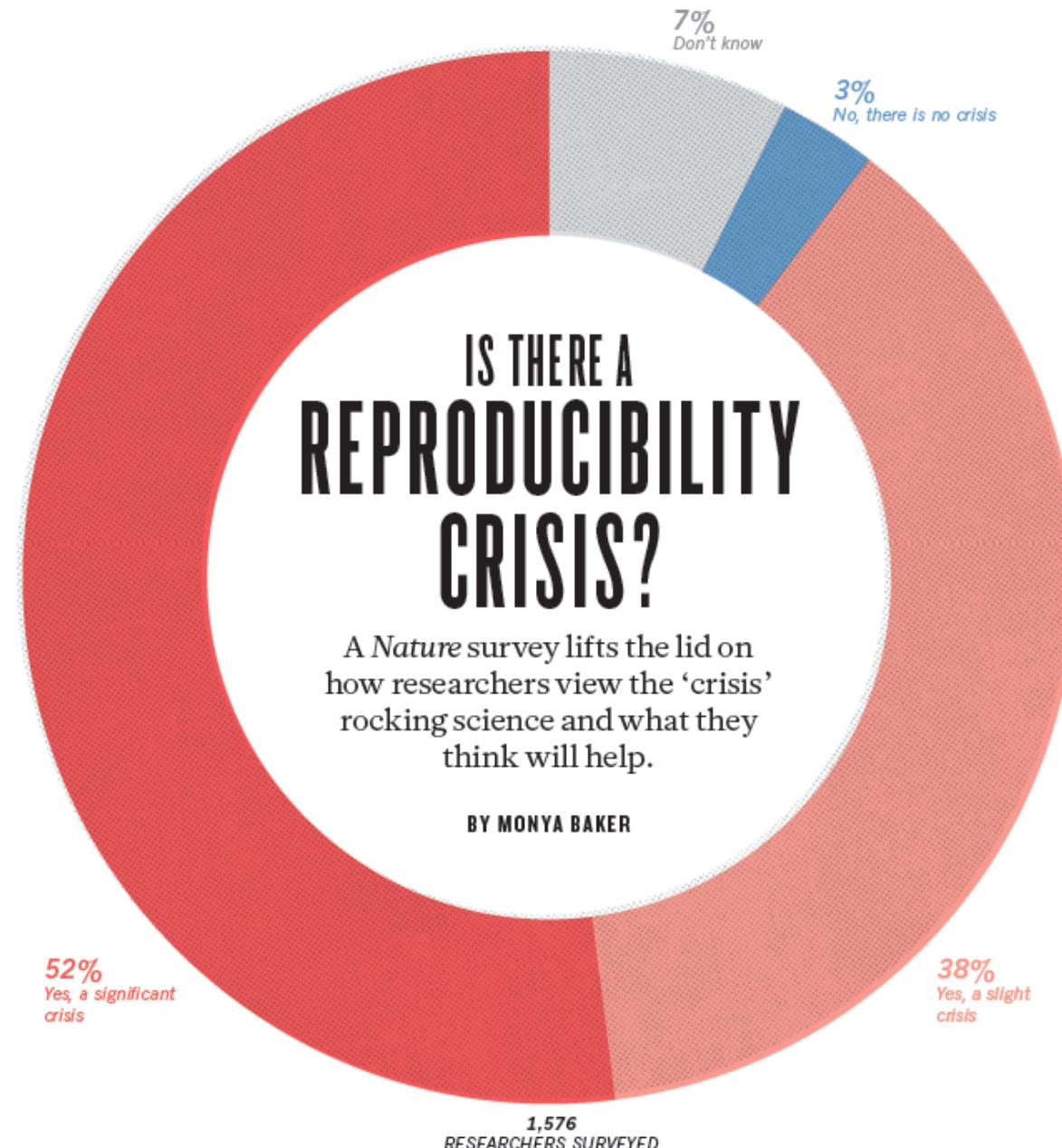


Reproducibility Crisis

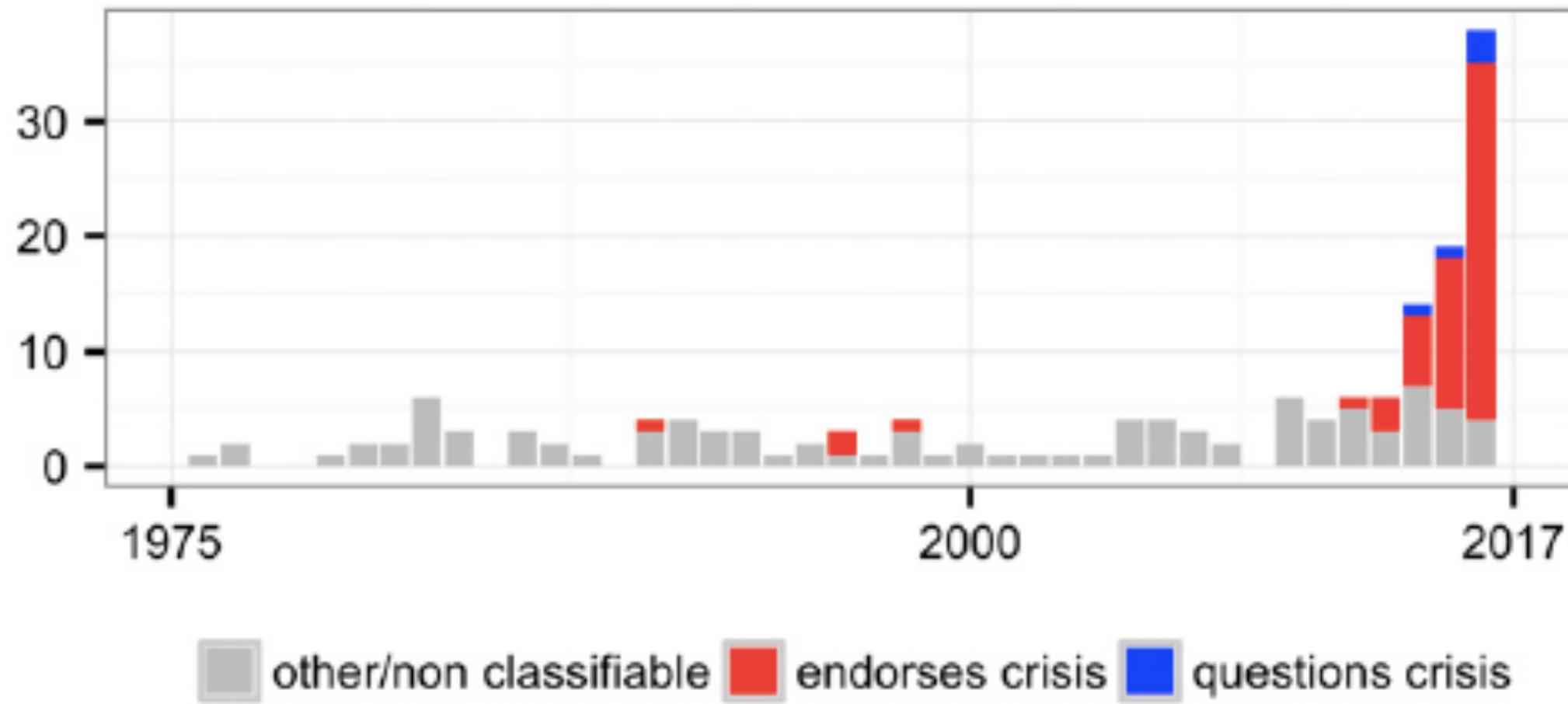
Cooduvalli Shashikant

Co-Director, Bioinformatics and Genomics Graduate Program

IS THERE A REPRODUCIBILITY CRISIS?



Frequency of Crisis Narrative in Web of Science Records



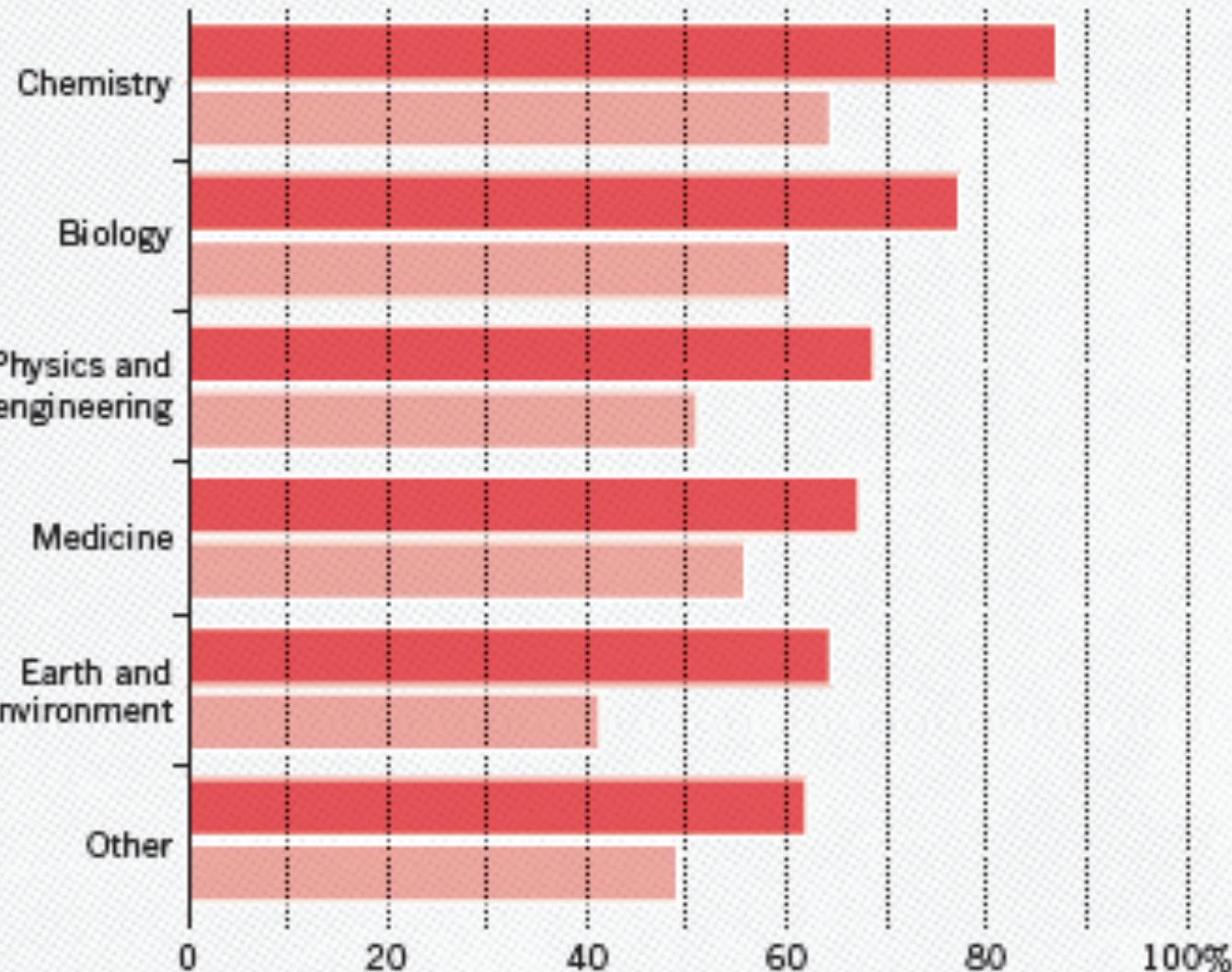
HAVE YOU FAILED TO REPRODUCE AN EXPERIMENT?

- Some one else's
- Your own

HAVE YOU FAILED TO REPRODUCE AN EXPERIMENT?

Most scientists have experienced failure to reproduce results.

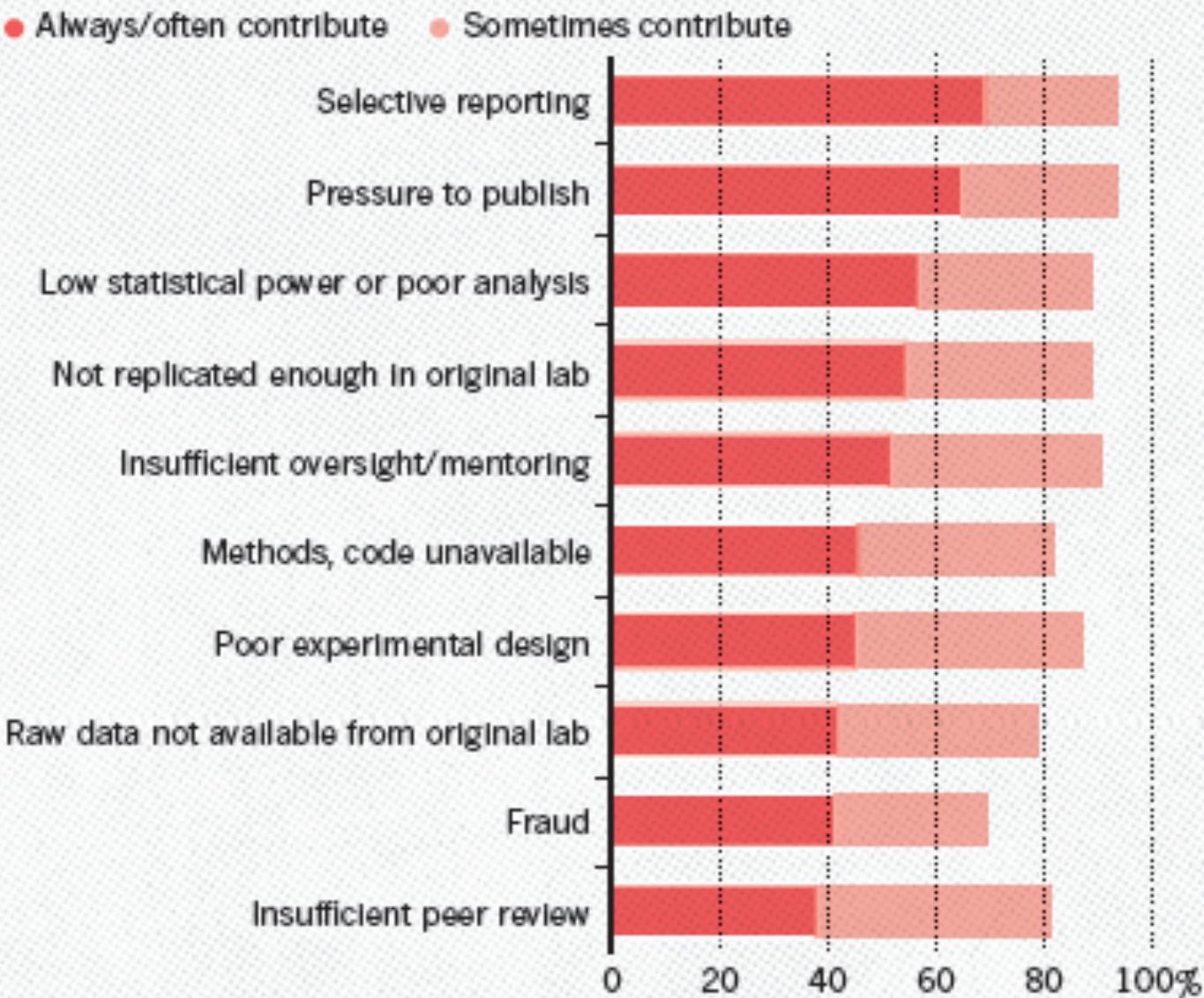
● Someone else's ● My own



WHAT FACTORS CONTRIBUTE TO IRREPRODUCIBLE RESEARCH?

WHAT FACTORS CONTRIBUTE TO IRREPRODUCIBLE RESEARCH?

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

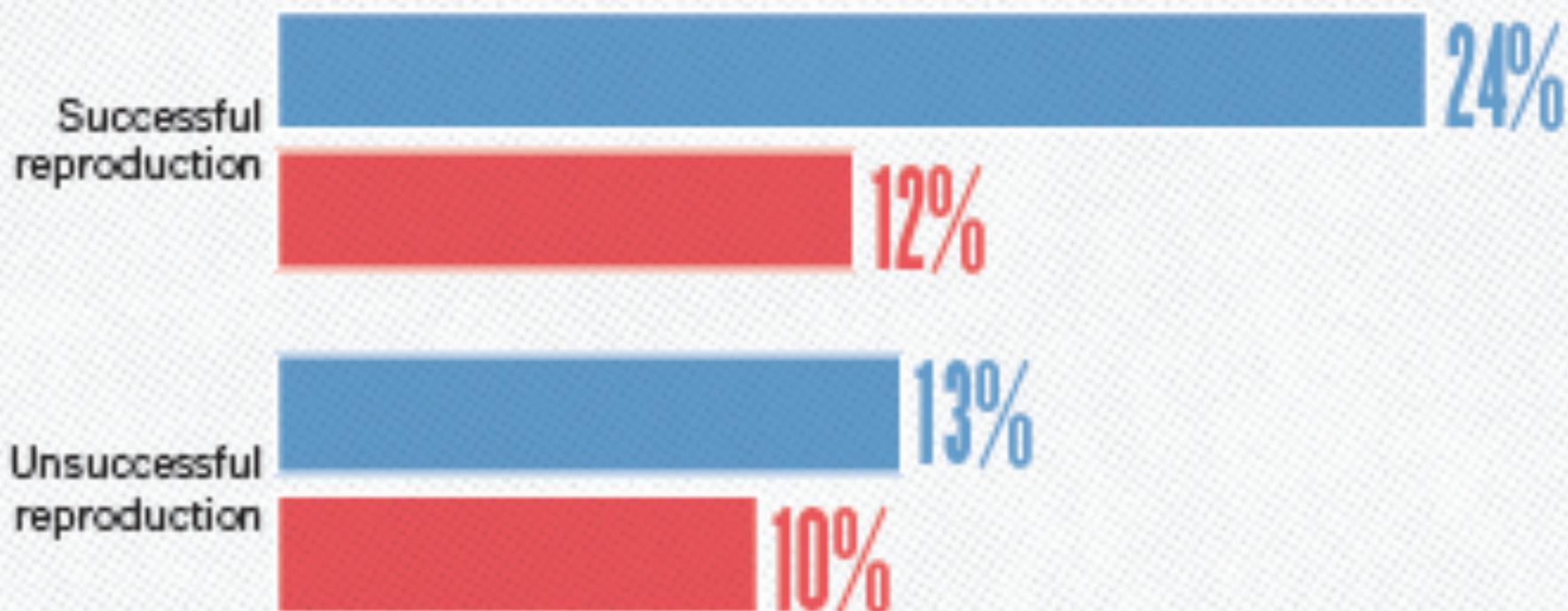


HAVE YOU EVER TRIED TO PUBLISH A
REPRODUCTION ATTEMPT?

HAVE YOU EVER TRIED TO PUBLISH A REPRODUCTION ATTEMPT?

Although only a small proportion of respondents tried to publish replication attempts, many had their papers accepted.

- Published
- Failed to publish



WHAT FACTORS COULD BOOST REPRODUCIBILITY?

WHAT FACTORS COULD BOOST REPRODUCIBILITY?

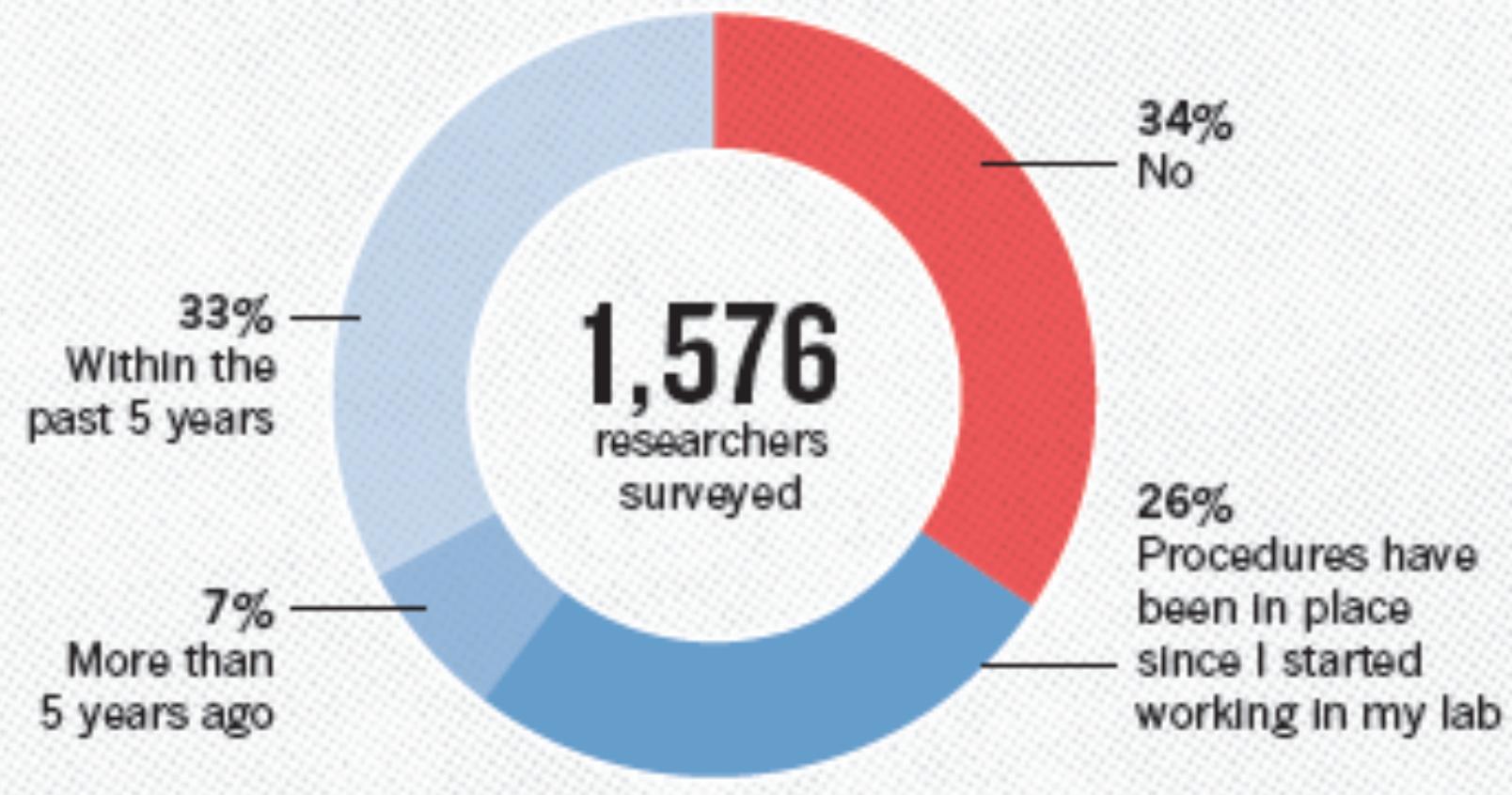
Respondents were positive about most proposed improvements but emphasized training in particular.



HAVE YOU ESTABLISHED PROCEDURES
FOR REPRODUCIBILITY?

HAVE YOU ESTABLISHED PROCEDURES FOR REPRODUCIBILITY?

Among the most popular strategies was having different lab members redo experiments.



The NIH initiative

- Students may not be receiving adequate training early in graduate school in experimental design and other skills related to conducting rigorous and reproducible research'

Training grants

- Training grants, Career Development and Individual fellowships will require formal instructions in
 - Rigorous experimental design
 - Transparency to enhance reproducibility
- Boot camp supported under ‘Administrative supplements to NIGMS Predoctoral Training Grants (PA-15-136)’
- PSU commitment to conduct boot camp for next five years

Teaching Rigor, Reproducibility and Ethics, 2019

- MCIBS 591-2 credit course
- Ethics, Rigor, Reproducibility and Conduct of Research in the Life Sciences:
 - Lack of Transparency
 - Blinding and Randomization
 - Biological and Technical Replicates
 - Sample size, outliers, and exclusion criteria
 - Cost of sloppy science and data reproducibility

Sources of Lack of Reproducibility

Sources of Lack of Reproducibility

- Fabrication, Falsification, plagiarism, misconduct
- Inadequate measures for data quality and reproducibility
- Biased reporting of results
- Inappropriate analysis
- Incomplete description of methods

Historic cases of Scientific Misconduct

- Charles Darwin
 - Origin of Pose: Saying ‘Cheese’ for Darwin NY Times, April 25, 1998
<http://www.nytimes.com/1998/04/25/books/origin-of-the-pose-saying-cheese-for-darwin.html>
- Louis Pasteur
 - Pasteur and culture wars, an exchange, The New York Review of Books, Dec 21, 1995; http://www.nature.com.ezaccess.libraries.psu.edu/search/adv_search?sp-q-1=nature.news
- Gregory Mendel
 - Beyond the Mendel-Fisher Controversy, Science, 350, 159, 2015,
<http://www.sciencemag.org.ezaccess.libraries.psu.edu/content/350/6257/159.full?sid=db800037-6596-432a-a00b-50bbe9d59686>

Fraud/Misconduct

- Mark Spector
 - <https://www.the-scientist.com/?articles.view/articleNo/26694/title/My-Favorite-Fraud/>
- Where are they now
 - <http://www.nature.com.ezaccess.libraries.psu.edu/articles/445244a>
- Scientific Misconduct, Ann. Rev. Psychology, 67, 693, 2016
 - <http://www.annualreviews.org.ezaccess.libraries.psu.edu/doi/full/10.1146/annurev-psych-122414-033437>

Fabrications



- William Summerlin (1974) Memorial Sloan-Kettering Research Institute
 - Transplant research: expected change in coat color; drew patches on mice with a black marker pen

How common are fraud, fabrication and falsification?

- 1-2% in anonymous survey admit falsification of data
- Much higher percentage admit dropping a data point or not publishing contradictory results
- Questionable research practices are much higher

Misrepresentation and Distortions

- More common than fraud, fabrication, falsification, plagiarism and misconduct of research

Concept of spin

“a form of propaganda, achieved by providing a biased interpretation of an event or campaigning to persuade public opinion in favor of or against some organization or public figure”



Spin

- A specific reporting that fails to faithfully reflect the nature and range of findings and that could affect the impression that the results produce in readers, a way to distort science reporting *without actually lying*
- Conscious, unconscious and unintentional
- Legitimate in some contexts
- In others, may create inaccurate impression of the study results

Spin

- The consequence of a lack of understanding of methodologic principles
- A parroting of common practices
- A form of unconscious behavior
- An actual willingness to mislead the reader
- Favors the author's vested interest (financial, intellectual, academic, and so forth)

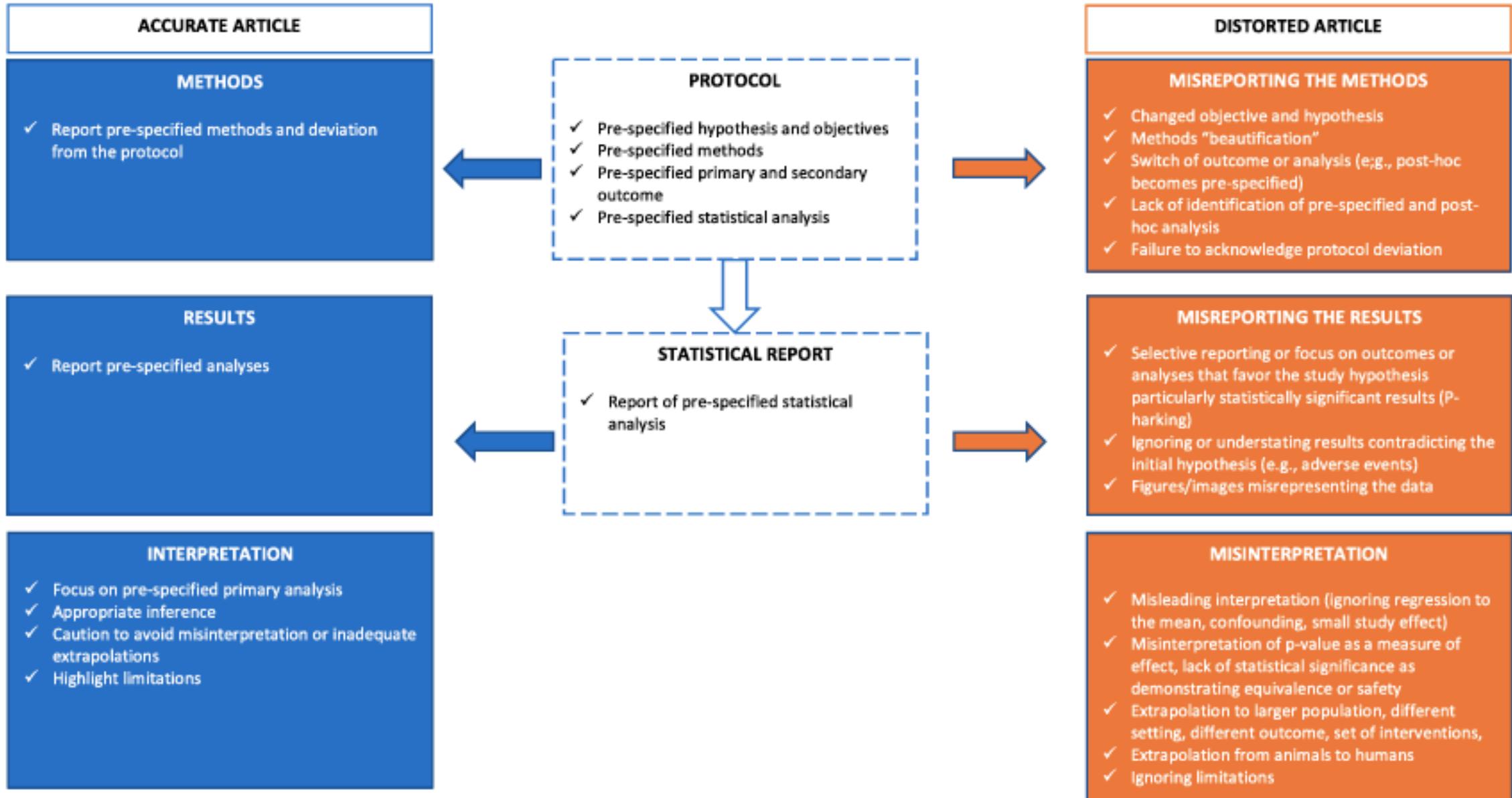


Fig. 1. Practices of spin in published reports.

Is science really facing a reproducibility crisis, and do we need it to?

Daniele Fanelli^{a,1}

- Published studies are getting longer, more complex and *richer in data*
- *Negative results* are increasingly getting embedded in longer publications
- *Globalization* of research is contributing to the rise in scientific misconduct in publication
- Rising power of information and communication technologies are transforming *scientific practices*

Reproducibility failures are essential to scientific inquiry

A. David Redish^{a,1}, Erich Kummerfeld^b, Rebecca Lea Morris^c, and Alan C. Love^d

Scientific Progress

- Observation
- Theory
- Replication
- Failure
- Re-integration
- *There is a widespread misunderstanding about the role of reproducibility in science*

Reproducibility and Scientific Progress

- Karry Mullis
 - Polymerase Chain Reaction
- Beatrice Mintz
 - Chimera of mouse embryonic cells +teratoma cells
 - Pluripotent stem cells
- Carl Illmensee
 - Cloning experiment
 - Imprinting: Surani, Solter
 - Vindicated?
- Rudolf Jaenisch
 - Reproduced important results of mouse cloning, induced pluripotent stem cells (iPS)



Fig. 1. Discussions about a “reproducibility crisis” often ignore what takes place when reproducibility fails: the integration of conflicting observations and ideas into a coherent theory. Image courtesy of Dave Cutler (artist).

Reproducibility Failures

- Time necessary to reconcile conflicting results
- Attention to the process of reconciling conflicting results
- Synthesis of diverse perspectives to be encouraged
- Theoretical integration leads to reliable results

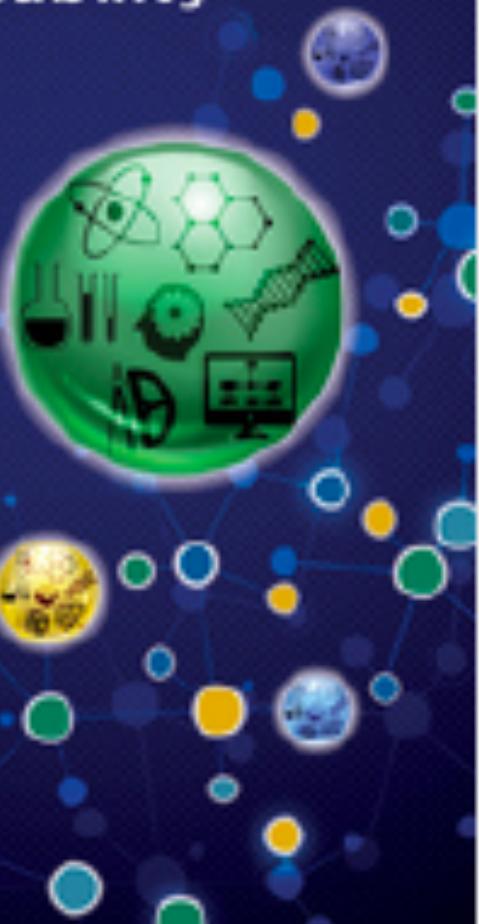
Scientific Progress

- Scientific discovery is an observation in under a given set of conditions
- When unable to replicate, one focuses on determining hidden variables
- Over a given time diverse outcomes including reproducibility failures get incorporated into a broader account

Failure to Generalize

In many of these cases, what have been called “failures to replicate” are actually failures to generalize across what researchers hoped were inconsequential changes in background assumptions or experimental conditions.

Reproducibility and Replicability in Science



Reproducibility, Replicability, Generalizability

- Reproducibility
 - obtaining consistent computational results using the same input data, computational steps, methods, and code, and conditions of analysis
- Replicability
 - obtaining consistent results across studies aimed at answering the same scientific question, each of which has obtained its own data.
- Generalizability
 - the extent that results of a study apply in other contexts or populations that differ from the original one.

Terminology for Reproducible Research

Term	Purpose	Description
Rerun	Robust	Variations on experiment and set-up, conducted in the same lab
Repeat	Defend	Same experiment, same set-up, same lab
Replicate	Certify	Same experiment, same set-up, independent lab
Reproduce	Compare	Variations on experiment and set-up, independent labs
Reuse	Transfer	Different experiment

Scientific progress despite irreproducibility:
A seeming paradox

It appears paradoxical that science is producing outstanding new results and theories at a rapid rate at the same time that researchers are identifying serious problems in the practice of science that cause many reports to be irreproducible and invalid.

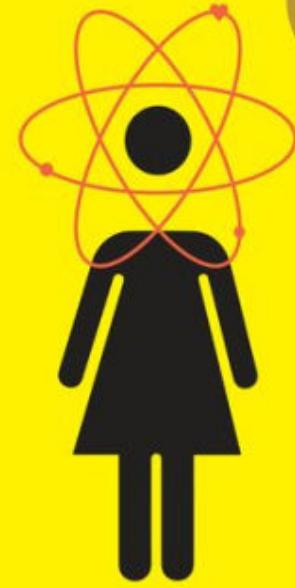
Confidence in Science

- Scientists
 - Avoid overstating implications of research
- Journalists
 - Report scientific results with as much context and nuance as the medium allows
- Policy makers
 - Avoid making serious decisions based on a single study
 - Recommendations of the National Academy Committee on Reproducibility and Replicability in Science, 2019

In science, perfect reproducibility
is the highest form of praise

"A comic and often precarious journey.
Told in a hilarious deadpan that recalls Gish Jen and Nora Ephron."
—O, *The Oprah Magazine*

Winner of the
PEN/Hemingway
Award



Chemistry
a novel by Weike Wang