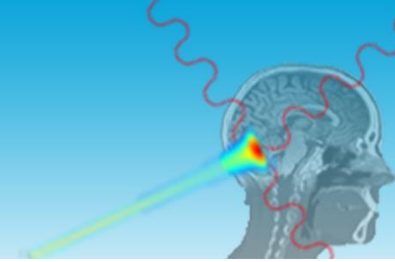


Advanced motion compensation in modern radiotherapy

Prof. Dr. Marco Riboldi

Lehrstuhl für Experimentalphysik – Medizinische Physik,
Ludwig-Maximilians-Universität München

Organisational information

- ***Contact data:***

Lehrstuhl für Experimentalphysik - Medizinische Physik

Am Coulombwall 1, 85748 Garching b. München

Telefon: +49(0)89 289-140171
Fax: +49(0)89 289-14072
E-Mail: marco.riboldi@physik.uni-muenchen.de

Consultation upon appointment

Presentation information

Duration of the seminar presentation:

- **1 h per candidate** (**40 minutes** + **20 minutes** for questions)

Deliverables:

- **Presentation slides**
- Folder with **research papers actually used in the presentation**

Sources

Research papers only, preferably indexed in:

- **Pubmed**
  - https://www.ncbi.nlm.nih.gov/pubmed/
- **ISI Web of Knowledge**
  - https://www.webofknowledge.com/
- **Scopus**
  - https://www.scopus.com/home.uri
- **IEEE Xplore**
  - http://ieeexplore.ieee.org/Xplore/home.jsp

Presentation structure

- **Brief introduction** to the topic
- General indications about the **research papers search** (search engine, keywords, timeframe, inclusion/exclusion criteria)
- **Current state-of-the-art**: reported clinical use of the motion compensated technique (if applicable)
- **General results** on evaluation/performance of the considered technique
- Suggested **modifications at a research level** (even if not yet clinical), with relative results (if any)
- **Comparison with other motion mitigation strategies** (if appropriate)
- General discussion/conclusion (**critical overview**)

Evaluation criteria

Main evaluation criteria:

- **Clarity** of the presentation
- **Structure** of slides
- **Timing**
- **Consistency** with the topic
- **Quality of the research material** used for the presentation
- **Adherence to reported results**
- **Answer to questions**

- **Active participation** (plus for those who are not presenting, participation is encouraged!)

SEMINAR TOPICS ASSIGNMENT

General reviews

Med Phys. 2006 Oct;33(10):3874-900. doi: 10.1118/1.2349696.

The Management of Respiratory Motion in Radiation Oncology Report of AAPM Task Group 76

Paul J Keall [1], Gig S Mageras, James M Balter, Richard S Emery, Kenneth M Forster, Steve B Jiang, Jeffrey M Kapatoes, Daniel A Low, Martin J Murphy, Brad R Murray, Chester R Ramsey, Marcel B Van Herk, S Sastry Vedam, John W Wong, Ellen Yorke

Affiliations + expand

PMID: 17089851 DOI: 10.1118/1.2349696

FULL TEXT LINKS

WILEY Full Text Article

FREE FULL TEXT FROM M LIBRARY

ACTIONS

Cite

Favorites

Review

Med Phys. 2018 Nov;45(11):e994-e1010. doi: 10.1002/mp.12679.

Motion Management in Particle Therapy

Shinichiro Mori [1], Antje-Christin Knopf [2], Kikuo Umegaki [3]

Affiliations + expand

PMID: 30421815 DOI: 10.1002/mp.12679

FULL TEXT LINKS

WILEY Full Text Article

ACTIONS

Cite

Favorites

LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

Seminar topics (1)

- Imaging for treatment planning under respiratory motion
  1. Time resolved CT
  2. Time resolved MRI
- Motion-encompassing methods (ITV)
  3. Radiotherapy
  4. Ion-beam therapy
- Breath-hold:
  5. Active breathing control
  6. Self-sustained (w/wo feedback)
- Shallow breathing with abdominal compression
  7. Radiotherapy
  8. Ion-beam therapy

Seminar topics (2)

- Respiratory gating:
  9. External surrogate (amplitude/phase based)
  10. Implanted markers / transponders
  11. Imaging based (e.g. MRI guidance, ultrasound)
  12. Respiratory gating in ion beam therapy
- Real-time tumor tracking:
  13. MLC tracking
  14. Robotic linac
  15. Gimbal (Vero)
  16. MRI Guidance
  17. Markerless tracking in X-ray imaging
  18. Tumor tracking in ion beam therapy

Topic assignment

- Check general reviews as introduction material
- Consider the list of topics and select 3 in order of preference:
  - Topic #1 (I would really like to present it!)
  - Topic #2 (Second choice in case #1 is taken)
  - Topic #3 (Third choice)
- Send your preference per e-mail to marco.riboldi@physic.uni-muenchen.de by April 27th, 2020
- Topic assignment (and calendar) will be discussed on April 28th, 2020 during the seminar
- We will try to follow the order of topics in slides 9-10 unless special needs apply

PUBLISHING A SCIENTIFIC ARTICLE: BRIEF OVERVIEW

Peer review

- The publication process is based on the principle of **peer review**
- Peer reviewed journals rely on **expert and objective review by knowledgeable researchers** to ensure the **quality of the papers** they publish
- Reviews are done on a voluntary basis, as a **contribution to the scientific community**
- Attention should be paid to **potential bias and conflict of interest**
- **Reviews are typically blind** (identity of authors and reviewers is not disclosed)

Peer review – who is contributing?

- **Journal staff** – oversees the receipt of manuscripts, manages communications with authors and reviewers and processes accepted manuscripts for publication
- **Scientific editors** - make the final decision as to whether a specific manuscript will be accepted for publication, returned for revisions, or rejected
- **Members of the editorial board / Associate editors** – read and review papers, select reviewers and monitor quality of reviews, and recommend actions to editor
- **Reviewers** – provide reviews of manuscripts, make recommendations concerning publication

Content of reviews

- Review form
- Comments to editor
- Comments to authors
  - General comments
  - Specific recommendations
- Journal may ask specific questions to ensure that specific points are addressed
  - Statistical analysis
  - others

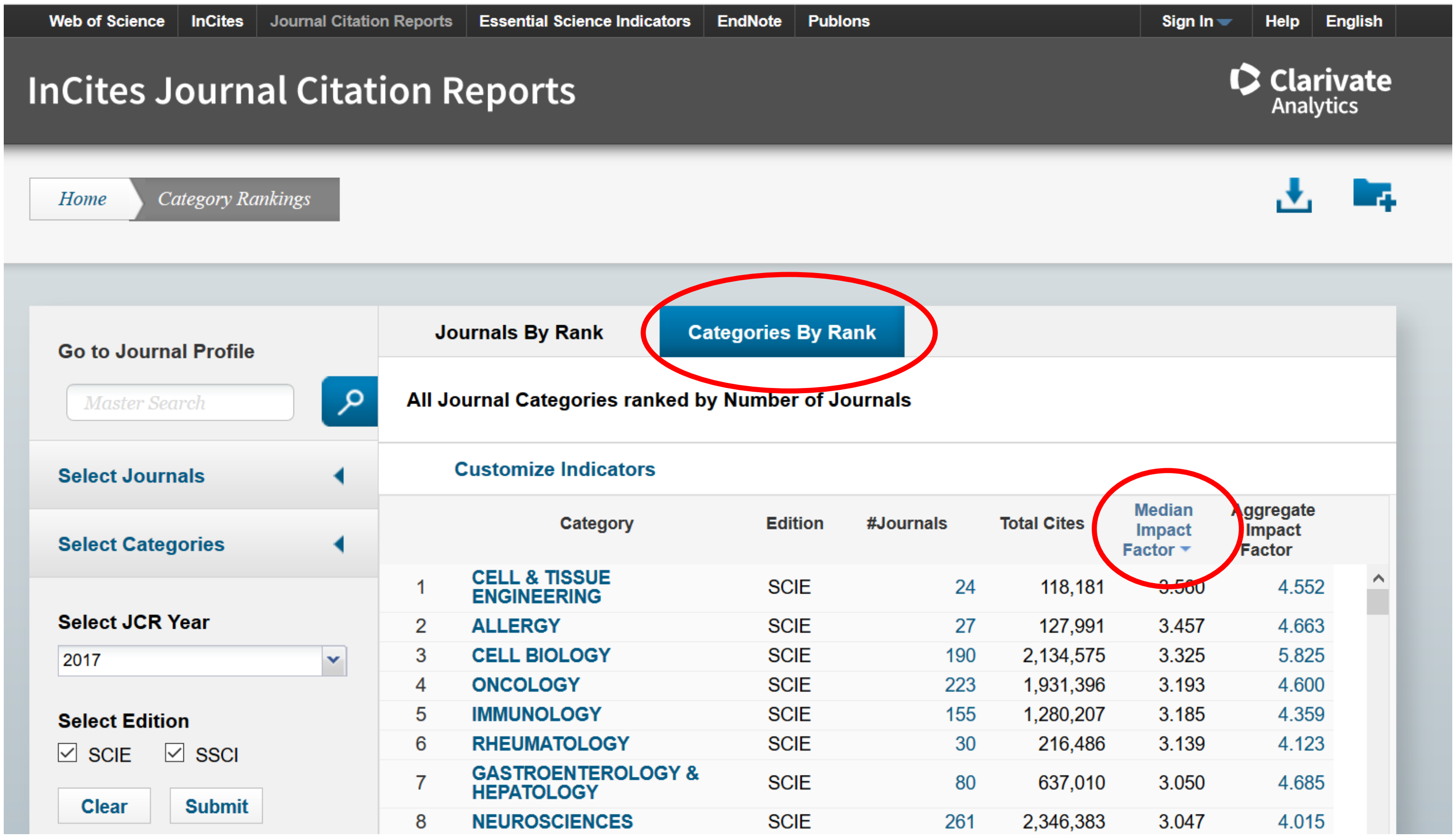
Bias and conflict of interest

- **Institutional affiliations**
  - Current or past institution (recent enough to have close associations)
  - Future institution (e.g. negotiating for a position)
  - Consultant to author's institution
- **Collaborators and colleagues**
  - How close? When?
- **Other relationships with the authors**
  - Family
  - Personal friends
  - People you would be reluctant or afraid to give a harsh review to
- **Financial conflicts of interest**
- **Others:**
  - **Participation in heated scientific debates in the area of the paper or with the authors**
  - **Studies so closely related to your own that you are in competition with the authors**
  - **Labs/groups with ongoing competitions in the general area of research**

Overview of the review process - reviewer's perspective

- Potential reviewer contacted by journal
- Given authors, title, abstract, and time frame for review
- Reviewer agrees to review paper (or declines)
- Reviewer receives paper
- Reviewer performs review
- Reviewer submits review to editors
- Editors examine reviews, obtain additional reviews if needed, and make decision
- Decision goes to author, with comments from reviewers
- Reviewer thanked; may be informed of decision; may receive copy of comments sent to author

Identify top journals in the field



JCR - Journal Citation Reports

from Thomson's InCites/ Web of Knowledge

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PHYSICS IN MEDICINE AND BIOLOGY

ISSN: 0031-9155
eISSN: 1361-6560
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TEMPLE CIRCUS, TEMPLE WAY, BRISTOL BS1 6BE, ENGLAND
ENGLAND

Go to Journal Table of Contents   Printable Version

TITLES
ISO: Phys. Med. Biol.
JCR Abbrev: PHYS MED BIOL

CATEGORIES
ENGINEERING, BIOMEDICAL - SCIE
RADIOLOGY, NUCLEAR MEDICINE & MEDICAL IMAGING - SCIE

LANGUAGES
Multi-Language

PUBLICATION FREQUENCY
24 issues/year

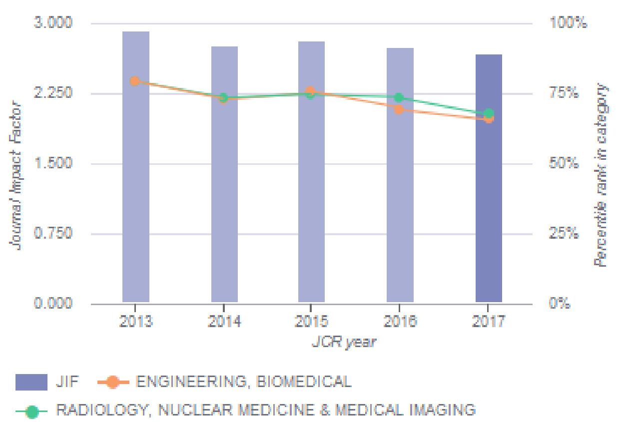
Current Year   All years

The data in the two graphs below and in the Journal Impact Factor calculation panels represent citation activity in 2017 to items published in the journal in the prior two years. They detail the components of the Journal Impact Factor. Use the "All Years" tab to access key metrics and additional data for the current year and all prior years for this journal.

Journal Impact Factor Trend 2017

Printable Version

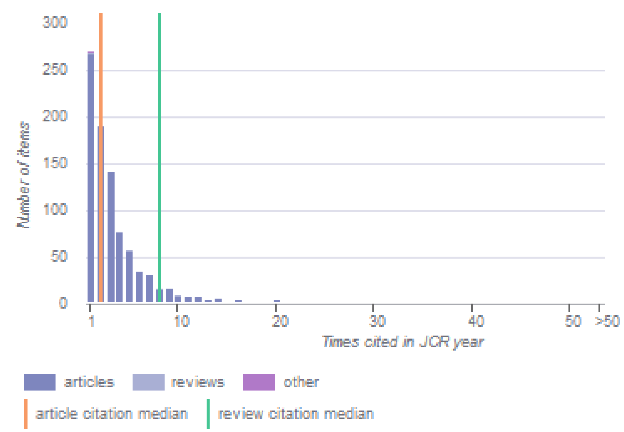
2.665
2017 Journal Impact Factor



Citation distribution 2017

Printable Version

2 Article citation median   **8** Review citation median



Journal Impact Factor Calculation

$$\text{2017 Journal Impact Factor} = \frac{3,030}{1,137} = 2.665$$

Journal Impact Factor contributing items

Show all

Citable items in 2016 and 2015 (1,137)   Citations in 2017 (3,030)

Journal Impact Factor Calculation

$$\text{2017 Journal Impact Factor} = \frac{3{,}030}{1{,}137} = 2.665$$

How is Journal Impact Factor Calculated?

$$\text{JIF} = \frac{\text{Citations in 2017 to items published in 2015 (1,762) + 2016 (1,268)}}{\text{Number of citable items in 2015 (572) + 2016 (565)}} = \frac{3{,}030}{1{,}137}$$

Journal Impact Factor contributing items

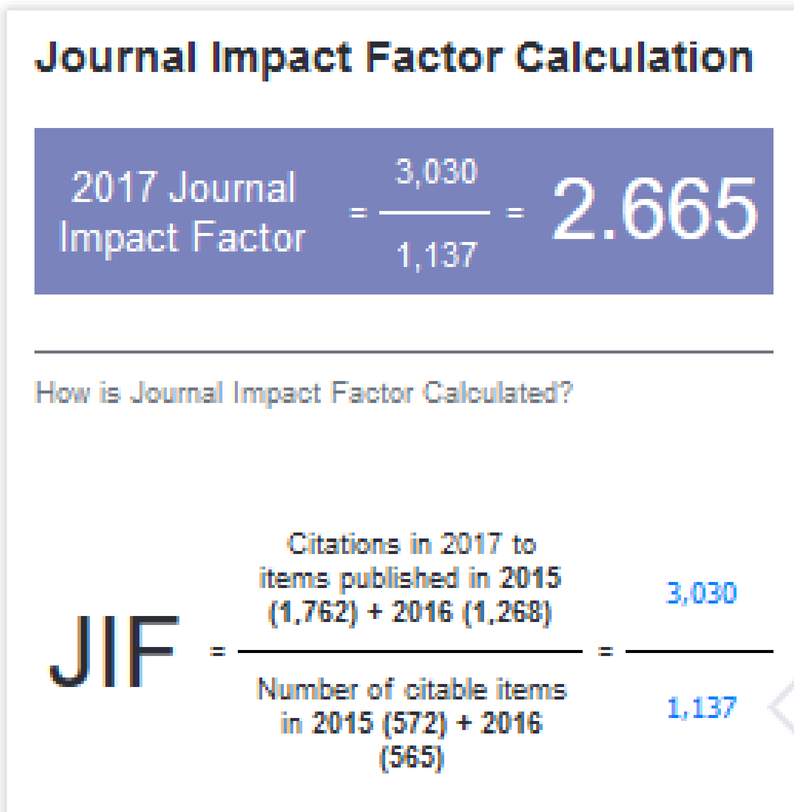
Show all

Citable items in 2016 and 2015 (1,137) Citations in 2017 (3,030)

TITLE	CITATIONS COUNTED TOWARDS JIF
A radiomics model from joint FDG-PET and MRI texture features for the prediction of lung metastases in soft-tissue sarcomas of the extremities By: Vallieres, M.; Freeman, C. R.; Skamene, S. R.; El Naqa, I. **Volume: 60 Page: 5471-5496 Accession number: WOS:000357620400010** **Document Type: Article**	42
Applications and limitations of radiomics By: Yip, Stephen S. F.; Aerts, Hugo J. W. L. **Volume: 61 Page: R150-R166 Accession number: WOS:000378094000002** **Document Type: Review**	35
A phenomenological relative biological effectiveness (RBE) model for proton therapy based on all published in vitro cell survival data By: McNamara, Aimee L.; Schuemann, Jan; Paganetti, Harald **Volume: 60 Page: 8399-8416 Accession number: WOS:000366108500013** **Document Type: Article**	29
Radiotherapy planning using MRI By: Schmidt, Maria A.; Payne, Geoffrey S. **Volume: 60 Page: R323-R361 Accession number: WOS:000366108900003** **Document Type: Review**	23
An evaluation of three commercially available metal artifact reduction methods for CT imaging By: Huang, Jessie Y.; Kry, Stephen F.; Kerns, James R.; Nute, Jessica L.; Liu, Xinming; et al. **Volume: 60 Page: 1047-1067 Accession number: WOS:000349438400014** **Document Type: Article**	21
PET-MRI: a review of challenges and solutions in the development of integrated multimodality imaging By: Vandenberghe, Stefaan; Marsden, Paul K. **Volume: 60 Page: R115-R154 Accession number: WOS:000349529100001** **Document Type: Review**	21
Evaluation of conventional imaging performance in a research whole-body CT system with a photon-counting detector array By: Yu, Zhicong; Ritman, Erik L.; McCollough, Cynthia H.; Leng, Shuai; Jorgensen, Steven M.; et al. **Volume: 61 Page: 1572-1595 Accession number: WOS:000370452500012** **Document Type: Article**	20

Impact factor

The **Journal Impact Factor** reflects the average number of citations to recent articles published in that journal. It is one measure of the *relative importance* of a journal within its field.



Suggested sources and impact factor

- The libraries suggested as sources (slide #4) include all **journals with impact factor** (i.e. indexed in ISI)
- Sources cover relevant libraries for **medical physics and engineering contributions** (might be relevant for motion management technologies)
- Selecting papers fro those sources is a **necessary condition to include high quality papers**
- **It is clearly not a sufficient condition**, as peer review is not exempt from errors

STATISTICAL TESTS IN SCIENTIFIC ARTICLES: A SHORT GUIDE

Data analysis and statistics

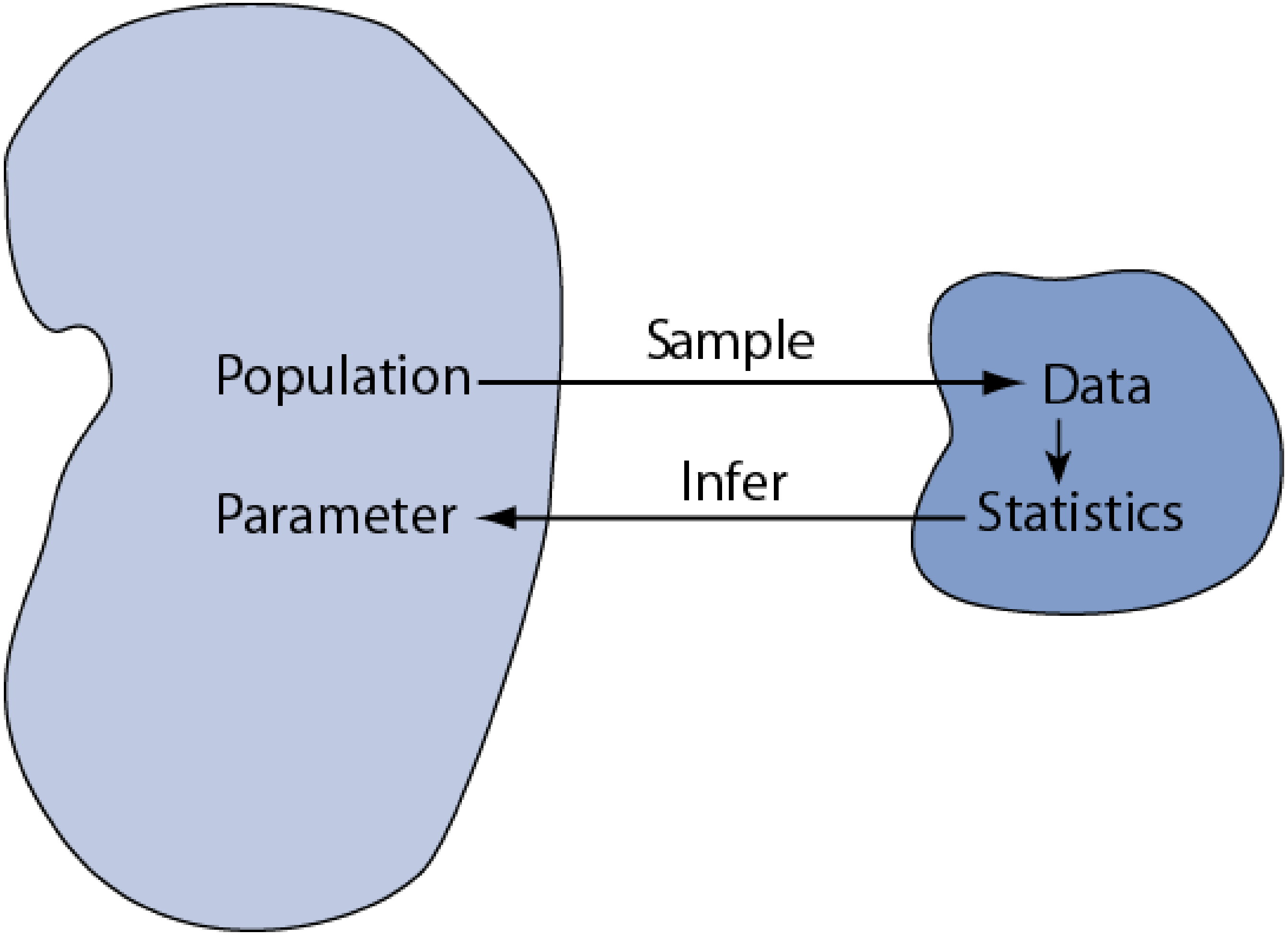
Statistics - a powerful tool for analyzing data

1. **Descriptive Statistics** - provide an overview of the attributes of a data set. These include measurements of *central tendency* (frequency histograms, mean, median, & mode) and *dispersion* (range, variance & standard deviation)
2. **Inferential Statistics** - provide measures of how well your data support your hypothesis and if your data are generalizable beyond what was tested (*significance tests*)

Statistics - definitions

- **Population** $\equiv$ all possible values of a given variable
- **Sample** $\equiv$ a portion of the population
- **Statistical inference** $\equiv$ generalizing from a sample to a population with a calculated degree of certainty
- Two forms of statistical inference
  - **Hypothesis testing**
  - **Estimation**
- **Parameter** $\equiv$ a characteristic of population, e.g., population mean μ
- **Statistic** $\equiv$ calculated from data in the sample, e.g., sample mean ($\bar{x}$)

Statistics - definitions



Significance testing

- Significance **testing tests a claim about a parameter** (e.g. mean value) **using evidence** (data in a sample)
- We can divide the process in the following **steps**:

A. Null and alternative hypotheses
B. Test statistic
C. P-value and interpretation (significance level)

Null and alternative hypothesis

- Convert a research question to null and alternative hypotheses
- The **null hypothesis (H_0)** is a claim of "no difference in the population"
- The **alternative hypothesis (H_a)** claims "H_0 is false"
- Collect data and seek evidence against H_0 as a way of supporting H_a (deduction)

Test statistics

- The test statistic *T* is a **scalar function of the observations** that reduces the data to one value that can be used to perform the hypothesis test

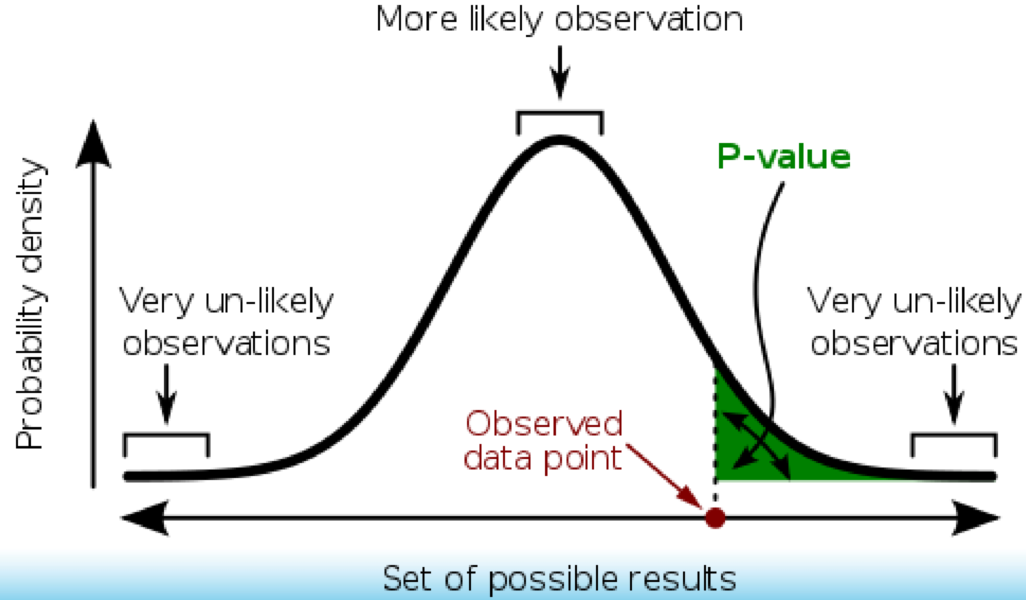
- The **distribution of *T* under the null hypothesis H_0** is assumed to be **known**

- The calculated scalar value (based on observations) is **compared to reference tables** (distribution of *T* under H_0)

- From the comparison we can derive the **probability that the calculated scalar value differs from the underlying null hypothesis**

P-value

- The **P-value** (**probability value**) is the probability that, when the null hypothesis H_0 is true, the test statistics would be greater than or equal to the actual value
- Thus, **smaller and smaller *P*-values provide stronger and stronger evidence against H_0**



Interpretation and significance level

- Let α ≡ probability of erroneously rejecting H_0
- Set **α threshold** (e.g., let α = 5%, 1%)
- **Reject H_0** when ***P-value* ≤ α**
- **Retain H_0** when ***P-value* > α**

Statistical errors

Your Statistical Decision	True state of null hypothesis	
	H_0 True (example: the drug doesn't work)	H_0 False (example: the drug works)
Reject H_0 (ex: you conclude that the drug works)	*Type I error (α)*	*Correct*
Do not reject H_0 (ex: you conclude that there is insufficient evidence that the drug works)	*Correct*	*Type II Error (β)*

Errors and power

- **Type I error rate** (or significance level): the probability of finding an effect that isn't real (**false positive**)
  - If we require p-value<.05 for statistical significance, this means that 1/20 times we will find a positive result just by chance.
- **Type II error rate**: the probability of missing an effect (false negative)
- **Statistical power**: the probability of finding an effect if it is there (the probability of not making a type II error)
  - When we design studies, we typically aim for a power of 80% (allowing a false negative rate, or type II error rate, of 20%).
  - It is related to the number of samples, the higher the number the higher is the power

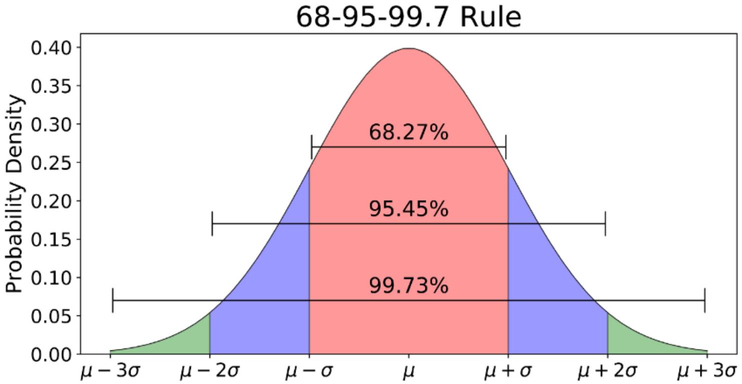
Common mistakes in interpretation

- **Over emphasize p-values**
  - Always check the magnitude of any statistically significant effect; it might be negligible even if significant
- **Statistical significance does not imply a cause-effect relationship**
- **High type II errors**
  - Results that are not statistically significant should not be interpreted as "evidence of no effect," but as "no evidence of effect"
  - Studies may miss effects if they are insufficiently powered
- **Comparing statistical significance**
  - "the effect was significant in the treatment group, but not significant in the control group" does not imply that the groups differ significantly
- **Multiple comparisons**
  - Significance values need to be adjusted for multiple comparisons in case a test that compares 2 groups is used (Bonferroni correction)
  - Use test for multiple comparisons is suggested

Parametric vs. non parametric tests

Data distribution

Normal (Gaussian) distribution | **Unknown distribution**



- If the sample is small (less than 100), **statistical tests should be performed to check the Gaussian distribution**: Kolomogorov-Smirnov, Lilliefors, Shapiro-Wilks.

- Otherwise it is safer to assume that the **distribution is unknown** (no risk to increase type I errors)

Parametric vs. non parametric tests

Statistical tests may fall into one of these categories:

- **Tests of differences between groups** (**independent samples**)
  - Same variable measured in different groups
  - Example: analyze age difference in different patient groups (numerosity may change)
- **Tests of differences between variables** (**dependent samples**)
  - Check difference within the same group
  - Example: before/after analysis in a given patient group (paired data analysis)
- **Tests of relationships between variables**
  - Correlation analysis

Difference between groups

Comparing 2 groups (A vs. B)

Parametric	Non parametric
T-test	Mann-Whitney U test
	Wald-Wolfowitz run test,
	Kolmogorov-Smirnov two-sample test

Comparing multiple groups (overall difference)

Parametric	Non parametric
Analysis of variance (ANOVA / MANOVA)	Kruskall-Wallis
	Median test

Difference between variables

Comparing 2 variables (X vs. Y)

Parametric	Non parametric
T-test for dependent samples	Wilcoxon's matched pair test
	McNemar's Chi-square test (binary variables)

Comparing multiple variables

Parametric	Non parametric
Repeated measures ANOVA	Friedman test
	Cochran Q Test (binary variables)

Relationship between variables

Parametric	Non parametric
Correlation coefficient	Spearman R
Pearson correlation	Kendall tau
	Coefficient Gamma