

December 5, 2020

Saturday 4:00 - 4:50 PM EST

**THE *UN*SCIENTIFIC METHOD:
CHALLENGES FACING
SCIENCE AS A DISCIPLINE**



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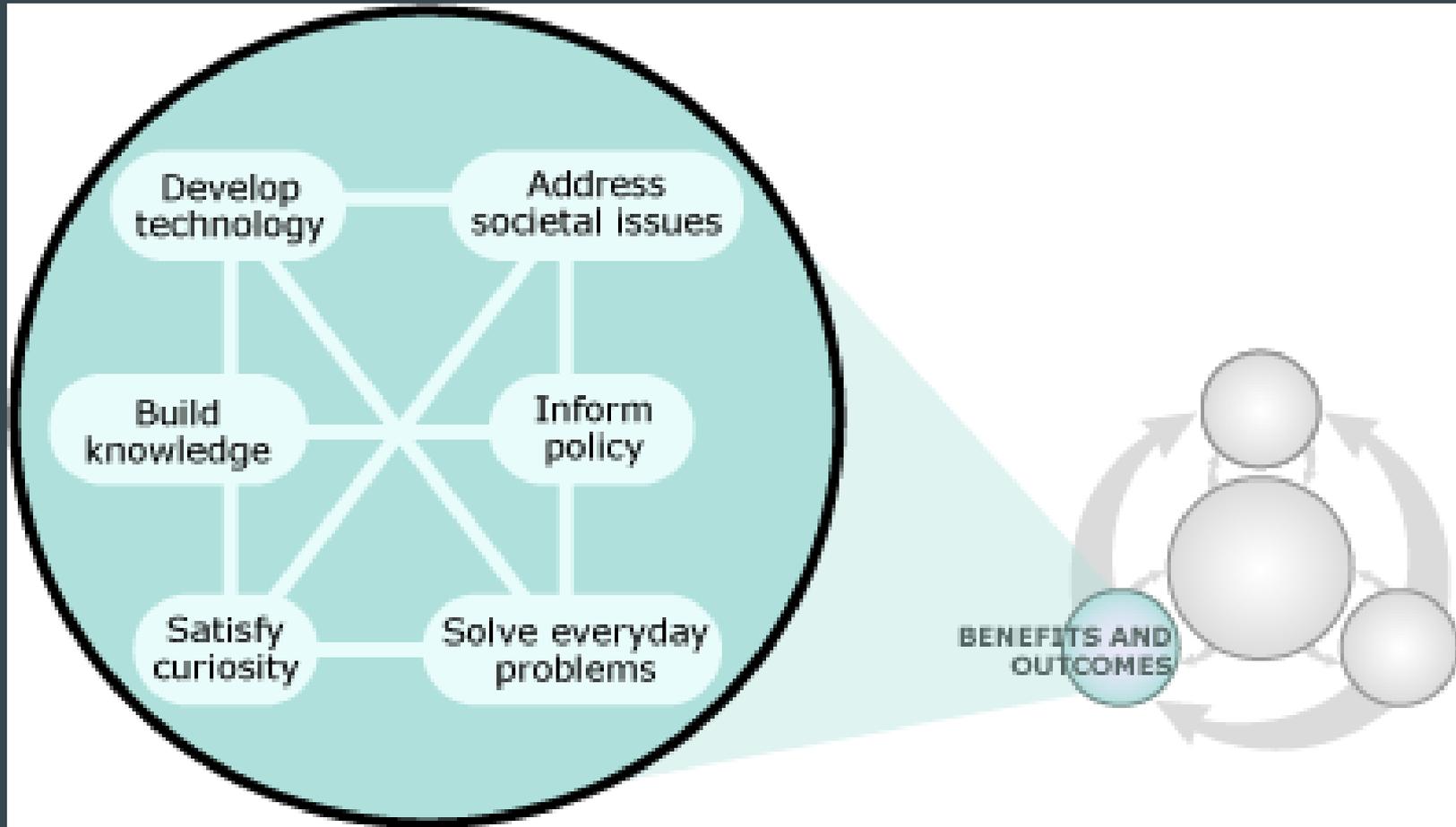
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IS THIS THE CLASS YOU ARE LOOKING FOR?

- This class gives an overview of challenges facing science as a discipline. We'll discuss how the Scientific Method should work and how it should play out in practice in terms of topics such as the the following:
 - Publishing
 - Peer review
 - Plagiarism
 - Scientific misconduct
 - Public relations
 - Unconscious bias
 - Reproducibility
- **Prerequisites**
Grades 10-12; Regents level science

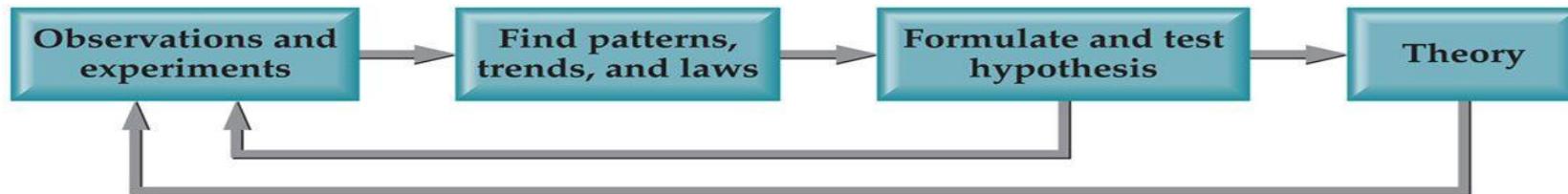
SCIENCE



THE SCIENTIFIC METHOD

Scientific Method

The scientific method is simply a systematic approach to solving problems.



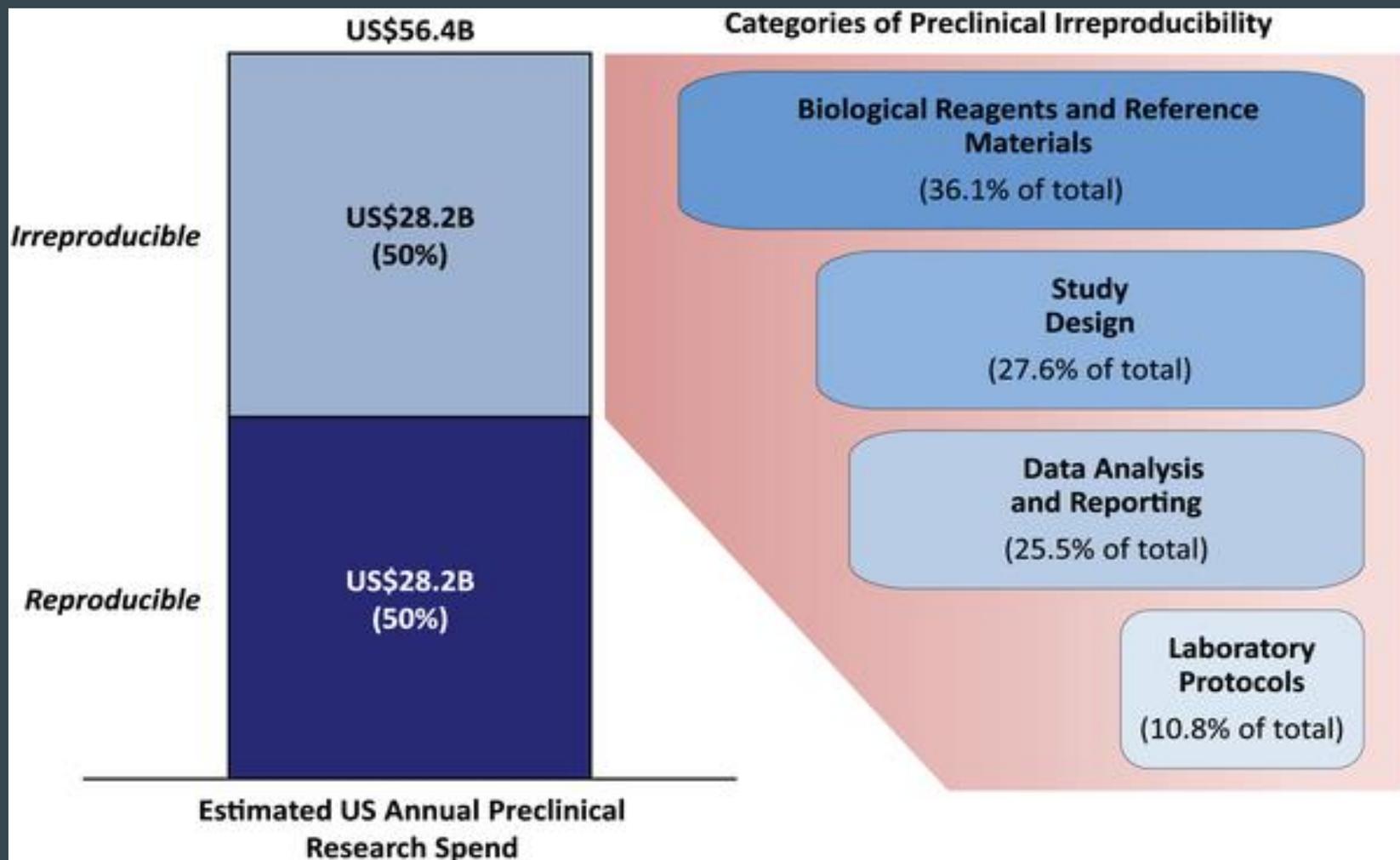
Matter
And
Measurement

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THE IMPORTANCE OF REPRODUCIBLE RESEARCH

- Scientists depend on the work done before them. If the work is not reproducible, then current science is being built on a false foundation.
- Depends on scientists being very careful and very explicit about what methods they use.

Fig 2. Estimated US preclinical research spend and categories of errors that contribute to irreproducibility.



Freedman LP, Cockburn IM, Simcoe TS (2015) The Economics of Reproducibility in Preclinical Research. PLoS Biol 13(6): e1002165. doi:10.1371/journal.pbio.1002165

<http://journals.plos.org/plosbiology/article?id=info:doi/10.1371/journal.pbio.1002165>

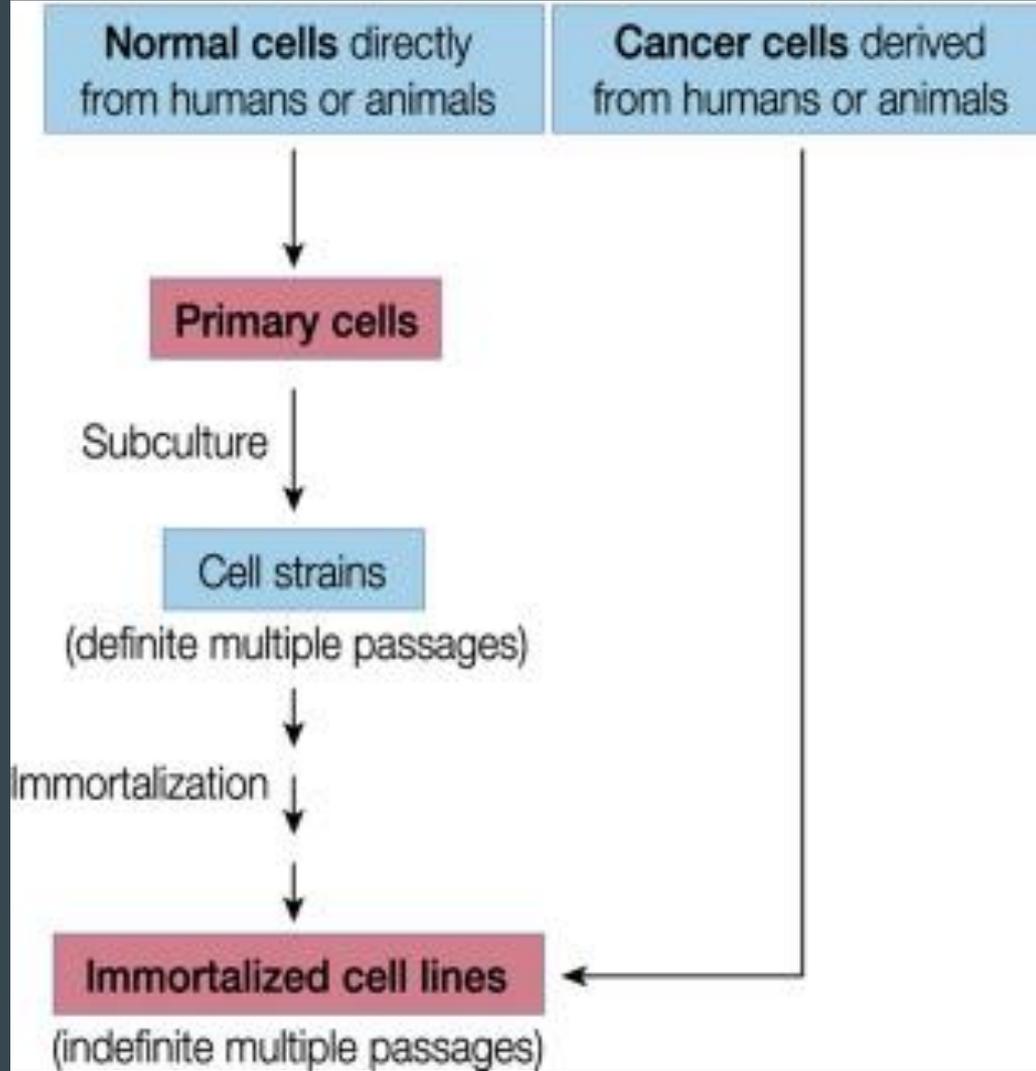
REPRODUCIBILITY

- “An analysis of past studies indicates that the cumulative (total) prevalence of irreproducible preclinical research exceeds 50%, resulting in approximately \$28,000,000,000 (\$28 billion)/year spent on preclinical research that is not reproducible” ~ Freedman, et al. (2015). *PLoS Biol*, 13(6), e1002165.
- “A 2015 study looked at 83 highly cited studies that claimed to feature effective psychiatric treatments. Only 16 had ever been successfully replicated. Another 16 were contradicted by follow-up attempts, and 11 were found to have substantially smaller effects the second time around. Meanwhile, nearly half of the studies (40) had never been subject to replication at all.” Vox

<http://www.sciencemag.org/news/2015/06/study-claims-28-billion-year-spent-irreproducible-biomedical-research>

<https://www.vox.com/2016/7/14/12016710/science-challenges-research-funding-peer-review-process>

CELL LINES



- <https://www.sciencedirect.com/topics/neuroscience/cell-lines>

CONTAMINATED CELL LINES

A tale of two impostors

Christopher Korch estimated the impact of research on two cell lines, HEp-2 and INT 407. Due to contamination long ago, both are now widely acknowledged to be composed of cancer cells called HeLa.

5789 ARTICLES in **1182** journals may have used HEp-2 inappropriately, producing an estimated **174,000** citations

1336 ARTICLES in **271** journals may have used INT 407 inappropriately, producing an estimated **40,000** citations

\$713 MILLION Estimated amount spent on the original articles published on **INT 407** and **HEp-2**

\$3.5 BILLION Estimated amount spent on subsequent work based on those papers

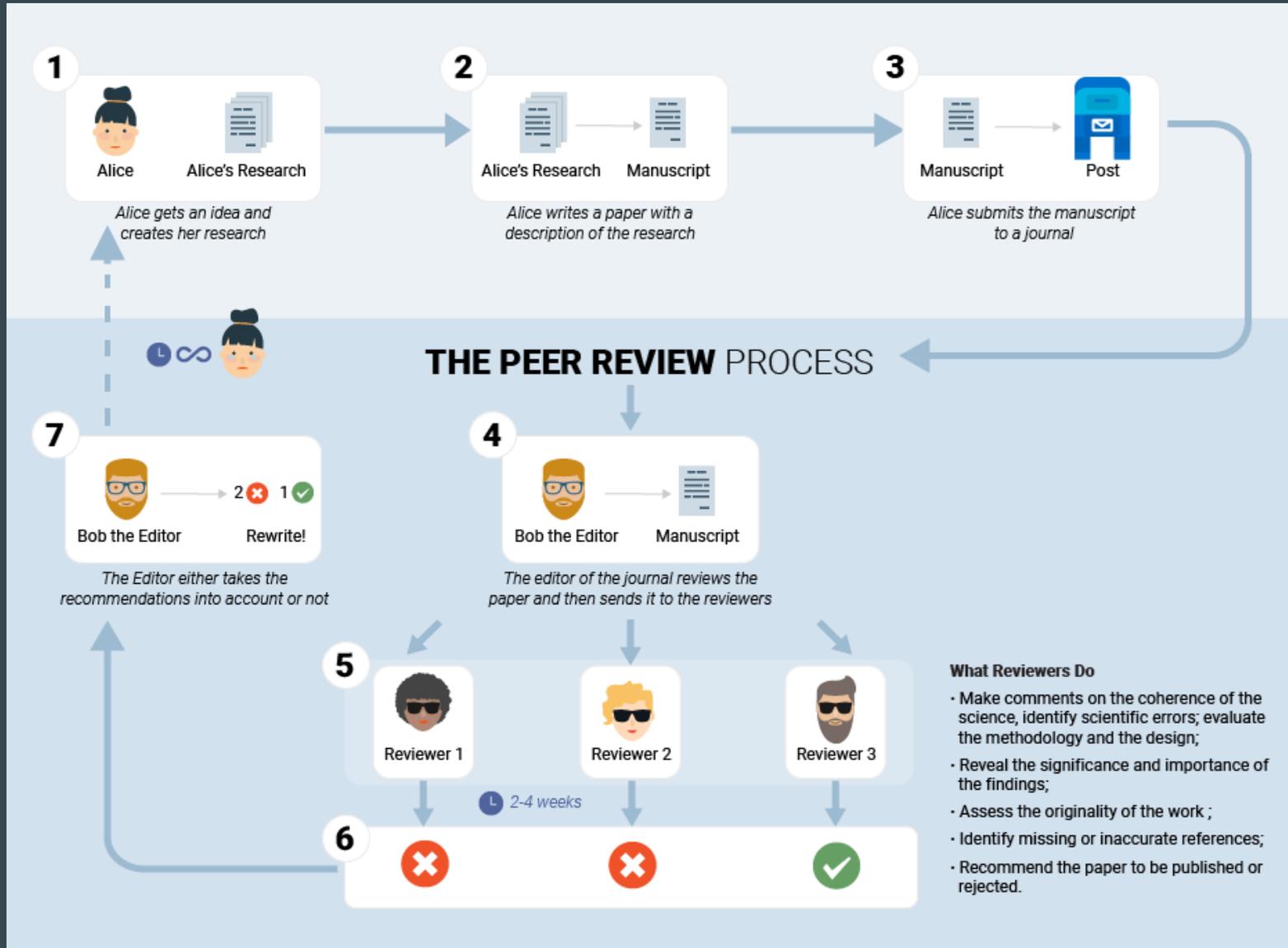
“All of this makes Korch optimistic at last. “I see the floodgates beginning to open, actually,” he says. “Scientists everywhere are starting to demand reproducibility. I hope my work is one extra push in the right direction. *We all want pyramids of literature built up solidly on sound foundations.*” (emphasis mine)

- Neimark, J. (2015). Line of attack. *Science*, 347(6225), 938-940.

THE IMPORTANCE OF PEER REVIEW

- The way we know scientists are not just making stuff up is by peer review where professionals in the field review the paper, often anonymously, and see if the results look believable with the methods employed and offer feedback.
- Reputable journals use this method to decide who is published.

PEER REVIEW

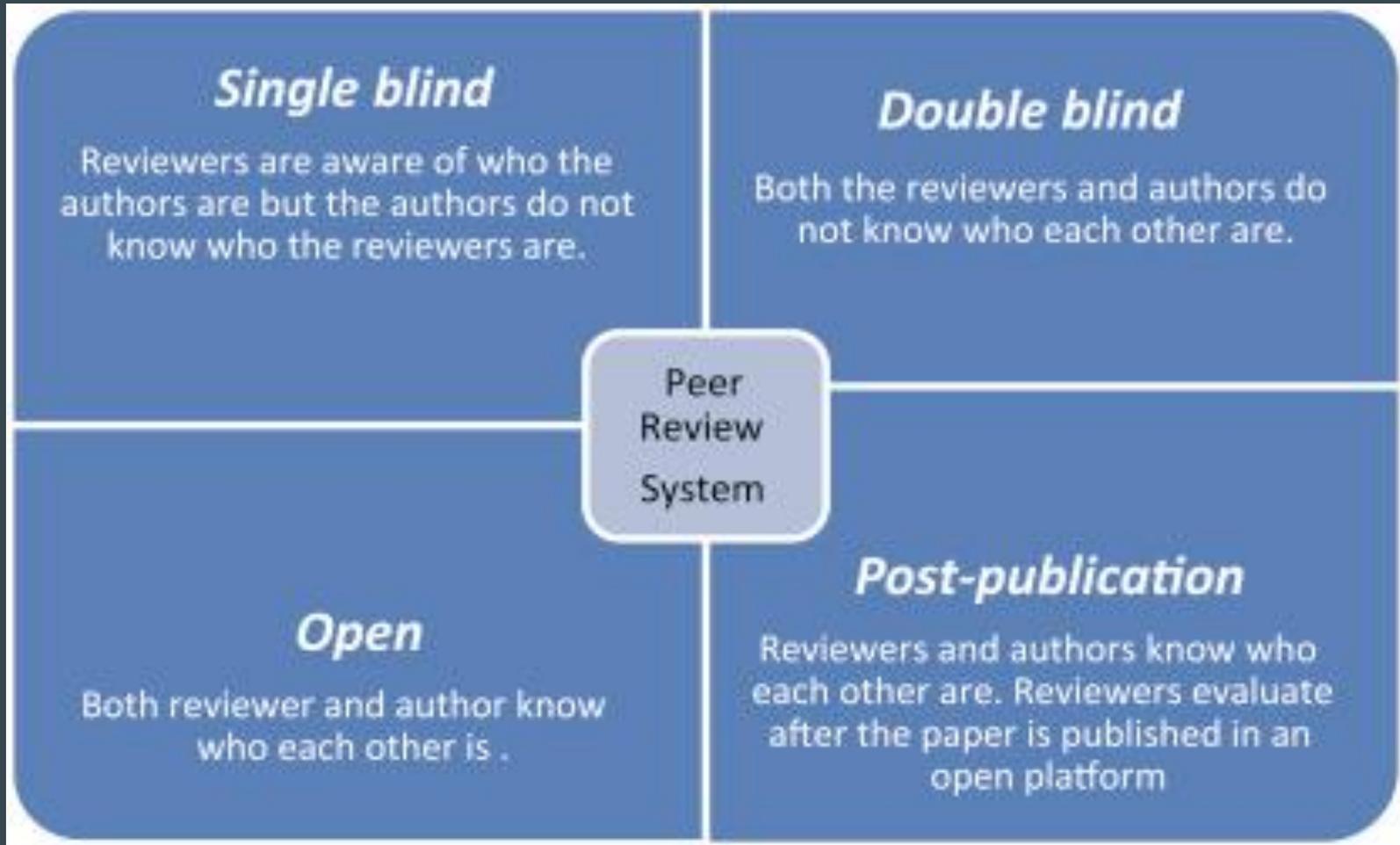


CHALLENGES IN PEER REVIEW

- Conflicts of interest, particularly competitors.
- (Un)conscious bias
 - Underrepresented minorities
 - “Third World” countries
- Unpaid labor.
- Usually no attempt at reproducing the paper - many things can be missed.
- Bias against negative studies.
- Standards used by reviewers are inconsistent.

Smith, Richard. J. Royal Soc. Med. 99, 4 (2006): 178-182.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1420798/>

KINDS OF PEER REVIEW



THE IMPORTANCE OF ETHICAL RESEARCH

- We rely on scientists to honestly report their findings and not misrepresent themselves as life and death decisions can be made on their science.
- They have to respect the rights of their research participants, human or otherwise.
- The careers of scientists are based on their publications, so they should not have data or text that is tampered with.
- People make important decisions based on what the media say about publications.

TYPES OF PLAGIARISM

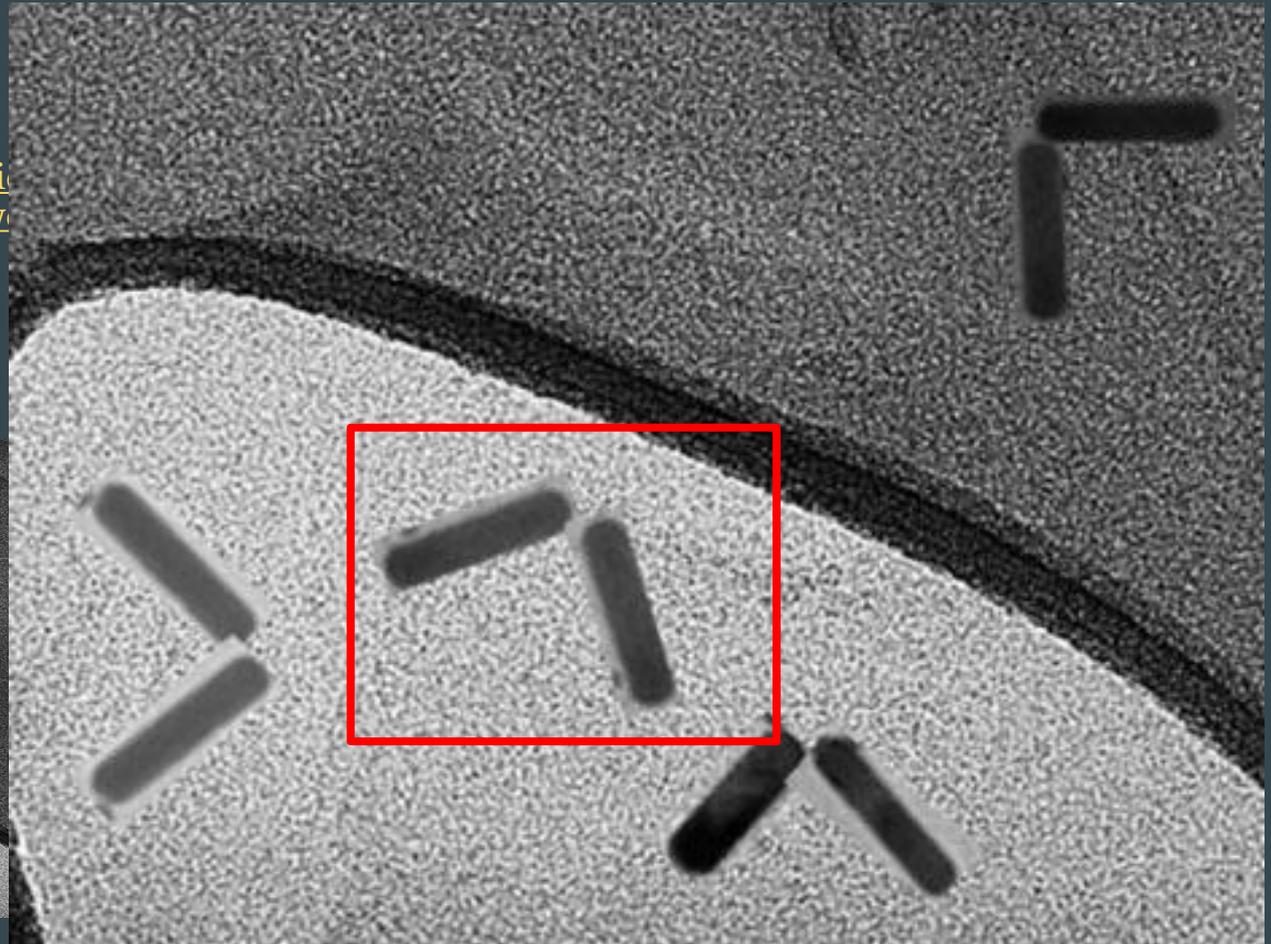
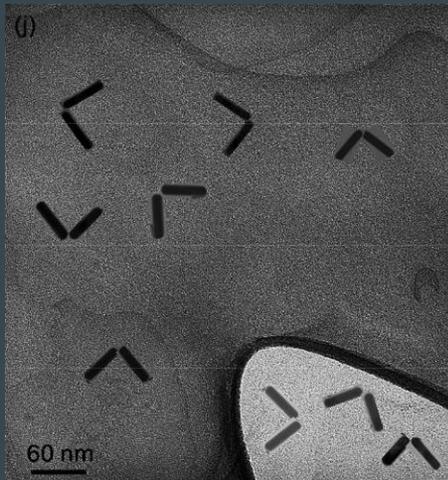
What is being copied?	Type of Offense	Typical Reason Given
Ideas		
Texts	Self-Plagiarism	Not knowing better
Texts	Collusion	Poor writing skills
Texts	Patchwriting	Poor writing skills

OTHER SCIENTIFIC MISCONDUCT

- Fabrication: creating results, funding sources, *and citations* out of nothing
 - Can be unintentional if insufficient controls were done!
- Falsification: Manipulating the data you have already *including removing “bad” data points*, especially if it is a well-known experiment.
- Ethical approval of studies especially regarding those involving animals, including humans!
- https://en.wikipedia.org/wiki/Scientific_misconduct#Forms_of_scientific_misconduct

NANO CHOPSTICKS

- Anumolu, R., Robinson, RETRACTED
- Courtesy: <https://retracti...paper-questioned-this-w>



TRY FOR YOURSELF

- Two third-year graduate students, Eustacia and Damien share lab space and work for the same PI* on different but related projects. Eustacia has come to question whether Damien is actually carrying out any of the experiments he claims to have because, although he often has very nice looking data to present at group meetings, he never orders any materials, produces any waste and never even appears to do anything.
 - (a) Does Eustacia have reasonable grounds for suspicion?
 - (b) Should Eustacia speak to her PI about her concerns
- *PI = boss of a academic research lab.
- Acknowledgments to Prof. Jonathan Parr, Yale Chem. Dept. for the scenario

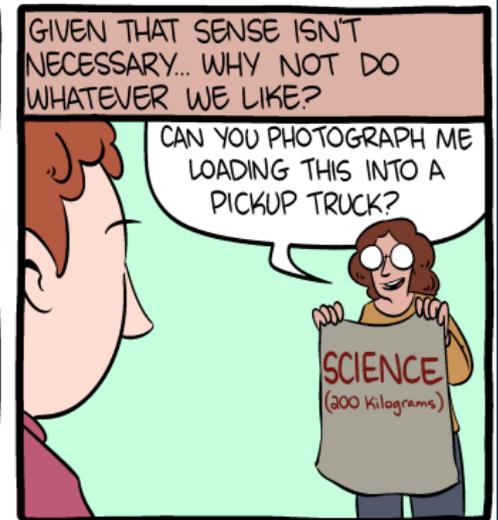
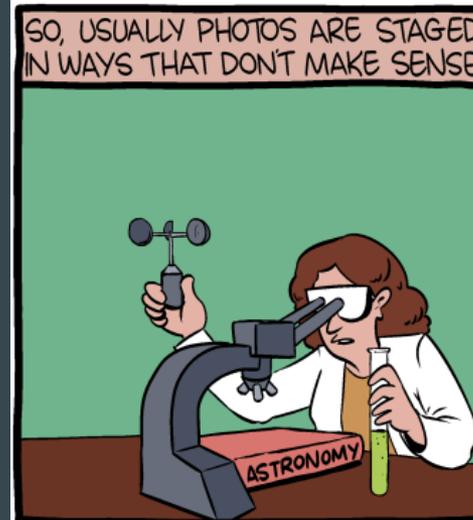
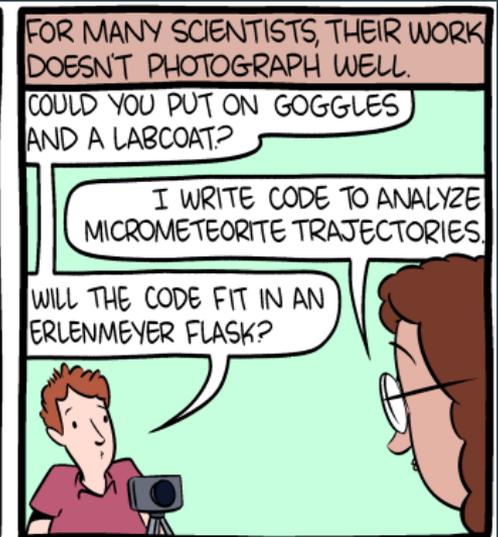
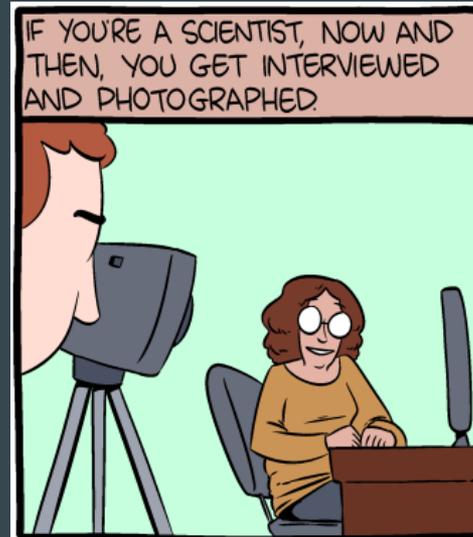
HOW BEN RESPONDED ~2 YEARS AGO

- a) Eustacia does have very reasonable grounds for suspicion since there is no evidence as to then doing any work in order to produce his very nice-looking data. She should make sure though if it is his responsibility to order chemicals or whether there is a more senior person in the lab who does it and whether he just works at times she usually does not e.g. may be in the middle of the night. Not producing any waste is also suspicious, but it may be hard to tell apart his waste from people who might share his lab space. She may want to ask him to let her shadow him to “learn his techniques” or to ask other lab members if they had the same suspicions.
- b) She should definitely speak to the PI about her concerns since his actions or lack thereof can reflect badly on the whole group. The PI may not be aware of what is going on since they may just be concerned with the logistics of managing the laboratory finances and publications.

GUILTY AS CHARGED?

- 7 people, including 6 scientists were found guilty of manslaughter and thus face six years in prison over L'Aquila earthquake where an official told the city that there was no risk of an earthquake after a series of shocks. It killed 29 people, many inside their homes.
- “In Italy you will now see many more false alarms in such situations, because experts will choose to cry wolf when in doubt. In the end they will become less and less credible.”
- Nosengo N. (2012). Italian court finds seismologists guilty of manslaughter. *Nature News*.
- Abbott N., Nosengo N. (2014) Italian seismologists cleared of manslaughter. *Nature News*.

SCIENCE-MEDIA RELATIONS



smbc-comics.com

THINGS TO THINK ABOUT WHEN READING ARTICLES

- Conflicts of interest
 - the source for this slide is biased towards industry
 - in articles, scientists or journalists may have a financial or political interest in a certain outcome and may misinterpret data.
- Journalists go for sensational headlines
 - e.g. cancer isn't one thing so you can't say something cures cancer, which is unlikely anyway
- Spurious correlations (hidden third variable explains connection between random things like lifespan of women and owning horses; often wealth).
- Journalists may not understand which journals are reputable.
- Many books particularly on food are not peer reviewed and have anecdotal evidence.

(UN)CONSCIOUS BIAS

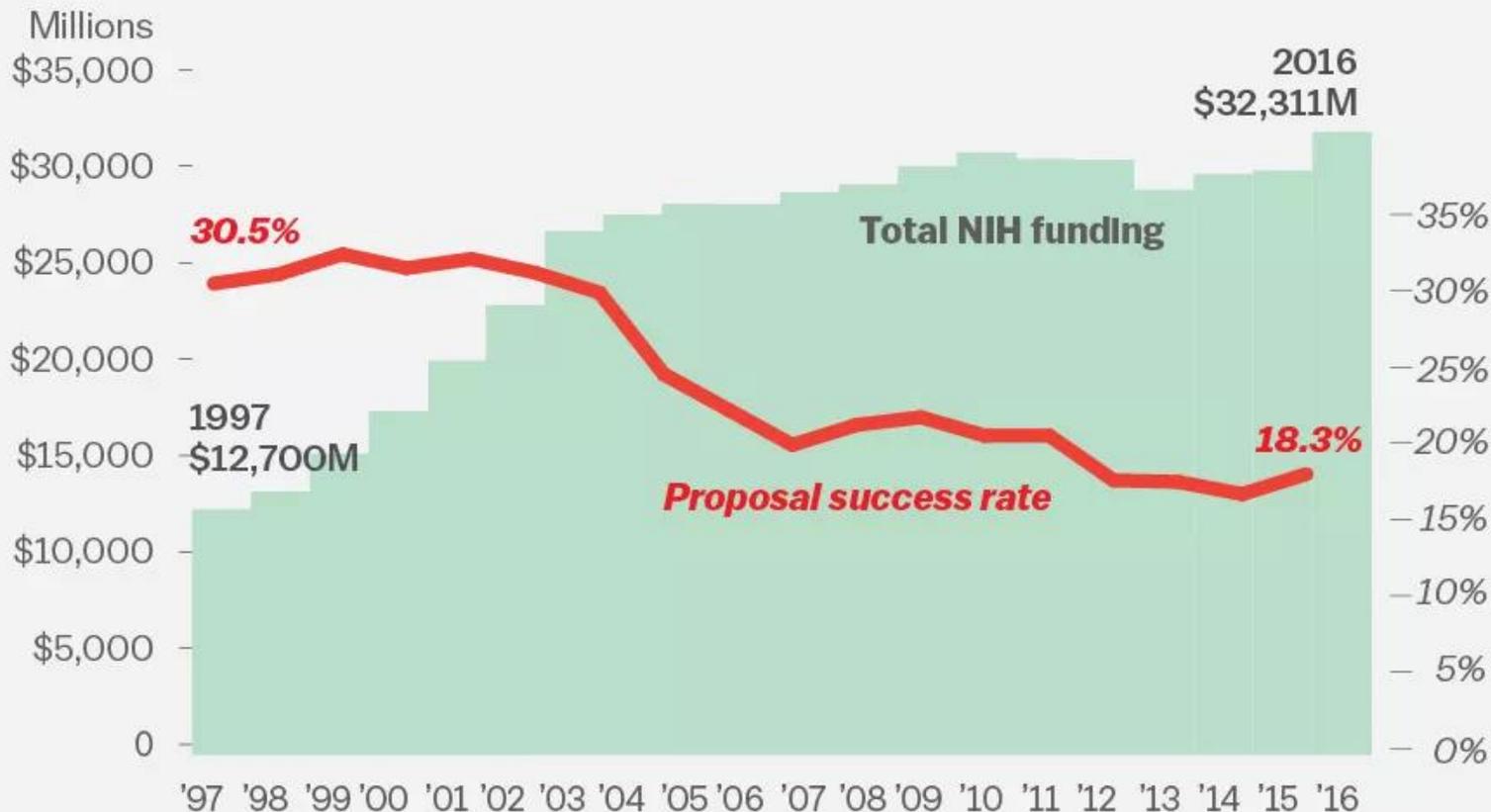
- Discrimination against scientists from underrepresented minorities leads to people leaving science.
- Lack of studies on women and minorities lead to issues in medical science.
 - Thalidomide: often causes birth defects
 - Cars not designed for women
- Bias against negative results, which may still be worth publishing.
- P-hacking: describes the conscious or subconscious manipulation of data in a way that produces a desired p-value (statistical significance)

COSTS

- Huge explosion of articles of variable quality.
- High pressure on researchers e.g. Sezen & Sames at Columbia
- Journals may not actually do peer review.
- For-profit publishers making money off of non-for-profit universities and librarians.
- Science funded by public locked beyond paywalls.
- People less willing to do high-risk research that may not result in a publication or support for a grant.
- People don't publish negative results, because they are not "interesting"

FUNDING

As NIH funding plateaued, grant applications grew much more competitive



SOURCE: NIH.gov

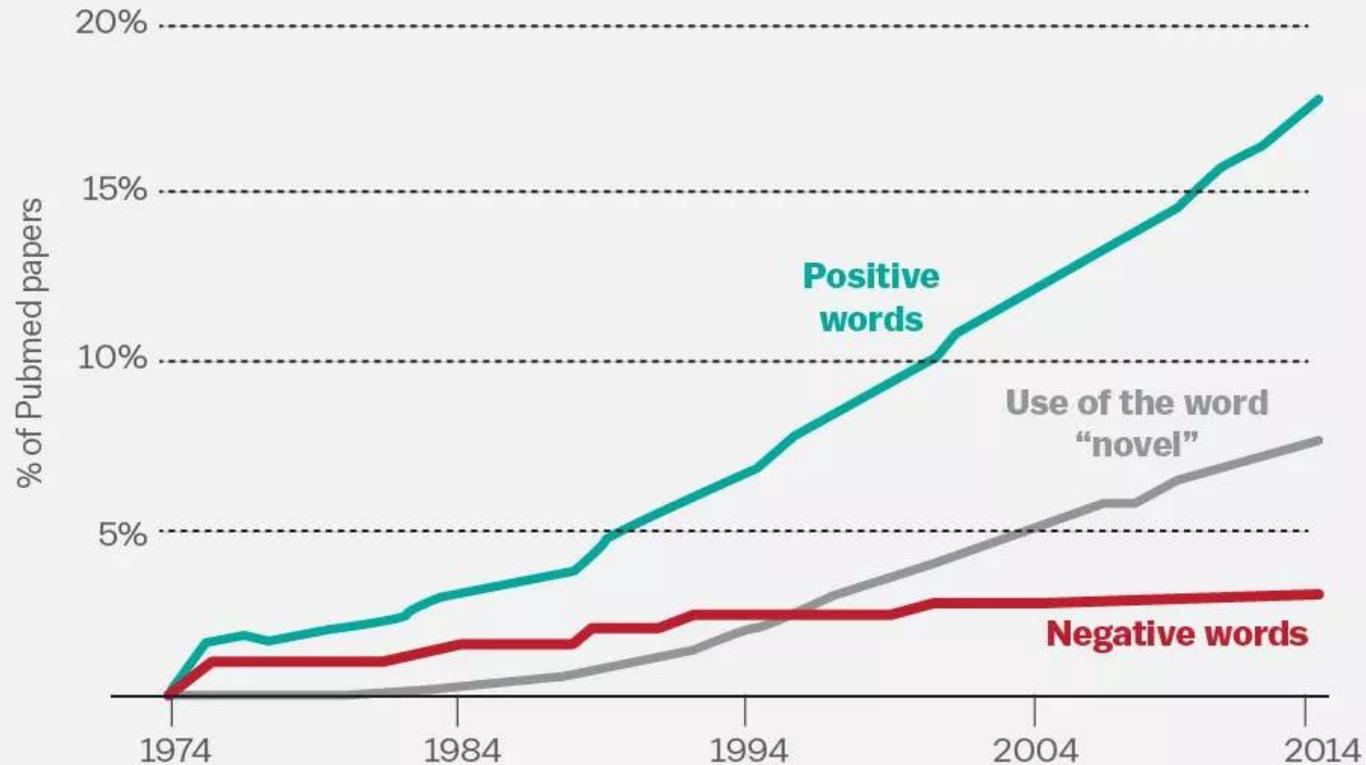
Vox

<https://www.vox.com/2016/7/14/12016710/science-challenges-research-funding-peer-review-process#1>

HYPE

Hype in science is on the rise

The use of positive words has increased in the titles and abstracts of research papers in PubMed.



SOURCE: BMJ/Nature

Vox

SOLUTIONS

- Open access
- Pre-print servers
- Government servers like PubMed
- More funding
- Fewer researchers (not very desirable)
- "I would make rewards based on the rigor of the research methods, rather than the outcome of the research," Simine Vazire
- Encourage people to publish studies testing if others are reproducible.
- Judge based on quality not quantity

THOUGHTS TO LIVE BY

- “I made the mistake that I wanted to manipulate the truth and make the world just a little more beautiful than it is.” ~ Diederik Stapel, who fabricated/manipulated data in his studies.
https://en.wikiquote.org/wiki/Diederik_Stapel
- “ Obviously, fraud is a terrible thing. Nothing provides as deep an existential threat to the scientific enterprise than making up data. But as bad as it is, there is something deeply ugly about the way the scientific community responds to misconduct. ” ~ Michael Eisen, whose father took his own life in 1987 after a member of his NIH lab committed scientific fraud.
<http://www.michaeleisen.org/blog/?p=1619>
- "Science, I had come to learn, is as political, competitive, and fierce a career as you can find, full of the temptation to find easy paths." — Paul Kalanithi, neurosurgeon and author of *When Breath Becomes Air*.
<https://www.vox.com/2016/7/14/12016710/science-challenges-research-funding-peer-review-process>
- "Is the point of research to make other professional academics happy, or is it to learn more about the world?" —Noah Grand, Former Lecturer In Sociology, UCLA (Vox)