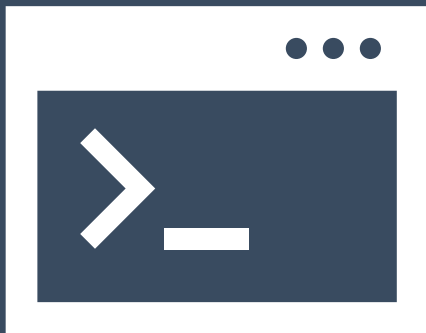


Foundations in Quarto

<https://tinyurl.com/hbc-quarto>



Harvard Chan Bioinformatics Core



Reproducibility means...

- ❖ The methods of an experiment can be repeated?

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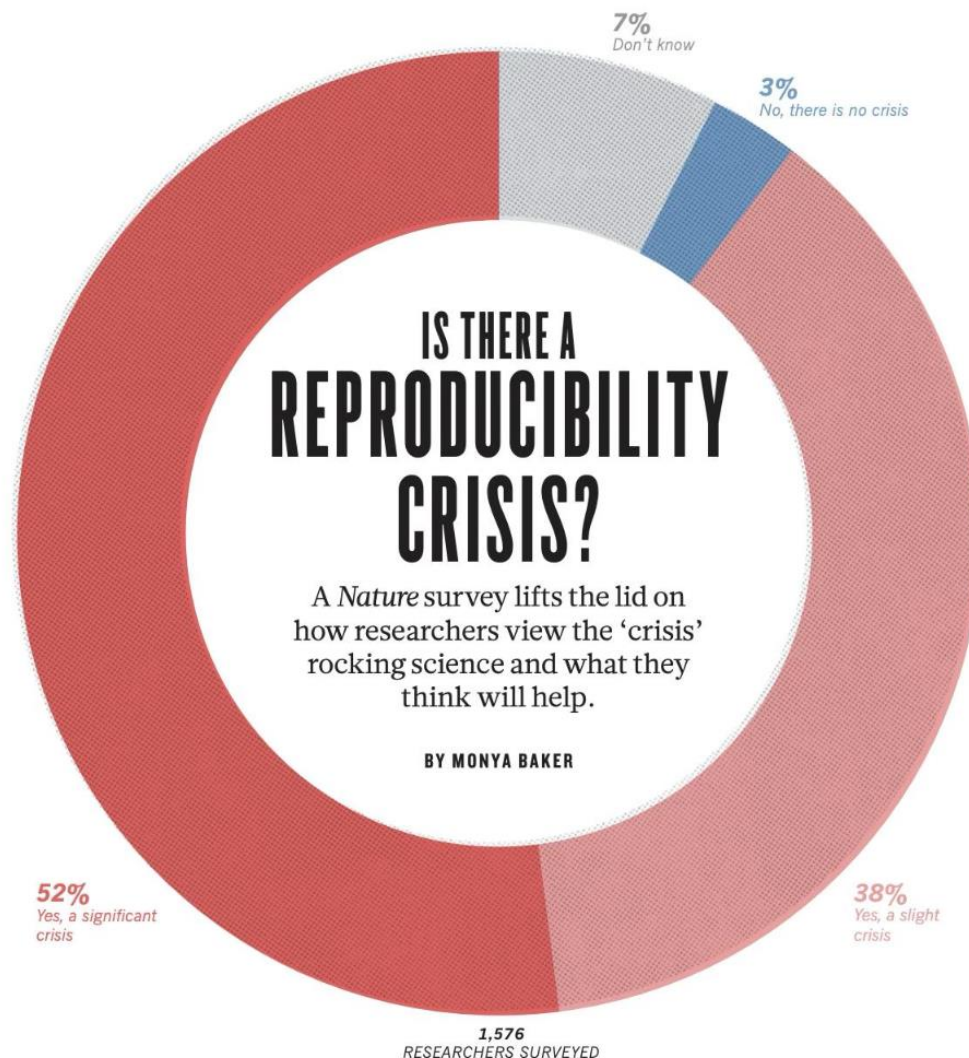
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Reproducibility means...

- ❖ The methods of an experiment can be repeated?
- ❖ The results of a subsequent experiment based on those methods would generate identical results?
- ❖ If two groups were analyzing the same data, they would reach the same conclusions?

“Reproducibility is a minimum necessary condition for a finding to be believable and informative.”

Goodman et al., 2016



NEWS FEATURE

a replication study. When work does not reproduce, researchers often assume there is a perfectly valid (and probably boring) reason. What's more, incentives to publish positive replications are low and journals can be reluctant to publish negative findings. In fact, several respondents who had published a failed replication said that editors and reviewers demanded that they play down comparisons with the original study.

Nevertheless, 24% said that they had been able to publish a successful replication and 13% had published a failed replication. Acceptance was more common than persistent rejection: only 12% reported being unable to publish successful attempts to reproduce others' work; 10% reported being unable to publish unsuccessful attempts.

Survey respondent Abraham Al-Ahmad at the Texas Tech University Health Sciences Center in Amarillo expected a "cold and dry rejection" when he submitted a manuscript explaining why a stem-cell technique had stopped working in his hands. He was pleasantly surprised when the paper was accepted³. The reason, he thinks, is because it offered a workaround for the problem.

Others place the ability to publish replication attempts down to a combination of luck, persistence and editors' inclinations. Survey respondent Michael Adams, a drug-development consultant, says that work showing severe flaws in an animal model of diabetes has been rejected six times, in part because it does not reveal a new drug target. By contrast, he says, work refuting the efficacy of a compound to treat Chagas disease was quickly accepted⁴.

THE CORRECTIVE MEASURES

One-third of respondents said that their labs had taken concrete steps to improve reproducibility within the past five years. Rates ranged from a high of 41% in medicine to a low of 24% in physics and engineering. Free-text responses suggested that redoing the work or asking someone else within a lab to repeat the work is the most common practice. Also common are efforts to beef up the documentation and standardization of experimental methods.

Any of these can be a major undertaking. A biochemistry graduate student in the United Kingdom, who asked not to be named, says that efforts to reproduce work for her lab's projects doubles the time and materials used — in addition to the time taken to troubleshoot when some things invariably don't work. Although replication does boost confidence in results, she says, the costs mean that she performs checks only for innovative projects or unexpected results.

Consolidating methods is a project unto itself, says Laura Shankman, a postdoc studying smooth muscle cells at the University of Virginia, Charlottesville. After several postdocs and graduate students left her lab within a short time, remaining members had trouble getting consistent results in their experiments. The lab decided to take some time off from new questions to repeat published work, and this revealed that lab protocols had gradually diverged. She thinks that the lab saved money overall by getting synchronized instead of troubleshooting failed experiments piecemeal, but that it was a long-term investment.

people mentioned this strategy. One who did was Hanne Watkins, a graduate student studying moral decision-making at the University of Melbourne in Australia. Going back to her original questions after collecting data, she says, kept her from going down a rabbit hole. And the process, although time consuming, was no more arduous than getting ethical approval or formatting survey questions. "If it's built in right from the start," she says, "it's just part of the routine of doing a study."

THE CAUSE

The survey asked scientists what led to problems in reproducibility. More than 60% of respondents said that each of two factors — pressure to publish and selective reporting — always or often contributed. More than half pointed to insufficient replication in the lab, poor oversight or low statistical power. A smaller proportion pointed to obstacles such as variability in reagents or the use of specialized techniques that are difficult to repeat.

But all these factors are exacerbated by common forces, says Judith Kimble, a developmental biologist at the University of Wisconsin–Madison: competition for grants and positions, and a growing burden of bureaucracy that takes away from time spent doing and designing research. "Everyone is stretched thinner these days," she says. And the cost extends beyond any particular research project. If graduate students train in labs where senior members have little time for their juniors, they may go on to establish their own labs without having a model of how training and mentoring should work. "They will go off and make it worse," Kimble says.

WHAT CAN BE DONE?

Respondents were asked to rate 11 different approaches to improving reproducibility in science, and all got ringing endorsements. Nearly 90% — more than 1,000 people — ticked "More robust experimental design" "better statistics" and "better mentorship". Those ranked higher than the option of providing incentives (such as funding or credit towards tenure) for reproducibility-enhancing practices. But even the lowest-ranked item — journal checklists — won a whopping 69% endorsement.

The survey — which was e-mailed to *Nature* readers and advertised on affiliated websites and social-media outlets as being 'about reproducibility' — probably selected for respondents who are more receptive to and aware of concerns about reproducibility. Nevertheless, the results suggest that journals, funders and research institutions that advance policies to address the issue would probably find cooperation, says John Ioannidis, who studies scientific robustness at Stanford University in California. "People would probably welcome such initiatives." About 80% of respondents thought that funders and publishers should do more to improve reproducibility.

"It's healthy that people are aware of the issues and open to a range of straightforward ways to improve them," says Munafò. And given that these ideas are being widely discussed, even in mainstream media, such

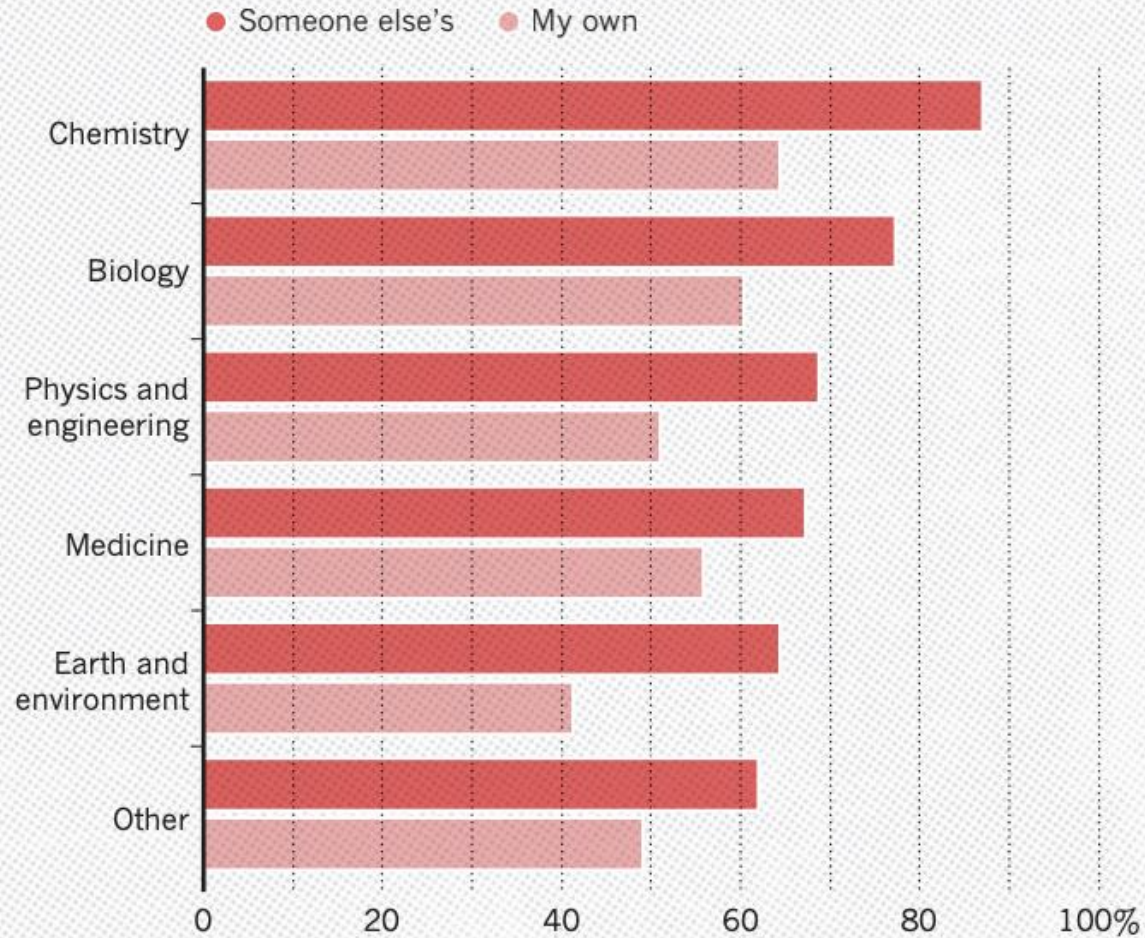
"REPRODUCIBILITY IS LIKE BRUSHING YOUR TEETH. ONCE YOU LEARN IT, IT BECOMES A HABIT."

Baker, Monya. 2016. "1,500 scientists lift the lid on reproducibility." *Nature News* 533(7604): 452-454.

<https://dx.doi.org/10.1038/533452a>

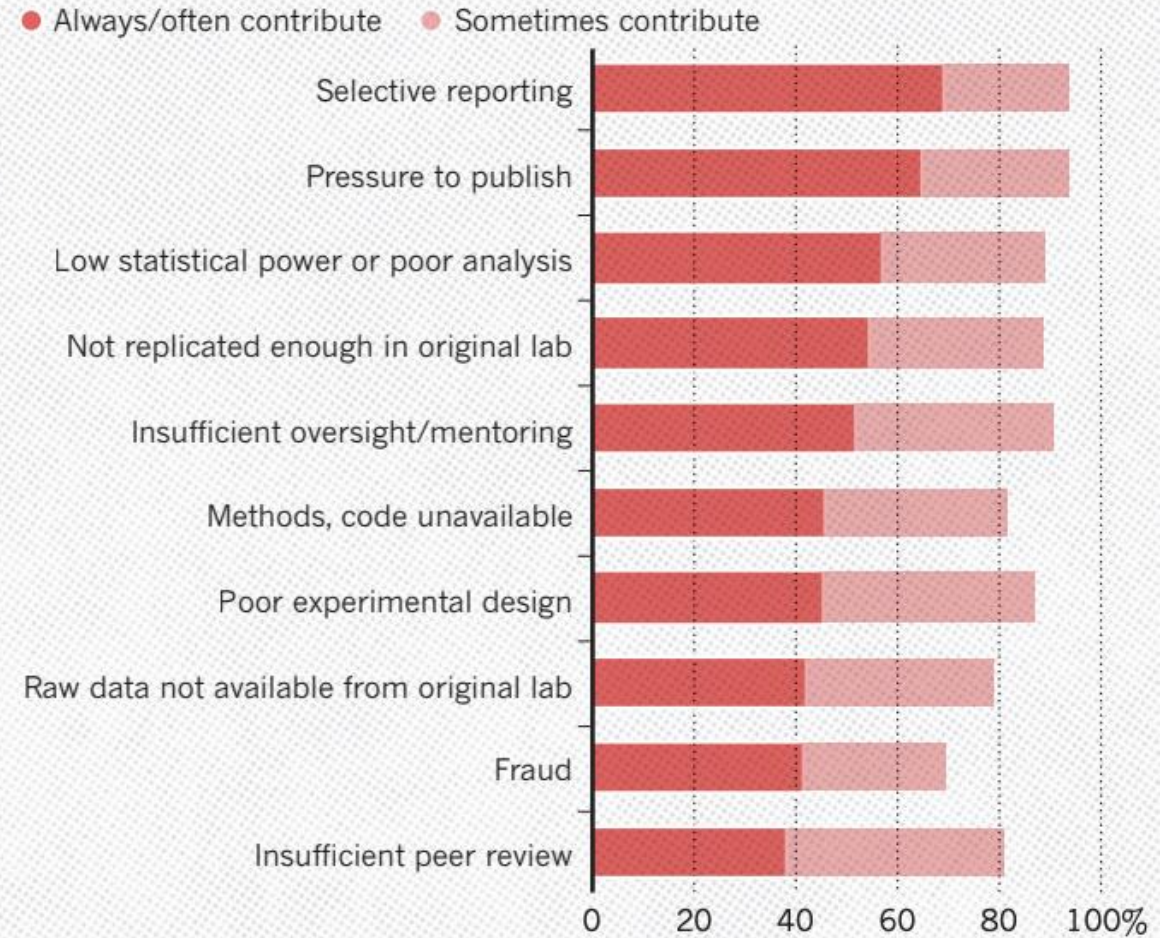
HAVE YOU FAILED TO REPRODUCE AN EXPERIMENT?

Most scientists have experienced failure to reproduce results.



WHAT FACTORS CONTRIBUTE TO IRREPRODUCIBLE RESEARCH?

Many top-rated factors relate to intense competition and time pressure.



Baker, Monya. 2016. "1,500 scientists lift the lid on reproducibility." *Nature News* 533(7604): 452-454.

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What can I do?

- ❖ Organize your data!
 - ❖ Make plans for appropriate storage of your data, both raw and processed
 - ❖ Have project directories created before starting a project
 - ❖ Keep data organized during the analysis

*You can't have any sort of reproducibility without
good **data management**.*



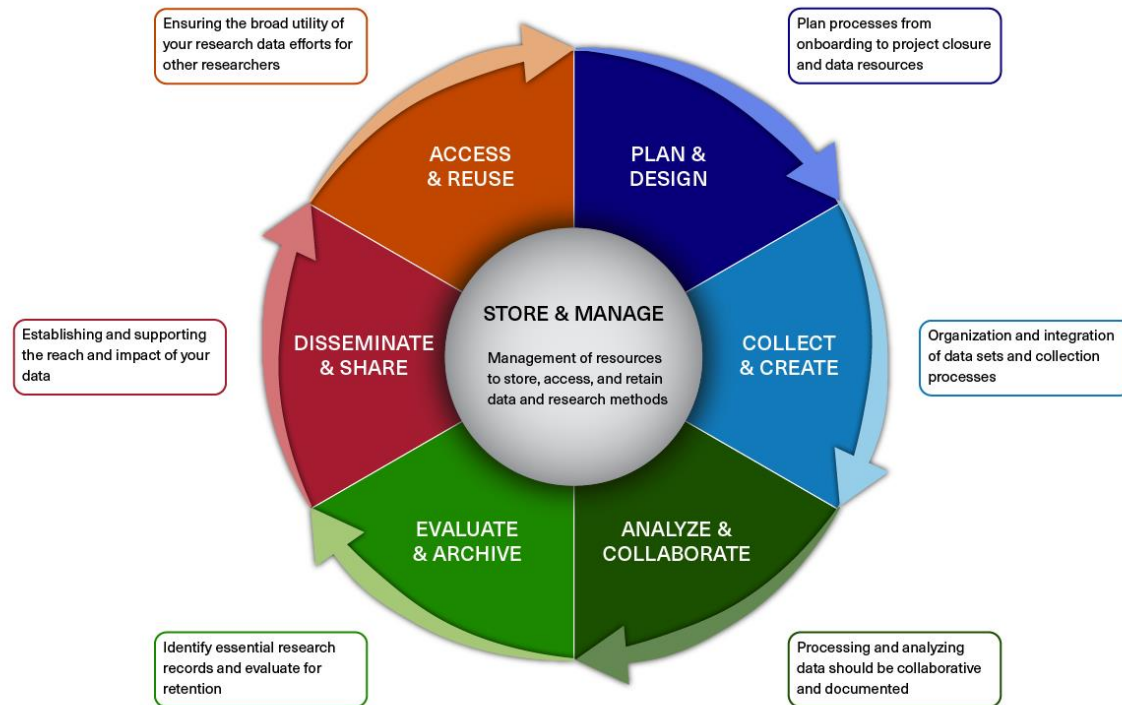
WWW.PHDCOMICS.COM

What can I do?

- ❖ Document everything!
- ❖ Create READMEs that detail data organization, analysis methods, dates, naming conventions, etc.
- ❖ Which tools and parameters have you tried, what were the version numbers? What were the results in each case?
- ❖ What were the exact commands you ran throughout the workflow?
- ❖ Annotate your code with comments
- ❖ Use version control to track code updates and changes to other text-based documentation

Research Data Management (RDM)

BIOMEDICAL RESEARCH DATA LIFECYCLE



Tools for documentation and version control

- ❖ Documentation - Quarto, Rmarkdown, Jupyter notebooks
- ❖ Version Control - Git, Subversion, Bitbucket
- ❖ Collaboration and Version Control - GitHub, Bitbucket
- ❖ Containerization to preserve workflows, tools and versions - Docker