Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

University of Zurich[UZH]

ZNZ Zentrum für Neurowissenschaften Zürich
Neuroscience Center Zurich

ZIHP

Data analysis and presentations:
Examples from basic statistics

Fri 01.06.2018 13:00-14:30
ZNZ MD/PhD Neuroscience Course, Module BIO628
Room Y35 F47

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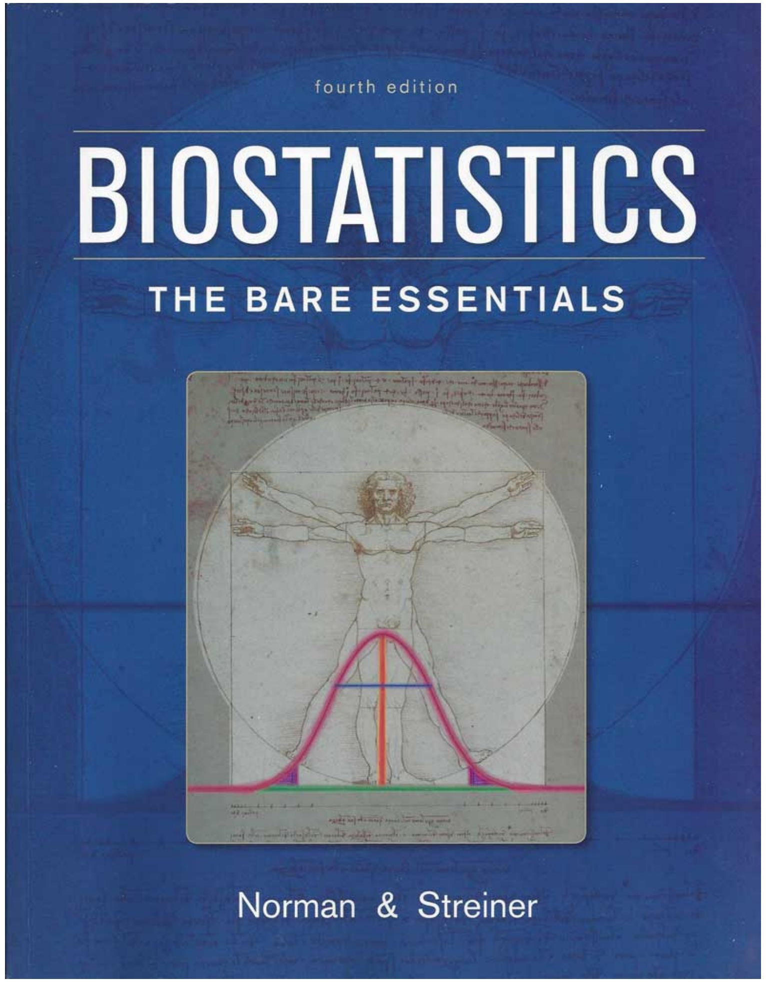
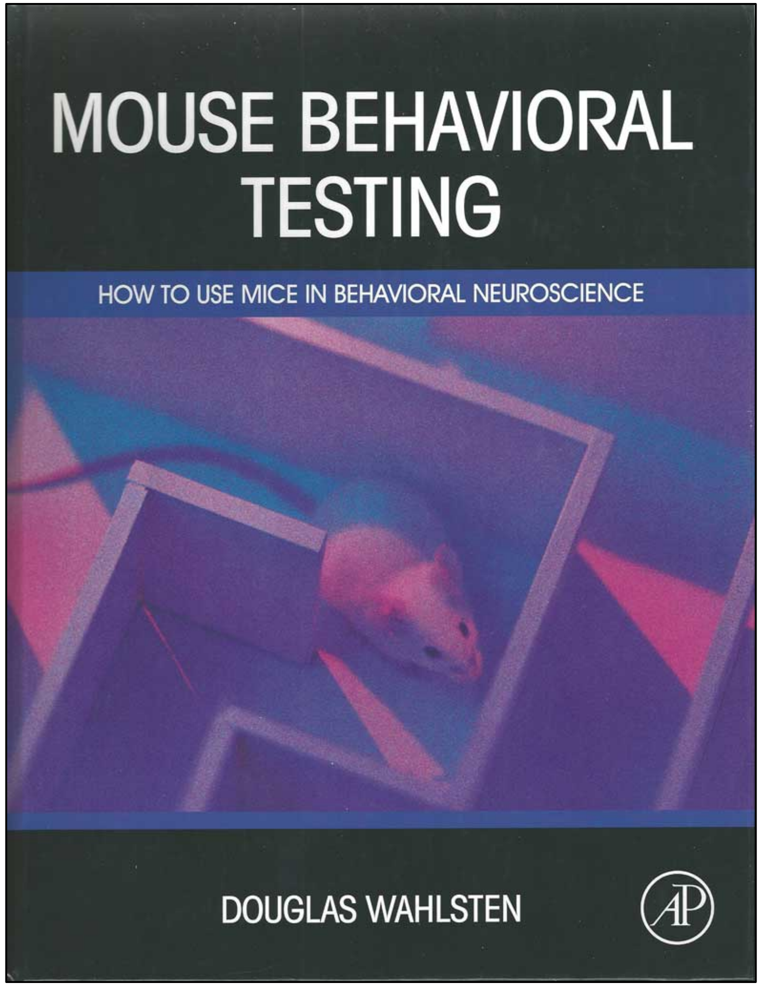


Norman GR, Streiner DL
Biostatistics, the bare essentials
BC Decker, 4. edition, 2014



Wahlsten D
Mouse Behavioral Testing
Academic Press, 1. edition, 2011

Population, sample and sampling error

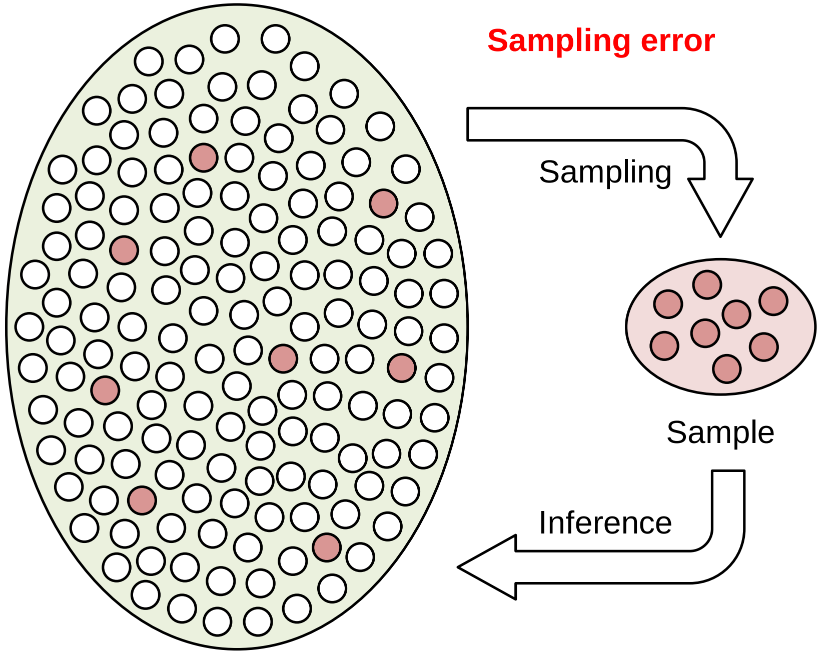
Population

$$\mu = \frac{\Sigma\,(X)}{N}$$

$$\sigma^2 = \frac{\Sigma\,(X-\mu)^2}{N}$$

σ

Sampling error



Population

Uncertainty

Sample

$$M = \frac{\Sigma\,(X)}{n}$$ mean

$$S^2 = \frac{\Sigma\,(X-M)^2}{n-1}$$ variance

S standard deviation

Sampling error

- *Due to sampling error, mean and standard deviation of samples always differ from the true population values, they are only estimates of the mean and standard deviation of the population*

- *If multiple samples are drawn from the same population, due to sampling error their means and standard deviations will always differ from each other*

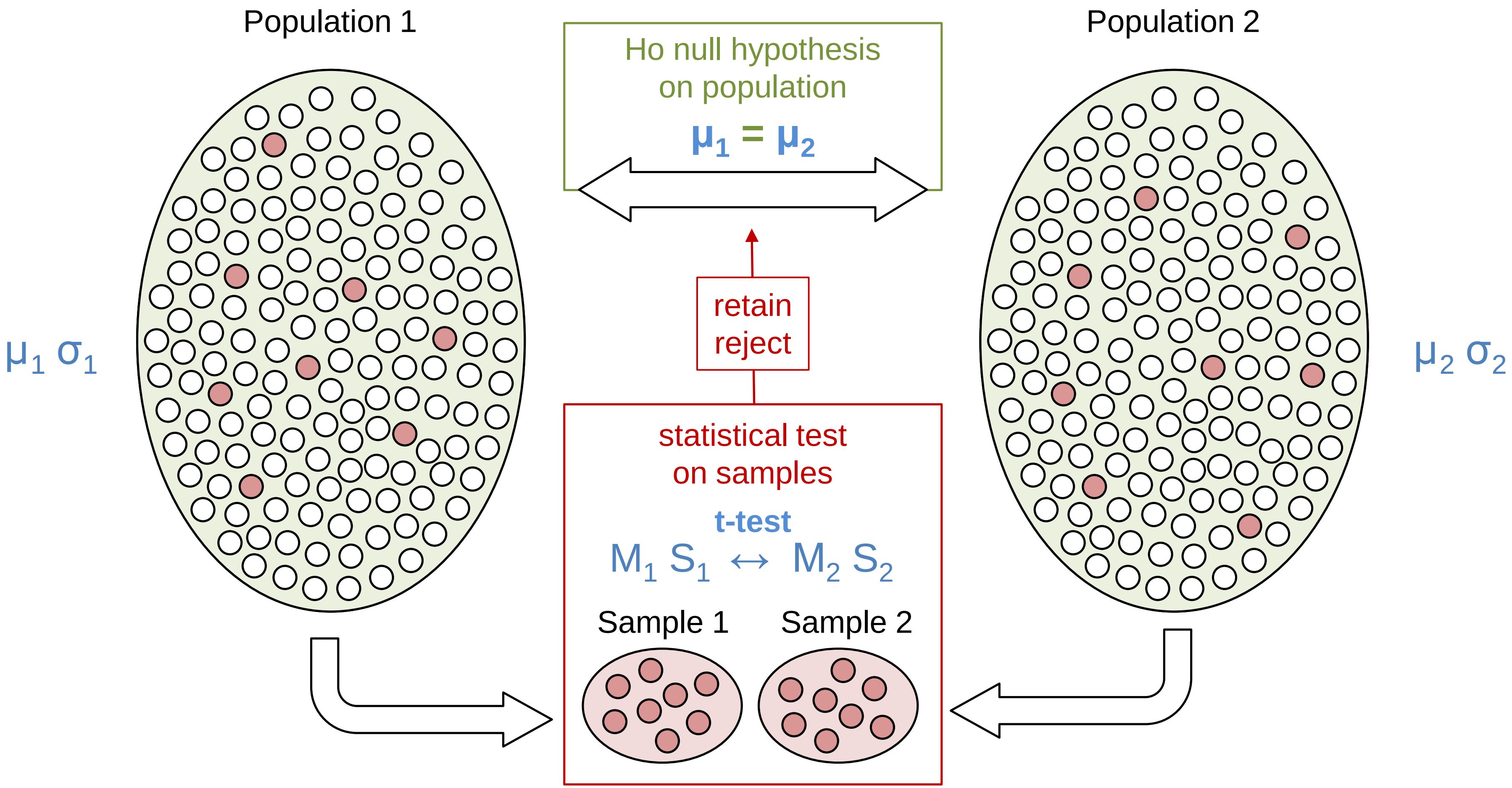
- *Repeated estimates of mean and standard deviations converge on the true population values, provided that*
  - *population data are normally distributed*
  - *sampling is unbiased*

- *Dispersion of estimates of mean and standard deviation decreases with increasing sample size:*

$$SE = \frac{s}{\sqrt{n}}$$

standard error of the mean

Statistical comparison of two populations



Hypothesis testing 1

	Ho false	Ho true
test positive: reject Ho	true positive	false positive
test negative: retain Ho	false negative	true negative

Sampling error:
We may be correct or not when using the results of a statistical test as criterion to reject or retain the null hypothesis

Hypothesis testing 1

<table>
<tr><th></th><th>Ho false</th><th>Ho true</th></tr>
<tr><td>test positive: reject Ho</td><td>true positive</td><td>α
P(reject Ho | Ho true)
Type I error
false positive</td></tr>
<tr><td>test negative: retain Ho</td><td>false negative</td><td>1-α
P(retain Ho | Ho true)
specificity
true negative</td></tr>
</table>

Type-I error

- *reject Ho when it is in fact true = false positive*
- *likelihood **α** estimated from experimental sample data by statistical tests*
- *Ho rejected if estimate ≤ threshold, typically **0.05***

Hypothesis testing 2

	Ho false	Ho true
test positive: reject Ho	**1-β** P(reject Ho | Ho false) power = sensitivity true positive	**α** P(reject Ho | Ho true) Type I error false positive
test negative: retain Ho	**β** P(retain Ho | Ho false) Type II error false negative	**1-α** P(retain Ho | Ho true) specificity true negative

Type-II error

- *retain Ho when it is in fact false = false negative*
- *likelihood β determined by experimental design:*
  - *- sample size*
  - *- type-I error threshold*
  - *- effect size*
- *Typically accepted $\beta \leq$ **0.2**, same as power 1-$\beta \geq$ **0.8***

Measures of effect size

	true effect size, population	estimated effect size, sample
t-test	$\delta = \Delta\mu/\sigma$ 0.2 = small 0.5 = medium 0.8 = large	$d = \Delta M/S_{pooled}$
ANOVA	$\omega^2 = \dfrac{\sigma^2 \text{ between groups}}{\sigma^2 \text{ total}}$ 5% = small 20% = large	$\eta^2 = \dfrac{S^2 \text{ between groups}}{S^2 \text{ total}}$

Hypothesis testing 2

<table>
<tr><th></th><th>Ho false</th><th>Ho true</th></tr>
<tr><td>test positive: reject Ho</td><td>1-β
P(reject Ho | Ho false)
power = sensitivity
true positive</td><td>α
P(reject Ho | Ho true)
Type I error
false positive</td></tr>
<tr><td>test negative: retain Ho</td><td>β
P(retain Ho | Ho false)
Type II error
false negative</td><td>1-α
P(retain Ho | Ho true)
specificity
true negative</td></tr>
</table>

Determining sample size:

- *before experiment is done!*
- *depends on*
  - *type-I error threshold, typically* $\alpha=0.05$
  - *expected effect size, eg.* $\delta=1$
  - *desired power, typically* $1-\beta=0.8$

Hypothesis testing 3

	Ho false	Ho true
test positive: reject Ho	**1-β** P(reject Ho | Ho false) power = sensitivity true positive	**α** P(reject Ho | Ho true) Type I error false positive
test negative: retain Ho	**β** P(retain Ho | Ho false) Type II error false negative	**1-α** P(retain Ho | Ho true) specificity true negative

***FDR** (false discovery ratio)*

P(Ho true | test positive)

FDR = 1 - PPV

$$FDR = \frac{\alpha}{(1-\beta)\cdot \mathbf{R} + \alpha}$$

R = Ho false / Ho true (pre-study odds)

Hypothesis testing 3

	Ho false	Ho true
test positive: reject Ho	**1-β** P(reject Ho | Ho false) power = sensitivity true positive	**α** P(reject Ho | Ho true) Type I error false positive
test negative: retain Ho	**β** P(retain Ho | Ho false) Type II error false negative	**1-α** P(retain Ho | Ho true) specificity true negative

PPV *(positive predictive value)*

P(Ho false | test positive)

PPV = 1 - FDR

$$PPV = \frac{(1-\beta)\cdot \mathbf{R}}{(1-\beta)\cdot \mathbf{R} + \alpha}$$

R = Ho false / Ho true
(pre-study odds)

Hypothesis testing 4

	Ho false	Ho true
test positive: reject Ho	**1-β** P(reject Ho | Ho false) power = sensitivity true positive	**α** P(reject Ho | Ho true) Type I error false positive
test negative: retain Ho	**β** P(retain Ho | Ho false) Type II error false negative	**1-α** P(retain Ho | Ho true) specificity true negative

***NPV** (negative predictive value)*

P(Ho true | test negative)

$$NPV = \frac{(1-\alpha)}{(1-\alpha) + \beta \cdot \mathbf{R}}$$

R = Ho false / Ho true
(pre-study odds)

Interpretation of test outcomes

- positive test outcome:
  type-I error p-value is not a measure of false discovery ratio

- false discovery ratio is typically larger than type-I error p-value, especially with
  - underpowered studies
  - low pre-study odds
  - multiple tests without correction

- Typically don't assume pre-study odds >1
  - ~ 1 in phase 3 clinical trials
  - pre-study odds <1 in basic research
  - <<1 for compound screening,
    "fishing expeditions" with poor hypotheses

- negative test outcome:
  absence of evidence is not necessarily evidence of absence of an effect

- negative predictive value is low and result inconclusive with
  - underpowered studies
  - high pre-study odds

- absence of effect should be demonstrated using dedicated tests for equivalence