Research quality and reproducibility: Developing resources for our members

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Who we are

- American Physiological Society has ~11,000 members who carry out basic physiological research in labs around the US and internationally
- Physiology has a role in pre-clinical and translational research
- Many of our members use animal models
- Member of FASEB

Understanding the problem

- 2012-2014: data comes to light showing lack of reproducibility
- Leaders in the scientific community, the scientific and lay press, and Congress have all taken notice
- Risk of undermining public support for research

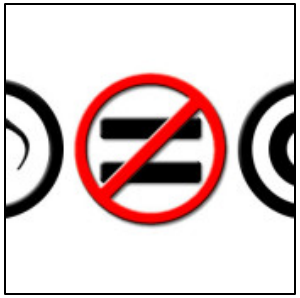
H.R. 34: 21st Century Cures Act

ENHANCING THE RIGOR AND REPRODUCIBILITY OF SCIENTIFIC RESEARCH

"…the Director of the National Institutes of Health, shall convene a working group under the Advisory Committee to the Director … to develop and issue recommendations through the Advisory Committee for a formal policy … to enhance rigor and reproducibility of scientific research funded by the National Institutes of Health.

Reaching our members

- Members of the scientific community have questions, among them, what does it mean to acknowledge this problem?
- Lack of research reproducibility does not equal research misconduct



April 2015 Science Policy Committee Symposium

- Reproducibility in Research: What are the problems? How can we fix them? What happens if we don't?
- Shai Silberberg, Malcolm Macleod, Richard Nakamura

- Resources: Journal club activity, recordings of presentations, video interviews

FASEB Report: Enhancing Research Reproducibility

- Goal of developing recommendations for stakeholder groups
- Symposium and series of roundtables focused on animal models, antibodies, developing recommendations
- Industry, academia, professional societies, publishers and others
- Available on the FASEB website: www.faseb.org

Over-arching recommendations

- Stakeholders should use precisely defined terms and definitions (offered in report)
- The inability to reproduce research findings may result from lack of sufficient detail in reporting
- Rigorous and transparent research is dependent on good research practices by all participants

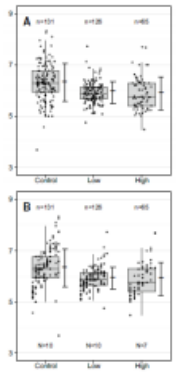
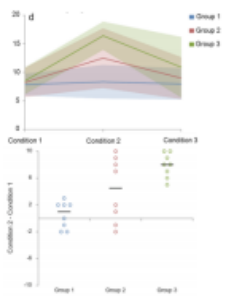
2017 Science Policy Committee Symposium

- Why scientific rigor matters and ways to improve it
  - Kristine Willis (NIH perspective)
  - Bradley Yoder (UAB training course)
  - Curt Sigmund (APS Publications)
  - Tracey Weissgerber (Mayo; statistics and data visualization)
- Resources: Reproducibility Toolbox handout (pdf), recordings of presentations

Data visualization

- Physiologists working with animal models often use small sample sizes

Data Visualization Resources for Small Studies

	Boxplots ▪ Independent data ▪ Clustered or grouped data Boxplots ▪ Independent data	Web-based tool (SHINY app) Web-based tool (SHINY app)	https://lancs.shinyapps.io/T Pallmann P, Hothorn LA. B in toxicology. 2015. doi:10 http://boxplot.tyerslab.com/ Spitzer M, Wildenhain J, R tool for generation of box p
	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. Weissgerber TL, Garovic V From static to interactive: T improve transparency. PLo doi:10.1371/journal.pbio.10
See paper for more info	Various different types of graphs	Excel R	http://faculty.washington.ed

APS Publications

- 14 peer-reviewed journals
- Publications chair participated in APS and FASEB efforts
- Committee developed new guidelines in information for authors
- Authors are encouraged to enhance reporting

Promoting Transparent Reporting in APS Publications to Enhance Data Reproducibility

Concerns about the lack of rigorous reporting of, and the failure to reproduce, studies published in research articles have been the topic of discussion at NIH, FASEB, APS, and other science organizations. In particular, APS Council and the APS Publications Committee have considered how APS journals could facilitate better reporting of experiments reported in the APS Journals and, in turn, increase the likelihood that studies could be reproduced.

As of August 2016, several guidelines in the APS Information for Authors have been updated, including the addition of a new section entitled "Experimental Details to Report in Your Manuscript" in effort to promote greater transparency in reporting relevant experimental information. As such, authors are ENCOURAGED* (as noted by the icon) to enhance in the following ways the reporting of:

Animal experiments

Authors are encouraged to refer to the **ARRIVE Guidelines Checklist** in preparation for reporting the methods and results of animal studies. Particular attention should be given to providing detailed information regarding:

- The animals used in the study (species, strain, sex, age, source of animals, genetic modification status, housing, diet, etc.)
- The controls used in the study (littermate, purchased, identical conditions, contemporaneous, historical, etc.)
- Precise details of all experimental procedures (drug formulation and dose, anesthesia and analgesia used, method of euthanasia, etc.)
- Steps taken to minimize subjective bias in the study design (randomization, blinding, etc.)

Antibody validation

Authors are encouraged to submit one representative full blot per antibody that generated the data for the paper, exclusive of loading controls. Lanes on the blot should be labeled to note the nonspecific and specific bands and exposure time should be indicated. These materials will be assessed during review.

Authors are encouraged to describe how antibodies were validated for specificity. Authors can reference prior publications or show positive or negative controls on the blot, as noted above, that is submitted as "Supporting Material for Reviewers Only."

Experimental details in figures and legends

Information reported in figures and legends should describe each individual experiment presented, including the number of samples or animals used per treatment. The statistics performed for each experiment should be reported as well. If concerns regarding the statistical analyses reported in the manuscript are raised during peer review, the Associate Editor may consult a statistician for guidance.

Authors are encouraged to present gels or blots in figures with the following:

- a molecular-weight size marker

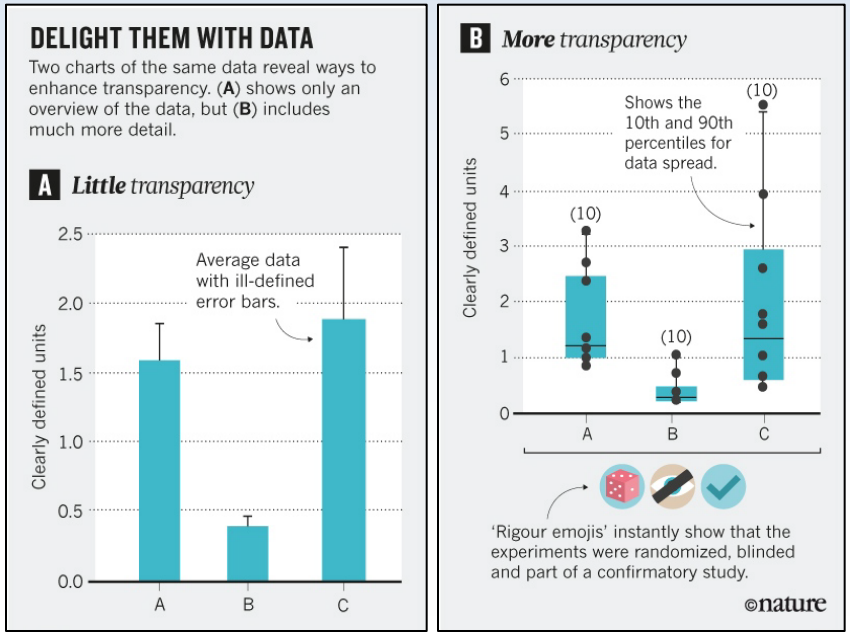
APS professional skills training course

- "Controls in Animal Studies Professional Skills Course"
  - Create a teaching module that develops skills in designing, analyzing, and reporting well-controlled animal studies, and to establish a community of practice for researchers using animal models
- NIH Clearinghouse for Training Modules to Enhance Data Reproducibility

NIH/FASEB Conferences Workshop

- Work presented at scientific meetings provides only a snapshot, can be difficult to evaluate information presented
- Call for ongoing efforts to improve communication at conferences
- Need for guidelines to promote transparency

FASEB piloting “rigor emojis”



- 2 small conferences
- Survey found that awareness was low, both for emojis and NIH policies
- Continue in 2018 with updated guidance for their use

***Nature* Commentary**
Nature 548, 153–154 (10 August 2017)
doi:10.1038/548153a

Resources

- www.the-aps.org/reproducibility
- APS Publications
  - Information for authors
- FASEB resources (www.faseb.org)
  - Enhancing reproducibility report
  - Link to *Nature* commentary

A lack of consistent reproducibility in some pre-clinical research has serious implications for translating those findings from bench to bedside. This is a problem that requires urgent corrective action. Restoring confidence in the rigor of pre-clinical biomedical research will require all stakeholders to be a part of the solution, including basic scientists, academic institutions, industry, and publishers.

Reproducibility Symposia

Why Scientific Rigor Matters and Ways to Improve It
Abstract and resource links for the 2017 EB symposium in which Kristine Willis (NIH), Bradley K. Yoder (University of Alabama-Birmingham), Curt D. Sigmund (University of Iowa), and Tracey Weissgerber (Mayo Clinic) described efforts to increase scientific rigor through training students in research design, more transparent reporting of research findings, and better approaches to data visualization.

Reproducibility in Research
Shai Silberberg (NINDS), Richard Nakamura (NIH-CSR), and Malcolm Macleod (Edinburgh University) identified issues that undermine scientific rigor and the importance of addressing them. (Experimental Biology 2015)

APS Resources

Reproducibility ToolBox
Resource collection handout made available during the Why Scientific Rigor Matters and Ways to Improve It Symposium [pdf]

Reproducibility Journal Club
Use this journal club activity to gain insight into the challenges of improving scientific rigor. It includes articles and sample questions recommended by speakers at the APS Reproducibility Symposium.

APS Advises NIH on Sex as a Biological Variable
The APS response to an NIH Request for Information (RFI, NOT-OD-14-128) on developing policies for the inclusion of sex as a biological variable in pre-clinical research studies involving animals and cells.

Professional Integrity: Best Practices for Publishing Your Research
APS Education Department's Professional Skills Training Course on Publication Ethics.

Outside Resources

NIH: Rigor and Reproducibility
Access point for NIH announcements and resources on improving scientific rigor.

NIH OER Rigor & Reproducibility Guidance
Information from the NIH Office of Extramural Research designed to assist the extramural community in addressing rigor and transparency in NIH grant applications and progress reports.

FASEB: Enhancing Research Reproducibility
A report by the Federation of American Societies for Experimental Biology (FASEB) with recommendations for a variety of stakeholders aimed at promoting the reproducibility and transparency of biomedical and biological research.

iBiology: Shai Silberberg Video on Unconscious Bias & Publications Bias
In a video produced by iBiology, NINDS Program Director Shai Silberberg discusses two key contributors to irreproducibility and offers suggestions for mitigating these factors.

ILAR Workshop Brief: Reproducibility in Research with Animal Models
A summary of the National Academy of Sciences's Roundtable on Science and Welfare in Laboratory Animal Use. The document is available as a free PDF download or to read online.

Click for more…

Future plans

- Launch of professional skills training on animal controls
- EB 2018 symposium in San Diego: Avoiding common pitfalls in preclinical animal research design
- Partnerships to enhance data visualization in our publications

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