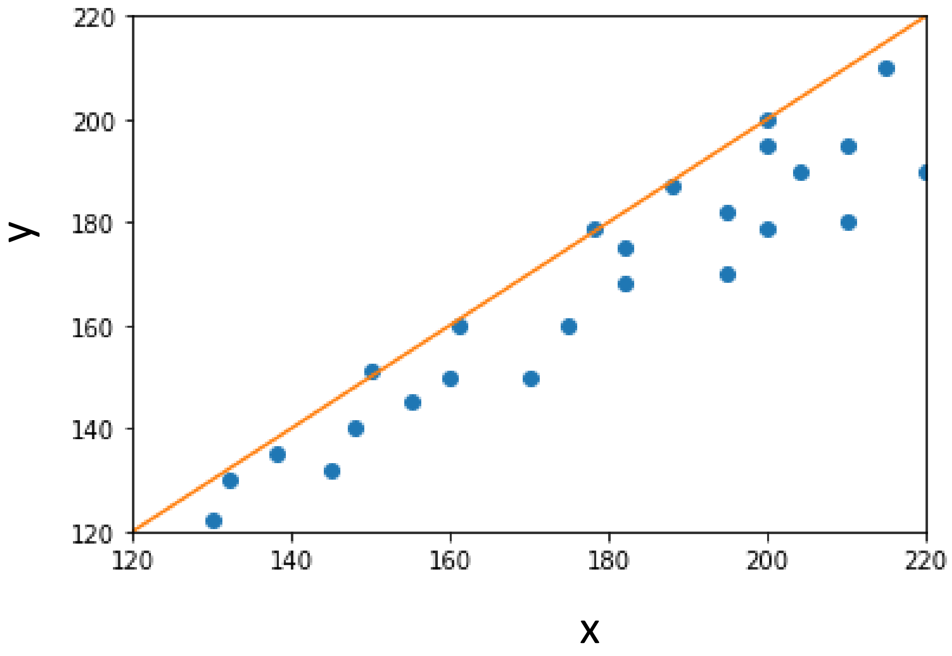
The "criterion of agreement was that the two methods gave the same mean measurement; 'the same' appears to stand for 'not significantly different'. Clearly, this approach tells us very little about the accuracy of the methods."[1]

[1] Altman & Bland, The Statistician 32, 1983

Correlation

- Are two methods doing the same if they correlate?
  - Correlation: Any kind of relationship.
  - Measurable; e.g. using Pearson's Correlation Coefficient *r* enumerated linear correlation.

Comparison of two methods of measuring systolic blood pressure (Data take from [1])



Expectation E

Mean average μ

$$r(X,Y) = \frac{E(X - \mu_X)(Y - \mu_y)}{\sigma_X \sigma_Y}$$

Standard deviation σ

Disclosure: Mean and standard deviation must be obtained from the whole population or from a sample set which is sufficiently large.

In practice *E* is the weighted sum:

$$r(X,Y) = \frac{\sum_{x \in X, y \in Y} \frac{(x - \mu_X)(y - \mu_Y)}{n}}{\sigma_X \sigma_Y}$$

Number of measurements *n*

[1] Altman & Bland, The Statistician 32, 1983

Correlation

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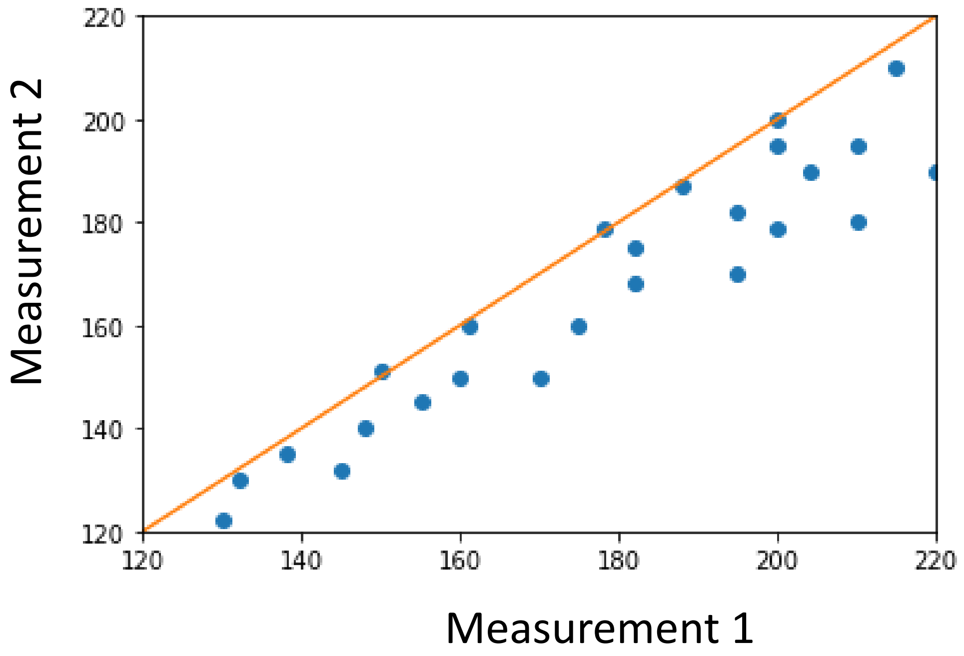


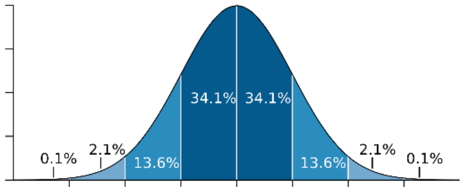
$$r(X,Y) = \frac{\sum_{x \in X, y \in Y} \frac{(x-\mu_X)(y-\mu_Y)}{n}}{\sigma_X \sigma_Y} = 0.94$$

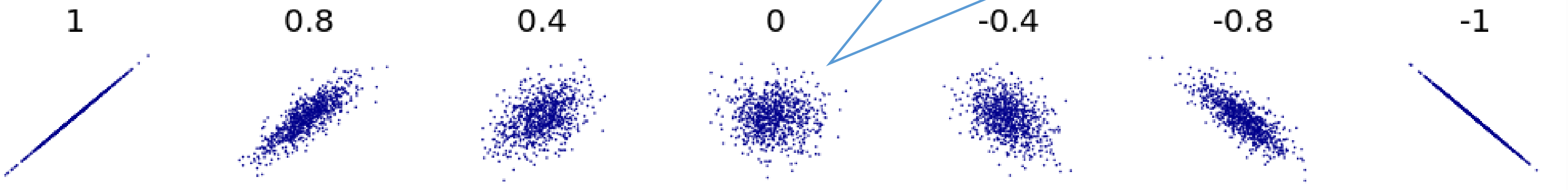
[1] Altman & Bland, The Statistician 32, 1983

Correlation: Pearson's *r*

- Pearson's *r* lies between -1 and 1
  - 1: Positive linear correlation
  - 0: No linear correlation
  - -1: Negative linear correlation

2-dimensional normal distribution





https://en.wikipedia.org/wiki/Pearson_correlation_coefficient#/media/File:Correlation_examples2.svg

Correlation

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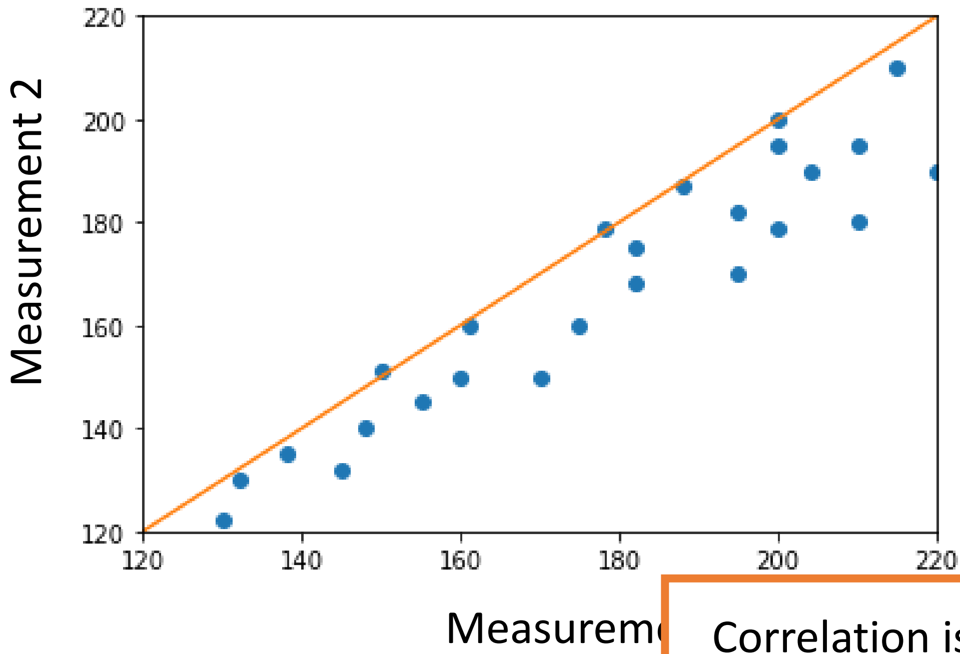


$$r(X,Y) = \frac{\sum_{x\in X, y\in Y} \frac{(x-\mu_X)(y-\mu_Y)}{n}}{\sigma_X \sigma_Y} = 0.94$$

"Positive linear correlation"

Measurement 1 is almost always larger than measurement 2

Correlation is necessary, but it is NOT sufficient!

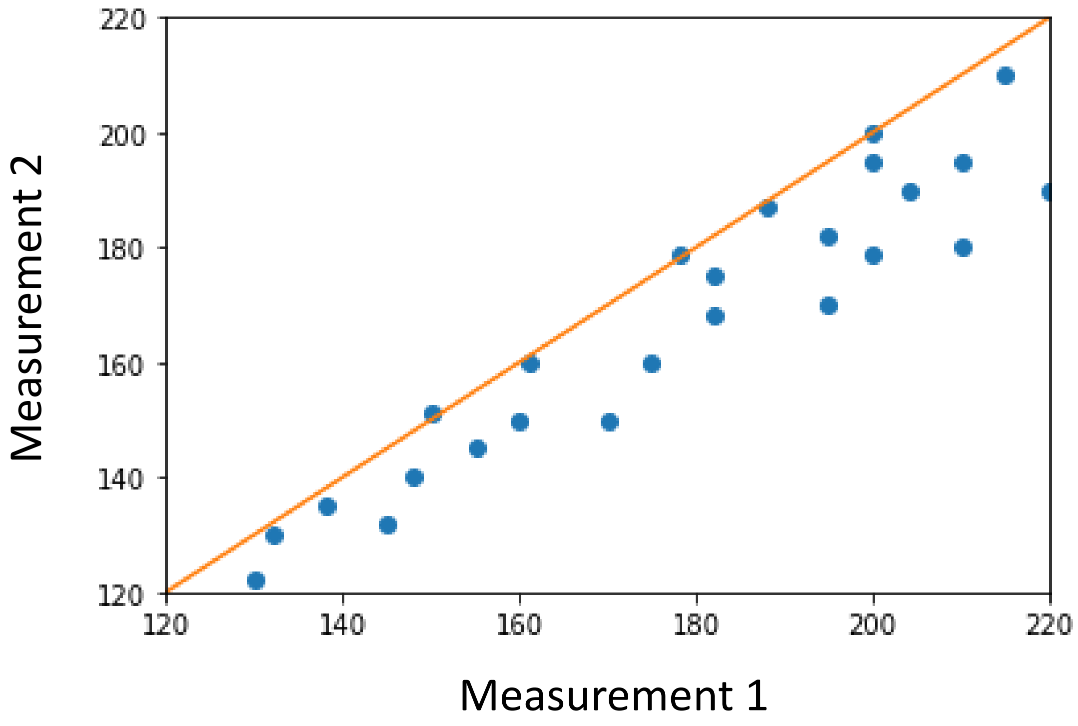
The scientific method: Show that a method doesn't work with *just one* example. And you have *proven* that the method doesn't work in general.

[1] Altman & Bland, The Statistician 32, 1983

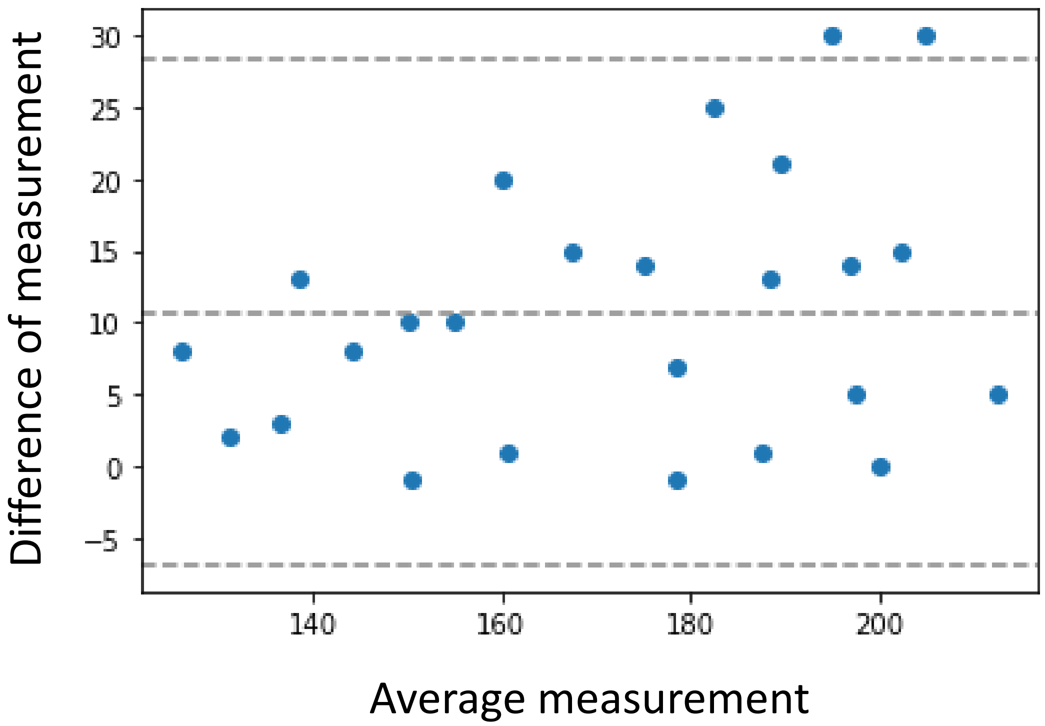
Bland-Altman plots

- In order to evaluate the difference between two methods, you should visualize them first.
- *“The purpose of computing is insight, not numbers.”*, Richard Hamming

Scatter plot



Bland-Altman plot



The confidence interval

- “The British Standards Institution (1979) define a coefficient of repeatability as ‘the value below which the difference between two single test results ... may be expected to lie with a specified probability; in the absence of other indications, the probability is 95 per cent’.”[1]

The confidence interval *CI* of agreement

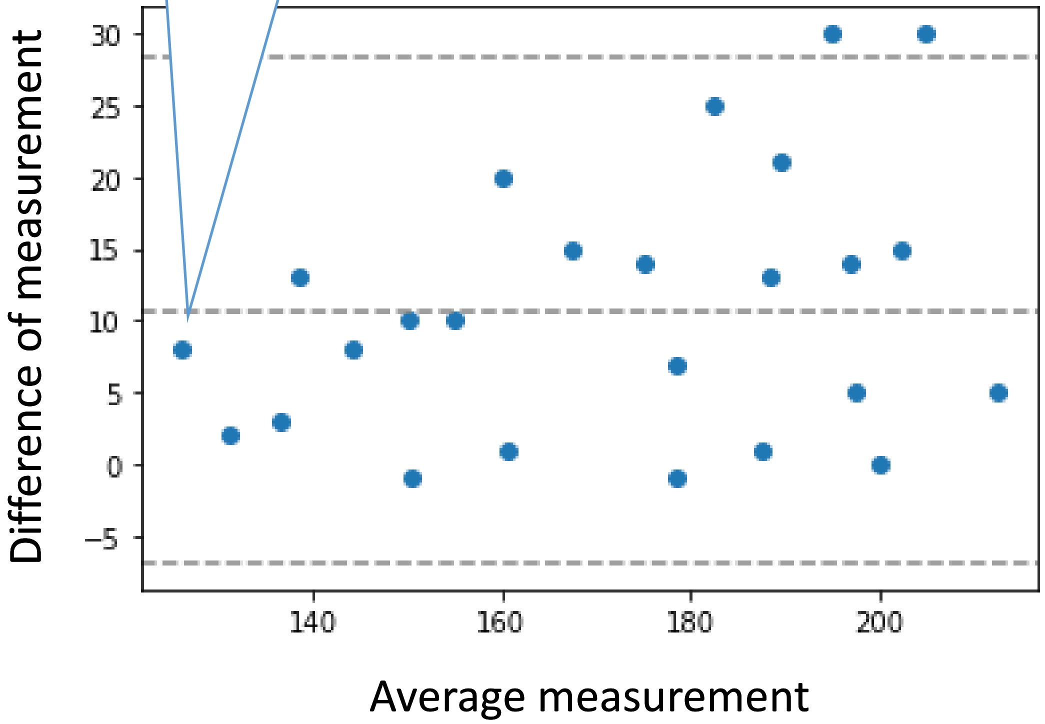
$$CI = (\mu - 2\sigma, \mu + 2\sigma)$$

Mean difference

Standard deviation of differences

The mean difference between the methods

Bland-Altman plot

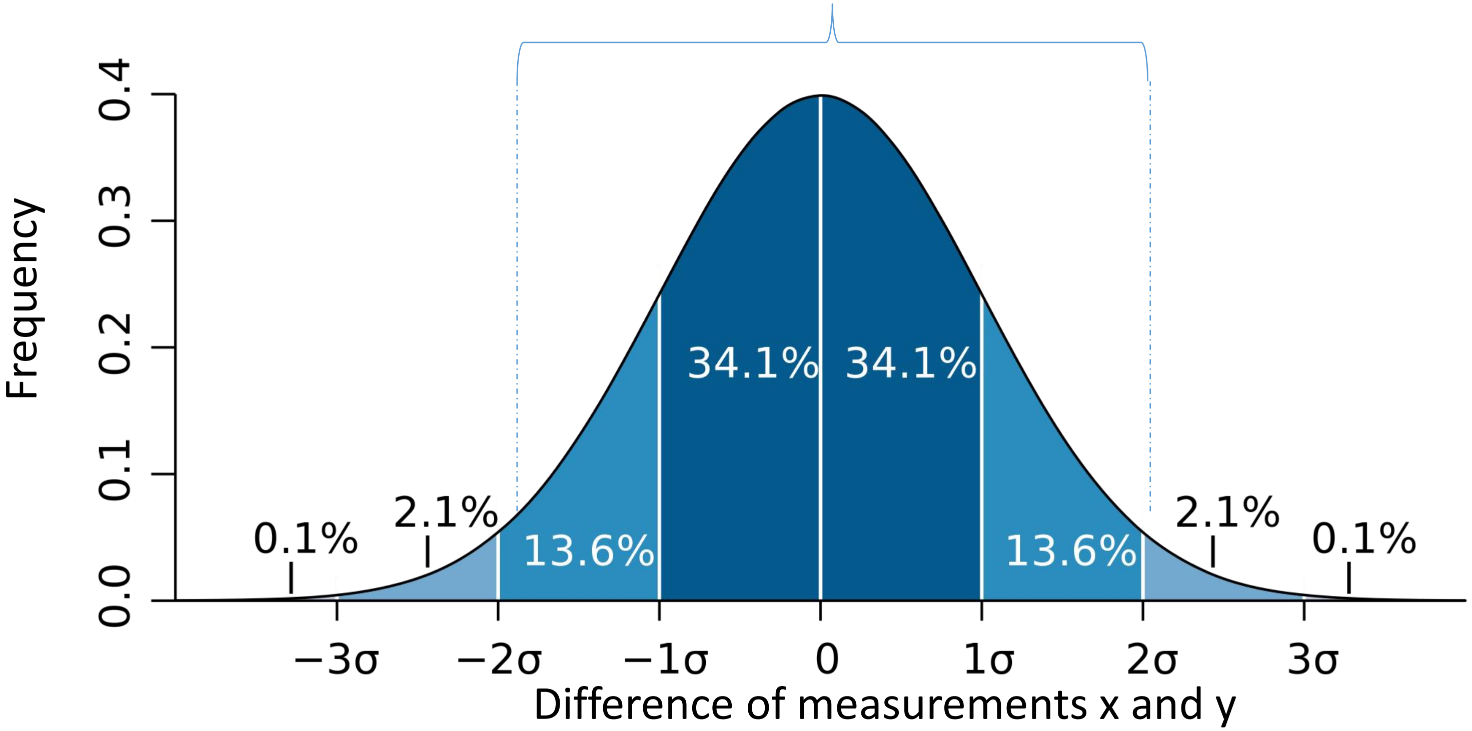


[1] Altman & Bland, The Statistician 32, 1983

The confidence interval & the coefficient of repeatability.

- "The British Standards Institution (1979) define a coefficient of repeatability as 'the value below which the difference between two single test results ... may be expected to lie with a specified probability; in the absence of other indications, the probability is 95 per cent'."[1]

In a normal distribution 95% of measurements lie in this area around the mean

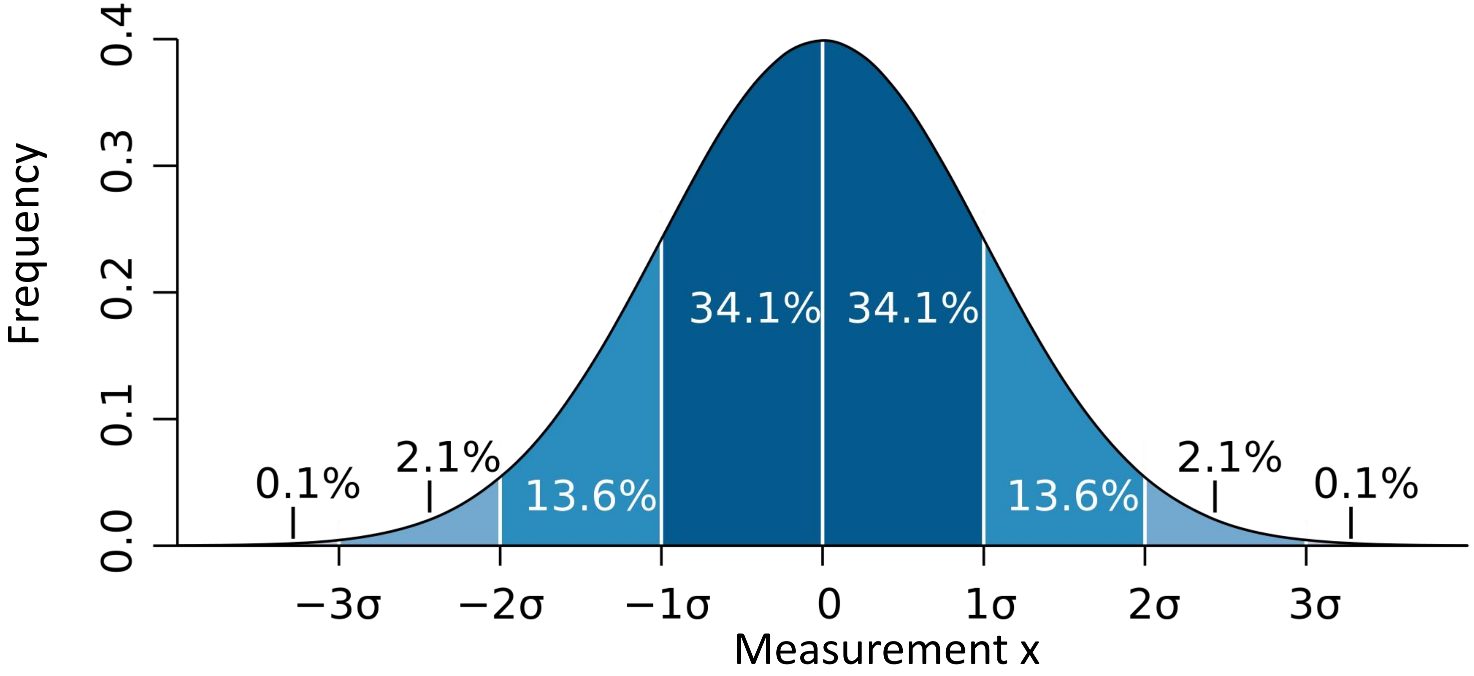


Graph adapted from: M. W. Toews - Own work, based (in concept) on figure by Jeremy Kemp, on 2005-02-09, CC BY 2.5, https://commons.wikimedia.org/w/index.php?curid=1903871

[1] Altman & Bland, The Statistician 32, 1983

The confidence interval & the coefficient of repeatability.

- "The British Standards Institution (1979) define a coefficient of repeatability as 'the value below which the difference between two single test results ... may be expected to lie with a specified probability; in the absence of other indications, the probability is 95 per cent'."[1]
- If the two measurements come from the same method which just repeated twice, we can assume that the main difference is zero. The coefficient of repeatability *CR* can then be estimated: It's the standard deviation of differences.[2]



$$\mathrm{CR}(X,Y) = \sqrt{\sum_{x\in X, y\in Y} \frac{(x-y)^2}{n}}$$

Graph adapted from: M. W. Toews - Own work, based (in concept) on figure by Jeremy Kemp, on 2005-02-09, CC BY 2.5, https://commons.wikimedia.org/w/index.php?curid=1903871

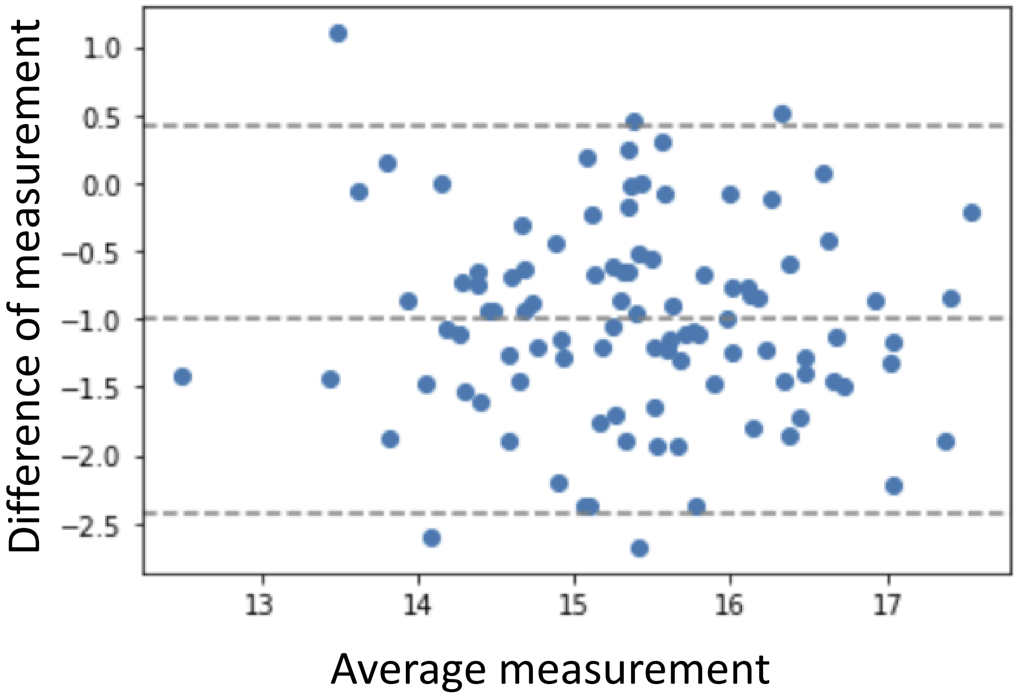
[1] Altman & Bland, The Statistician 32, 1983

2 Bland & Altman, Lancet , 1986

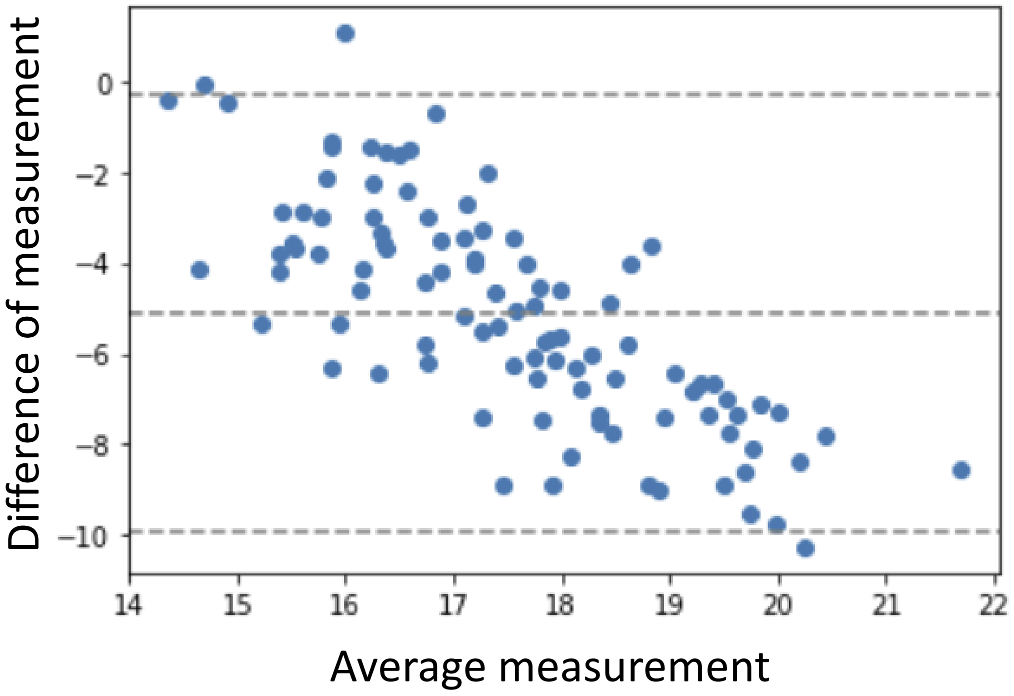
In practice:

- Bland-Altman plots allow us to differentiate various kinds of bias.

Agreement with additive error (offset)



Multiplicative bias



Processing tables with Python

Robert Haase

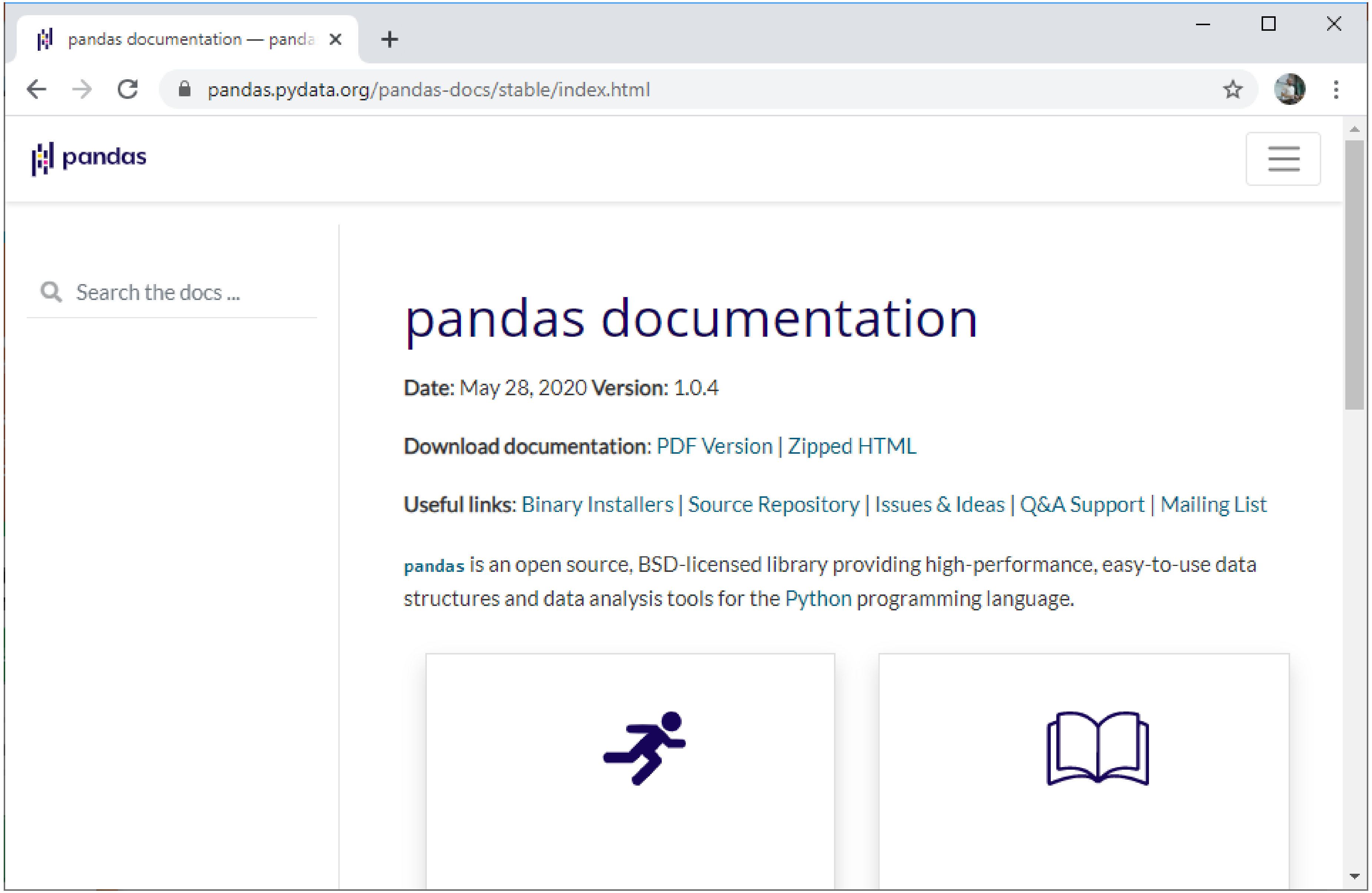
June 2021

@haesleinhuepf

Pandas

- pandas is a library providing high-performance, easy-to-use data structures and data analysis tools for the Python programming language.

```
conda install pandas
```



Processing tables with pandas

- Typical use-case:
  - You get data from a colleague in form of a table.
  - Using pandas, you can analyze it in python.

Results

File Edit Font Results

	Area	Mean	Circ.	AR	Round	Solidity
1	2610	96.920	0.773	1.289	0.776	1.000
2	2100	90.114	0.660	2.333	0.429	1.000
3	27	110.222	0.108	27.000	0.037	1.000

- Loading a table in python using pandas:

```python
import pandas as pd

data_frame = pd.read_csv("Measurements_ImageJ.csv", delimiter=',')
data_frame
```

		Area	Mean	Circ.	AR	Round	Solidity
0	1	2610	96.920	0.773	1.289	0.776	1.0
1	2	2100	90.114	0.660	2.333	0.429	1.0
2	3	27	110.222	0.108	27.000	0.037	1.0

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3	27	110.222	0.108	27.000	0.037	1.000

- Accessing a column

```
data_frame["Mean"]
```

```
0     96.920
1     90.114
2    110.222
Name: Mean, dtype: float64
```

- Determining mean of a column

```
import numpy as np
np.mean(data_frame["Mean"])
```

```
99.08533333333332
```

- Accessing an individual cell

```
data_frame["Mean"][0]
```

```
1.2890000000000001
```

Processing tables with pandas

- Creating tables with pandas

- Creating a new table

```
header = ['A', 'B', 'C']

data = [
    [1, 2, 3],  # this will later be colum A
    [4, 5, 6],  #                          B
    [7, 8, 9]   #                          C
]

# convert the data and header arrays in a pandas data frame
data_frame = pd.DataFrame(data, header)

# show it
data_frame
```

	0	1	2
A	1	2	3
B	4	5	6
C	7	8	9

- Rotate a table

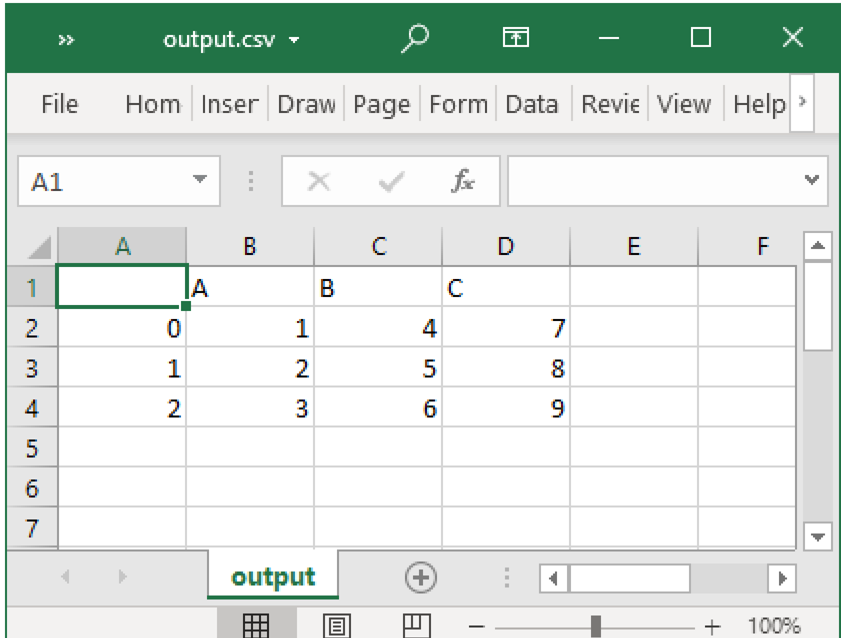
```
# rotate/flip it
data_frame = data_frame.transpose()

# show it
data_frame
```

	A	B	C
0	1	4	7
1	2	5	8
2	3	6	9

- Save it to disc

```
# save a dataframe to a CSV
data_frame.to_csv("output.csv")
```



Selecting rows and columns

	City	Country	Population	Area_km2
0	Tokyo	Japan	13515271	2191
1	Delhi	India	16753235	1484
2	Shanghai	China	24183000	6341
3	Sao Paulo	Brazil	12252023	1521
4	Mexico City	Mexico	9209944	1485

- Selecting columns

```
cities[['City', 'Country']]
```

	City	Country
0	Tokyo	Japan
1	Delhi	India
2	Shanghai	China
3	Sao Paulo	Brazil
4	Mexico City	Mexico

- Selecting rows

```
cities[cities['Area_km2'] > 2000]
```

	City	Country	Population	Area_km2
0	Tokyo	Japan	13515271	2191
2	Shanghai	China	24183000	6341

Combining tables

- The big art in data science is the ability of combining information from multiple sources to gain new insights.

	Country	Population
0	Japan	127202192
1	India	1352642280
2	China	1427647786
3	Brazil	209469323
4	Mexico	126190788

	City	Country	Population	Area_km2
0	Tokyo	Japan	13515271	2191
1	Delhi	India	16753235	1484
2	Shanghai	China	24183000	6341
3	Sao Paulo	Brazil	12252023	1521
4	Mexico City	Mexico	9209944	1485

```
combined = countries.merge(cities, on='Country', suffixes=['_country', '_city'])
combined
```

	Country	Population_country	City	Population_city	Area_km2
0	Japan	127202192	Tokyo	13515271	2191
1	India	1352642280	Delhi	16753235	1484
2	China	1427647786	Shanghai	24183000	6341
3	Brazil	209469323	Sao Paulo	12252023	1521
4	Mexico	126190788	Mexico City	9209944	1485

```
# compute ratio
combined['City_Country_population_ratio'] = combined['Population_city'] / combined['Population_country']

# only show selected columns
combined[['City', 'City_Country_population_ratio']]
```

	City	City_Country_population_ratio
0	Tokyo	0.106250
1	Delhi	0.012386
2	Shanghai	0.016939
3	Sao Paulo	0.058491
4	Mexico City	0.072984

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Functional parameters in Python

Robert Haase

June 2021

@haesleinhuepf

Functional parameters

- So far, we know variables can contain numbers, list, strings, images, …
- We also know functions.
- Variables can also be functions.

```python
def double_number(x):
    return x * 2
```

```python
double_number(values)
```

```
array([ 2,  4,  6,  8, 20])
```

```python
import numpy as np

values = np.asarray([1, 2, 3, 4, 10])
```

```python
my_function = double_number

my_function(values)
```

```
array([ 2,  4,  6,  8, 20])
```

Functional parameters

- Using the same concept, you can pass over a function to a function.
- Function will then execute function.

```python
import matplotlib.pyplot as plt
from skimage.measure import label

def count_blobs(image, threshold_algorithm):
    # binarize the image using a given
    # threshold-algorithm
    threshold = threshold_algorithm(image)
    binary = image > threshold

    # show intermediate result
    # plt.imshow(binary)

    # return count blobs
    labels = label(binary)
    return labels.max()
```

```python
from skimage.filters import threshold_otsu

count_blobs(blobs_image, threshold_otsu)
```

```
64
```

```python
from skimage.filters import threshold_yen

count_blobs(blobs_image, threshold_yen)
```

```
67
```

Useful for method comparison ;-)

Summary

- Descriptive statistics
    - Method comparison
        - Comparison of means (not sufficient!)
        - Pearson's correlation coefficient
        - Scatter plots
        - Bland-Altman plots
        - Confidence interval
        - Coefficient of repeatability.
- Coming up next
    - Hypothesis testing