# Scientific Rigor & Reproducibility Tool Box

Presented by the American Physiological Society Science Policy Committee

## APS Publications

The American Physiological Society has added two pages to the Information for Authors that are intended to encourage transparent reporting and enhance data reproducibility.

The pages are:

- Promoting Transparent Reporting in APS Journals: **https://www.physiology.org/author-info.promoting-transparent-reporting**
- Experimental Details to Report in Your Manuscript: **https://www.physiology.org/author-info.experimental-details-to-report**

## Animal Research

The Experimental Design Assistant (EDA) is an online tool to guide researchers through the design of their experiments, helping to ensure that they use the minimum number of animals consistent with their scientific objectives, methods to reduce subjective bias, and appropriate statistical analysis. **https://eda.nc3rs.org.uk/**

This site also has some additional experimental design general information: **https://www.nc3rs.org.uk/experimental-designstatistics**

## Statistics

### Online Statistics Courses

Data Analysis for Life Sciences 1: Statistics and R

An introduction to basic statistical concepts and R programming skills necessary for analyzing data in the life sciences. **https://online-learning.harvard.edu/course/statistics-and-r**

NIH's Clearinghouse for Training Modules to Enhance Data Reproducibility

Includes video modules produced by NIH and Society for Neuroscience. These cover the basics of experimental design, data analysis, and data management. Good resource for training and provide an overview. **https://www.nigms.nih.gov/training/pages/clearinghouse-for-training-modules-to-enhance-data-reproducibility.aspx**

### Textbooks on Responsible Conduct of Research (suggested on U Penn's site)

Scientific Integrity, F.L. Macrina, 4th ed. **https://www.amazon.com/Scientific-Integrity-Responsible-Conduct-Research/dp/1555816614**

Responsible Conduct of Research, A.E. Shamoo and D.B. Resnick, 3rd ed. **https://www.amazon.com/Responsible-Conduct-Research-Adil-Shamoo/dp/019536824X**

### CITI Training Course on Responsible Conduct of Research

(Requires institutional subscription or $/course)

**https://about.citiprogram.org/es/serie/responsible-conduct-of-research-rcr/**

**Find more info at the-aps.org/ReproducibilityTools**

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## NIH Resources

NIH Policies on Rigor and Reproducibility (NIH Rigor and Reproducibility Description)

The NIH offers guidelines, training, and up to date announcements on rigor and reproducibility. Under Frequently asked Questions (FAQs), of Rigor and Transparency, important information is summarized for all scientists to consider when validating scientific findings.

Most funding applications (new submissions, resubmissions and renewals as well as research, career development and training grants) must address rigor and transparency. The following areas should be addressed in the Research Strategy of the applications (in the existing page limits): **Scientific premise**, **Scientific rigor**, **Relevant biological variables**, and **Key biological and/or chemical resource authentication plan**.

If an awardee encounters challenges with meeting the rigor and transparency strategies, they must provide program officials with clear explanations of the difficulties and actions the investigator has taken to overcome them in the progress report. Program officials will suggest alternative approaches to resolve the difficulties and in extreme cases, support may end early for the project.

### 1. Scientific premise

- Include in the Significance section
- Scientific premise is rated by the quality and strength of the research (published and unpublished) in support of the application.
- Applicants should address gaps in rigor or reporting of rigor and how these gaps will be addressed in the application.
- Scientific premise is a retrospective consideration of the foundation of the application, rather than what will happen if the aims are achieved in the grant application.

### 2. Scientific rigor

- Include in the Approach section
- Application of the scientific method to the proposed study to ensure:
- Robust and unbiased experimental design (solid, well-controlled experiments that can be reproduced; may vary across scientific disciplines)
- Methodology (must be described in detail within the experimental design)
- Analysis, interpretation and reporting of results

The full transparency of reporting experimental details allowed other to reproduce and extend the reported findings. An example of appropriately presented data: “10 males and 10 females will



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be randomized to blinded treatment and control groups, giving 80% power to detect a treatment effect size of 65% compared to a baseline response of 5% at a significance level of 0.05."

## 3. Relevant biological variables

- Included in the Approach section and considered as part of review score for research strategy
- Biological variables to consider: sex, age, weight, underlying health conditions
- In particular, sex needs to be considered in the research design, analyses and reporting, or strong justification for studying only one sex needs to be included. For clinical research studies, this is mandated by law.
- Sex should be accounted for when using primary cells and tissue explants and is encouraged to be reported for cell lines when possible

Studies incorporating both males and females should disaggregate the data, whether the study was statistically powered to detect sex differences or not. This enables its use for further study; for example, reporting descriptive statistics for males and females separately contributes to understanding of male and female biology. Considering the possible role of sex early in the research continuum may save time and money by revealing differences/similarities that need to be taken into consideration in subsequent phases of study.

An NIH RFI on sex as a biological variable (SABV), found agreement that considering SABV is good science, but scientists and other stakeholders have noted concerns (i.e.: cost, methodological constraints, experimental design). Based on respondent requests, NIH is developing SABV training resources and scientific tools such as courses, workshops, and online resources to help applicants, reviewers, and NIH program staff.

## 4. Key biological and/or chemical resource authentication

- The Authentication Plan should be brief (< 1 page) and is a separate attachment (Item 15 in the Research Plan)
- The plan should include the methods proposed to authenticate key established resources prior to use and at regular intervals, if appropriate
- Established resources used in the proposal include: specialty chemicals, antibodies, cell lines (including those obtained from outside sources) and other biologics
- The plan is considered in the review, but not considered in the overall impact score
- The plan does not need to include actual data demonstrating that authenticated resources are available; plans for the authentication of data sets, databases, machinery, or electronics.
- Applicants proposing to generate a new key biological and/or chemical resource (such as a human cancer cell line) should describe development and authentication of the resource in the Approach section.



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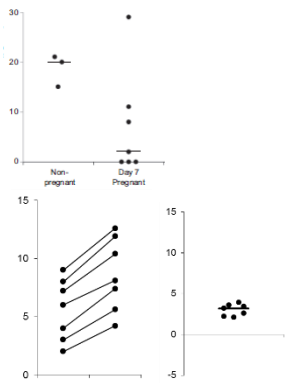
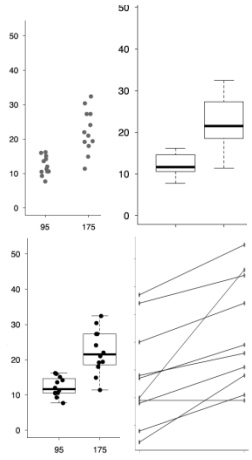
**Data Visualization Resources for Small Studies**

| Graphic | Graph Type | Program | Link & Reference |
|---|---|---|---|
|  | Univariate scatterplots<br>▪ Independent data<br>▪ Paired data (1-2 groups, 2 conditions/group) | Excel (templates)<br><br>Graph Pad PRISM (instructions)<br><br>SPSS (code) | http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1002128<br><br>Weissgerber T, Milic N, Winham S, Garovic VD. Beyond Bar Graphs: Time for a New Data Presentation Paradigm. PLoS Biol. 2015;13: e1002128<br><br>**Updated Excel templates and SPSS code posted at CTSpedia:** https://www.ctspedia.org/do/view/CTSpedia/TemplateTesting |
| Same as above | Replication of graphs shown in Weissgerber et al., PLOS Biol 2015;13: e1002128 | R | https://cdn.rawgit.com/benmarwick/new-data-presentation-paradigm-using-r/582a80eaba654237231fe4b06d3eda5a61587d73/Weissgerber_et_al_supplementary_plots.html<br><br>This repository includes all information as a zip file:<br>Marwick, Ben. 2015. Using R for the examples in Weissgerber et al. 2015 "Beyond Bar and Line Graphs: Time for a New Data Presentation Paradigm". http://dx.doi.org/10.5281/zenodo.18613 |
|  | Univariate Scatterplots<br><br>Boxplots | R | http://www.ashander.info/posts/2015/04/barchart-alternatives-in-base-r/<br><br>Blog post: Ashander J. 2015. Easy alternatives to bar charts in native R graphics, Rapid evolution: Theory, computation and inference. April 28, 2015. |



Compiled by: Tracey Weissgerber (@T_Weissgerber)

**Data Visualization Resources for Small Studies**

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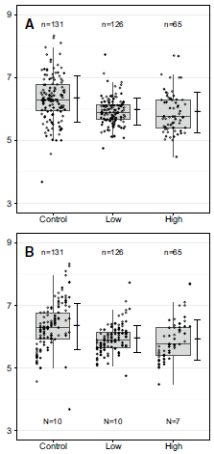
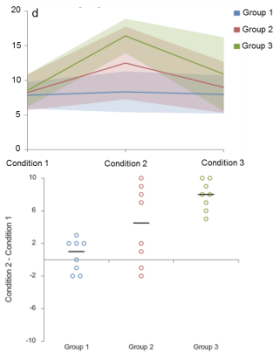
|---|---|---|---|
|  | Boxplots<br>▪ Independent data<br>▪ Clustered or grouped data<br><br>Boxplots<br>▪ Independent data | Web-based tool (SHINY app)<br><br>Web-based tool (SHINY app) | https://lancs.shinyapps.io/ToxBox<br><br>Pallmann P, Hothorn LA. Boxplots for grouped and clustered data in toxicology. 2015. doi:10.1007/s00204-015-1608-4.<br><br>http://boxplot.tyerslab.com/<br><br>Spitzer M, Wildenhain J, Rappsilber J, Tyers M. BoxPlotR: a web tool for generation of box plots. Nature methods 2014;**11**(2):121-2. |
|  | Interactive line graphs for scientific publications, also allows authors to save tif files of static figures for print publication | Web-based tool | http://statistika.mfub.bg.ac.rs/interactive-graph/<br><br>Weissgerber TL, Garovic VD, Savic M, Winham SJ, Milic NM. From static to interactive: Transforming data visualization to improve transparency. PLoS Biology 4(6): e1002484. doi:10.1371/journal.pbio.1002484. |
| See paper for more info | Various different types of graphs | Excel<br>R<br>Stata | http://faculty.washington.edu/kenrice/heartgraphs<br><br>Rice K, Lumley T. 2016. Graphics and statistics for cardiology: comparing categorical and continuous variables. Heart 102(5):349-355 |

The free statistical software package R offers many options for creating different types of graphics. Maria Nattestad has created a very accessible series of short video lectures that teaches learners who have not used R before to import data and make different types of plots. For those who are new to R, this tutorial provides valuable background information for the “R” resources listed in the table above.

Maria Nattestad. Plotting in R for Biologists: The Course.

https://www.youtube.com/watch?v=sf_li1XV664&list=PL-IR12W3BZkXGfIjRtMgAw1Ff0liWX_Aj



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