Fraud, misconduct and shortcoming

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Istem

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Unreliable research Trouble at the lab The economist

Summary

- Scientific misconduct
  - Definitions
- Fraud and errors
  - Examples
- Misconduct and reproductibility
  - Reproductibility /repetability
- What's wrong ?
- Initiatives and recommendation

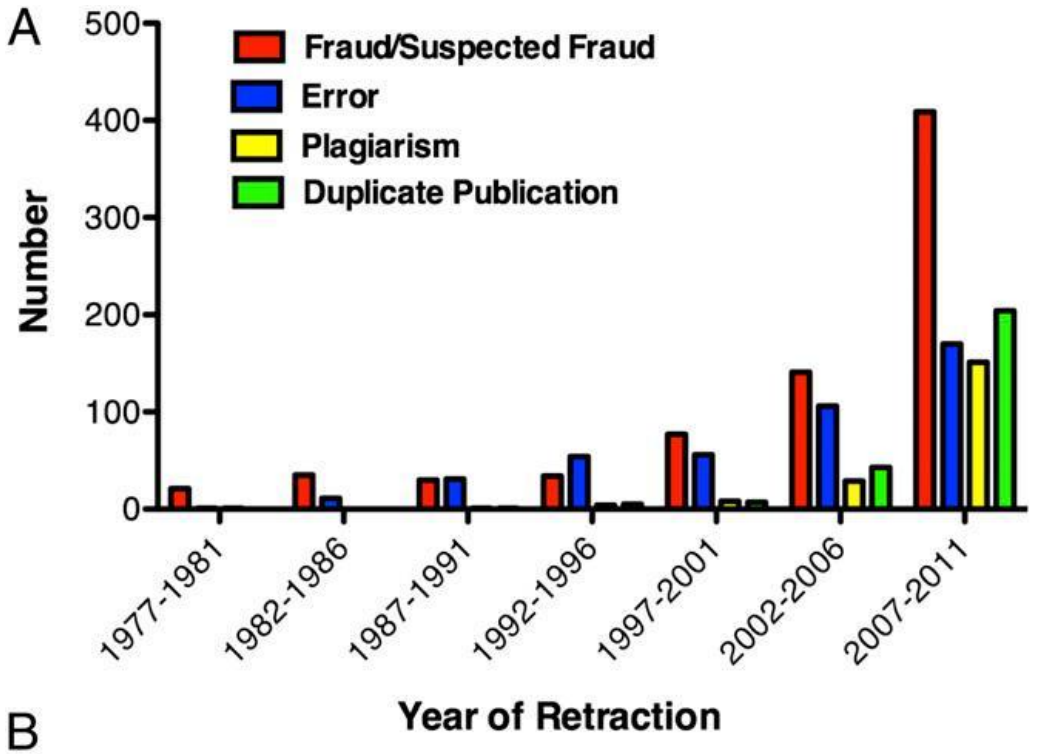
Scientifc misconduct

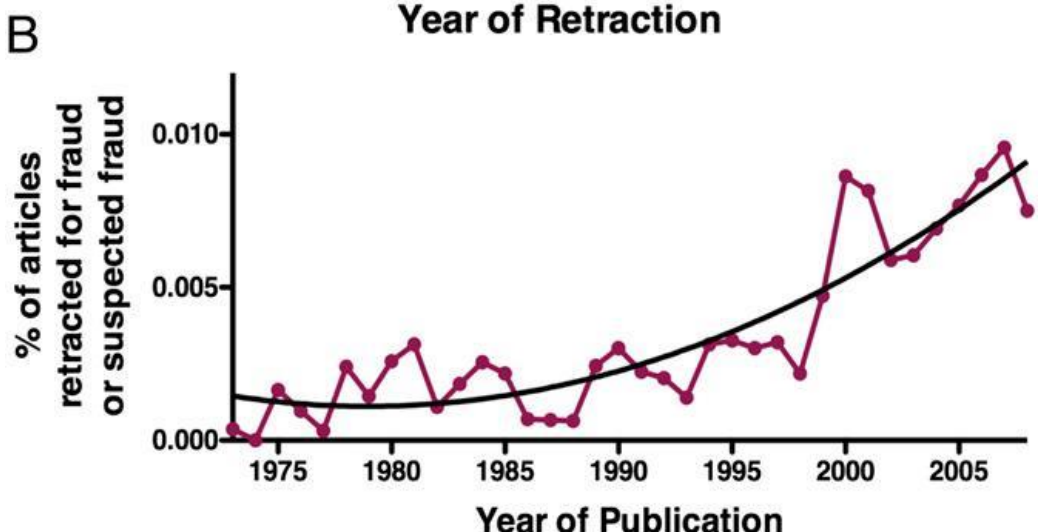
- The U.S. National Science Foundation defines three types of research misconduc: fabrication, falsification, and plagiarism
- *Fabrication* is making up results and recording or reporting them.
- *Falsification* is manipulating research materials, equipment, or processes or changing or omitting data or results such that the research is not accurately represented in the research record.
- *Plagiarism* is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit. One form is the appropriation of the ideas and results of others, and publishing as to make it appear the author had performed all the work under which the data was obtained.

Scientific misconduct and shortcomings

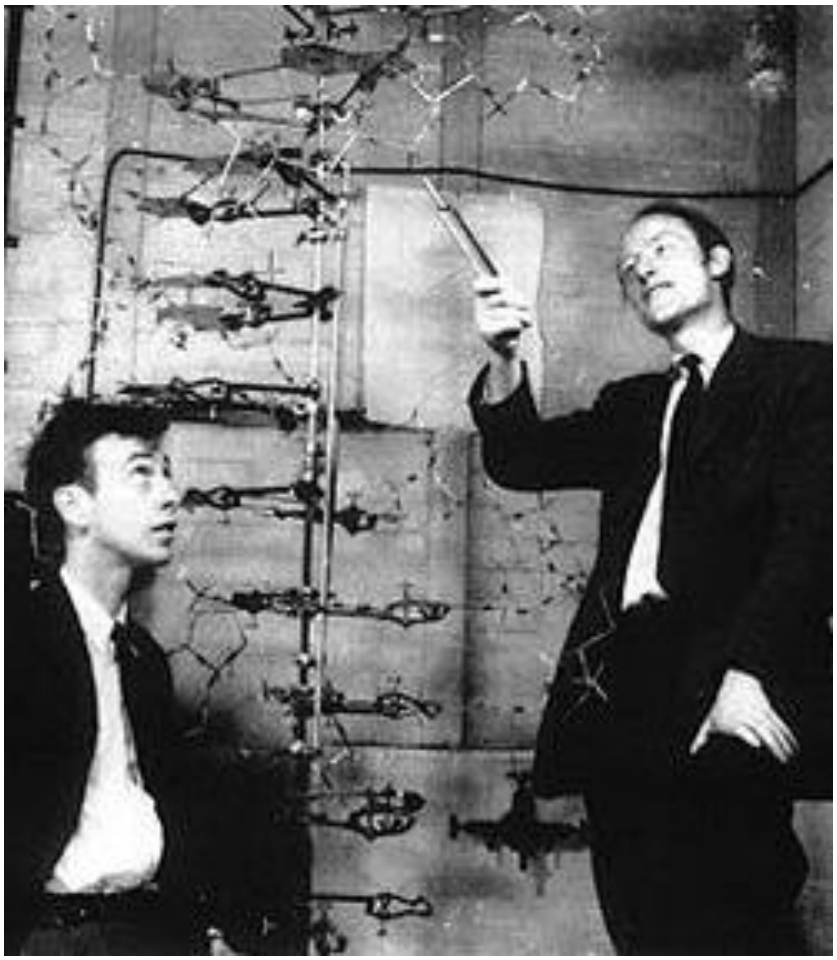
- There are numerous highly competent scientists that have used unorthodox or flawed methods and arrived at false conclusions, but still have been excellent researchers. The history of science teaches us this.
- It is therefore important to understand the difference between misconduct, which is a ***moral transgression, and various scientific shortcomings***.
- In the second place, even if misconduct (proper) and scientific shortcomings can have similar consequences, there are different ways to cope with the problems.

Fraud and error





Famous fruitful misconduct



Nature on 25 April 1953 Watson and Crick without Rosalind Franklin.
Franklin was the first to discover and formulate these facts,
which in fact constituted the basis for all later attempts to build a model of the molecule
X-ray diffraction studies provided crucial clues to the structure of DNA

A giant scientific breakthrough that turned out to be a fraud.

- Mark Spector, the most spectacular cases of scientific fraud in the second half of the 20th century.
- Spector as a thesis project the molecular characterization of the Na-K pump from mouse ascites cells, a type of cancer cell that can be grown easily in large quantities and therefore was suitable for biochemical studies.
- A manuscript reporting these findings was submitted to the Journal of Biological Chemistry (JBC) in June of 1980, i.e. about one half year after Spector came to Cornell.
- I***n the following few months the story was elaborated further with the emergence of a "kinase cascade"***
- Spector claimed to show that the phosphorylation of the ATPase and of the three kinases took place on the amino acid tyrosine
- Similarly and also just preceding Spector's ATPase work, the oncogenic protein encoded by the chicken retrovirus Rous sarcoma virus (RSV) was itself shown to be a tyrosine kinase Thus, in a short time the emerging molecular biology of cancer seemed to have converged on a central role for tyrosine phosphorylation

A giant scientific breakthrough that turned out to be a fraud.

- One post doc in a famous lab said openly that Spector's phospho-amino acid analyses clearly were faked, ***because the radioactive"spots" visible on the two-dimensional plate were far too small.***

- But Spector obviously was highly intelligent and really understood the biology and biochemistry of his and others' work. ***And he had an answer for everything when challenged.***

- The kinase cascade collapsed in summer 1981, only a month after the world-wide publicity from the Cold Spring Harbor meeting and from the various talks that Racker had given on Spector's work over the past year. In fact, the cascade was totally faked.

- None of the kinases ever existed, nor did the purified ATPase that Spector claimed to have prepared

A giant scientific breakthrough that turned out to be a fraud

- In cases of scientific fraud, the denouement in the form of a published retraction sometimes brings both clarity and closure to the case. That retraction was ambiguous, and to many researchers it seemed almost pathetic. "*We have recently discovered a major discrepancy in an unpublished experiment involving the kinase cascade. This, together with several other findings, makes us doubt the correctness of the results reported in our paper published in Cell in July 1981. In particular, we believe that the immunological identification of PKF and the phosphoamino acid analyses may not be right. Thus, until we or others are able to reproduce the purification and the characterization of the kinase, the conclusions* ***of the article must be regarded as unsubstantiated"***.
- ***Perhaps more important, the concepts underlying the cascade proved to be entirely valid***
- "How could Spector's falsification of data fail to have been detected over the one and a half years he was at Cornell, despite abundant warning signals?
- Some would say that preventing scientific fraud requires more oversight of research workers, by mentors and coworkers and even perhaps by governmental agencies.

Suspect Drug Research Blamed for Massive Death Toll

- Poldermans, a prominent researcher who published more than 300 papers, was fired in November 2011 after a university investigation concluded that he had engaged in misconduct, including data fabrication
- He was the lead author on two influential trials examining whether **β**-blocker drugs can protect patients undergoing surgery that doesn't directly involve the heart.
- ***May have led to the deaths of 800,000 people in Europe***, Darrel Francis and Graham Cole of Imperial College London wrote in a provocative article

Suspect Drug Research Blamed for Massive Death Toll

- It is also a reminder, some scientists say, of the huge effects that a few uncertain and potentially flawed studies can have on clinical practice.“***This is unfortunately what happens when you write a guideline that affects large numbers of people in a relatively common situation,***” Francis says.
- Even if 800,000 deaths is a provocative exaggeration, Francis and Cole are making
- After misconduct, the forces slowing down any public health response often ***“are far stronger than those people who are brave enough to write such a provocation,”*** Antes says. “I know many examples where ***a bit more provocation would be helpful to stir things up***, so they get the attention they deserve.”

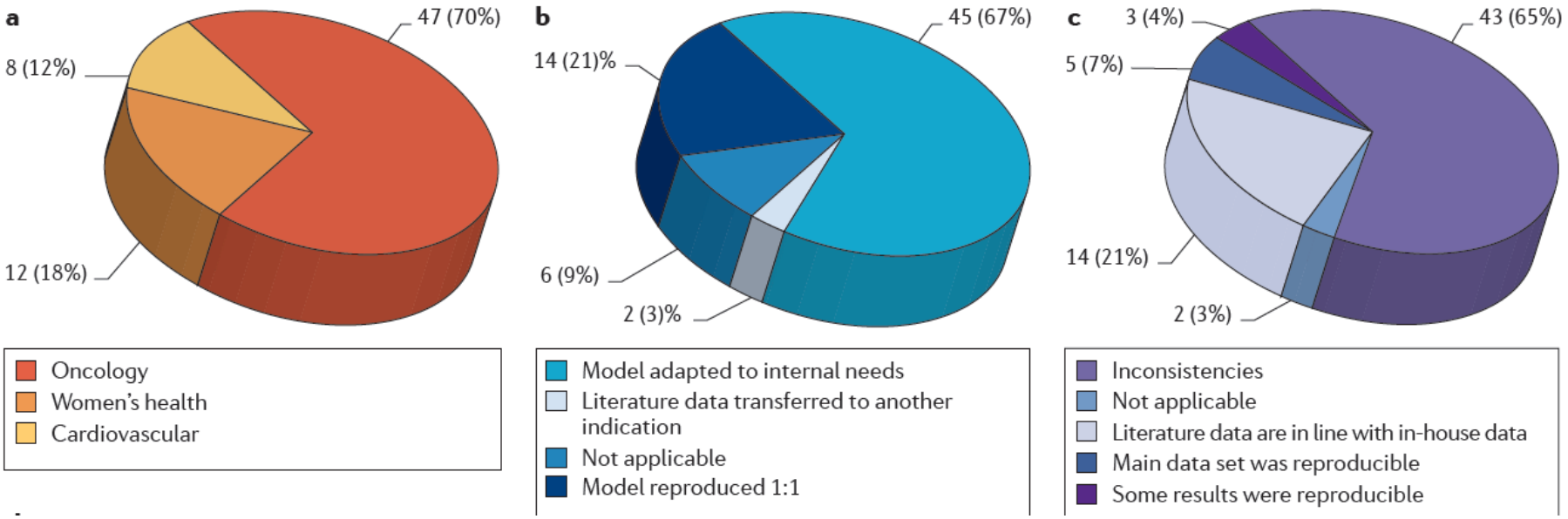
Misconduct and reproductibility

- From alarming estimates derived from studies by ***Bayer and Amgen*** that some ***60–70% of biomedical research papers may contain irreproducible results***, it would seem that our time would be better spent investigating experimental irreproducibility rather than hunting down fraudsters.
- **William Gunn** *Mendeley and the Reproducibility Initiative, California, USA.*

Believe it or not: how much can we rely on published data on potential drug targets? *Florian Prinz, Thomas Schlange and Khusru Asadullah*

- The validity of published data on potential targets is crucial when deciding to start novel projects.
- However, validation projects that were started in our company based on ***exciting published data have often resulted in disillusionment when*** key data could not be reproduced.
- Indeed, ***our analysis revealed that the reproducibility of published data did not significantly correlate with journal impact factors***, the number of publications on the respective target or the number of independent groups that authored the publications.
- Among the more obvious yet unquantifiable reasons, there is immense competition among laboratories and a pressure to publish. It is conceivable that this may sometimes result in negligence over the control or reporting of experimental conditions
- There is also a bias towards publishing positive results, as ***it is easier to get positive results accepted in good journals.***
- We are not reporting fraud, but a lack of reproducibility

Believe it or not: how much can we rely on published data on potential drug targets? *Florian Prinz, Thomas Schlange and Khusru Asadullah*



Raise standards for preclinical cancer research

C. Glenn Begley and **Lee M. Ellis** propose how methods, publications and incentives must change if patients are to benefit.

- The results of preclinical studies must therefore ***be very robust and very predictive to withstand the rigours and challenges of clinical trials.***
- The scientific community assumes that the claims in a preclinical study can be taken at face value . Unfortunately, this is not always the case.
- Scientific findings were confirmed in only 6 (11%) cases. Even knowing the limitations of preclinical research, ***this was a shocking result.***
- Investigators frequently presented the results of one experiment, such as a single Western-blot analysis.
- Some non-reproducible preclinical papers ***had spawned an entire field, with hundreds of secondary publications that expanded on elements of the original observation, but did not actually seek to confirm or falsify its fundamental basis.***
- ***Addressing these systemic issues will require tremendous commitment and a desire to change the prevalent culture***.

Raise standards for preclinical cancer research

C. Glenn Begley and **Lee M. Ellis** propose how methods, publications and incentives must change if patients are to benefit.

- ***The academic system and peer-review process tolerates and perhaps even inadvertently encourages such conduct.*** To obtain funding, a job, promotion or tenure, researchers need a strong publication record, often including a first-authored high-impact publication.

- Journal editors, reviewers and grant-review committees often look for a scientific finding that is simple, clear and complete — a 'perfect' story. It is therefore tempting for investigators to submit selected data sets for publication, or even to massage data to fit the underlying hypothesis

- ***There are no perfect stories in biology, but we like perfect stories***

- ***Journals and grant reviewers must allow for the presentation of imperfect stories***, and recognize and reward reproducible results, so that scientists feel less pressure to tell an impossibly perfect story to advance their careers.

Raise standards for preclinical cancer research

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REPRODUCIBILITY OF RESEARCH FINDINGS

Preclinical research generates many secondary publications, even when results cannot be reproduced.

Journal impact factor	Number of articles	Mean number of citations of non-reproduced articles*	Mean number of citations of reproduced articles
>20	21	248 (range 3–800)	231 (range 82–519)
5–19	32	169 (range 6–1,909)	13 (range 3–24)

Results from ten-year retrospective analysis of experiments performed prospectively. The term 'non-reproduced' was assigned on the basis of findings not being sufficiently robust to drive a drug-development programme.
*Source of citations: Google Scholar, May 2011.

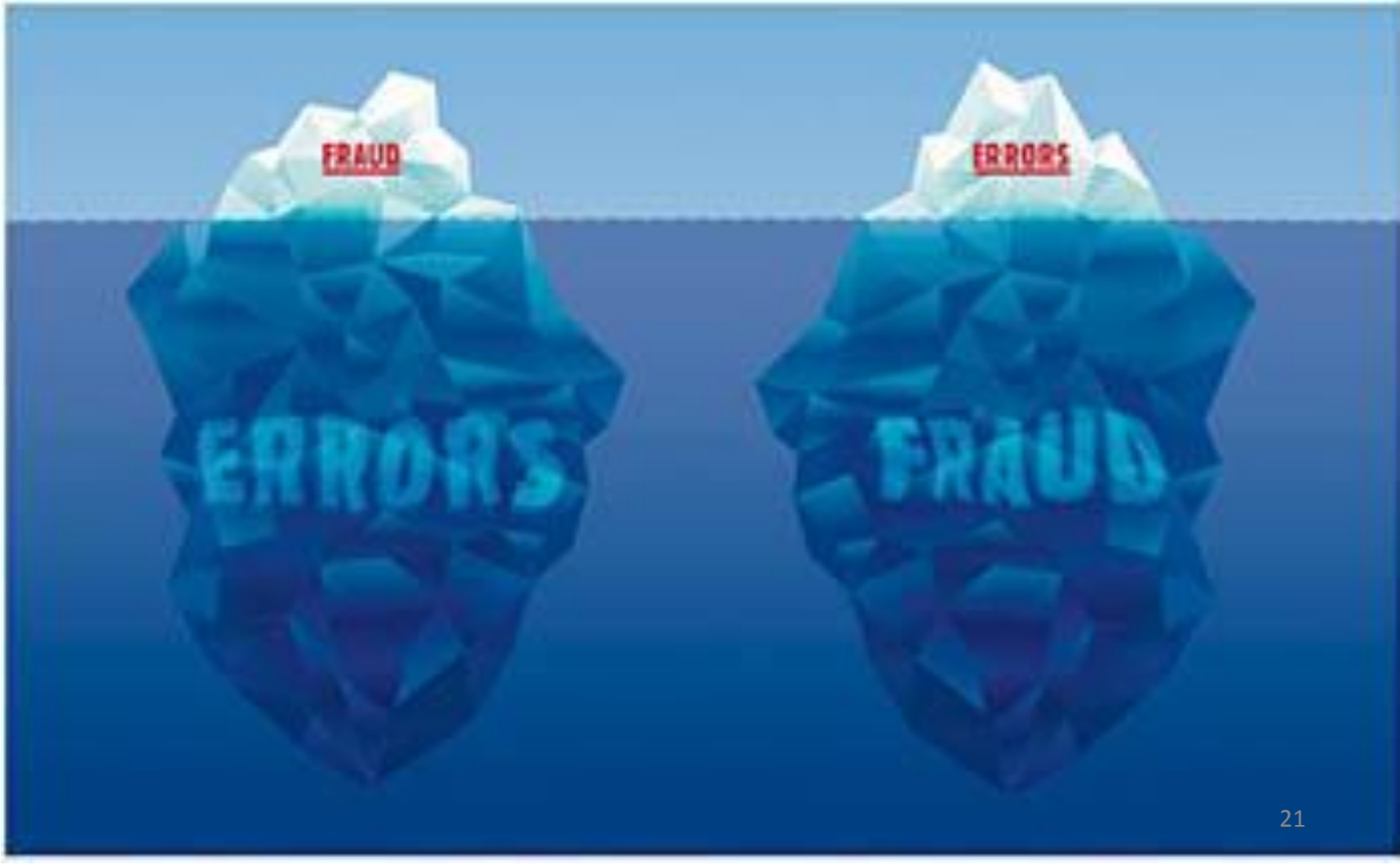
Scientific frauds : tip of the irreproductibility iceberg

- Dr. Casadevall disagreed. ***"It convinces me more that we have a problem in science,"*** he said.
- While the fraudulent papers may be relatively few, he went on, their rapid increase is a sign of a **winner-take-all culture** in which getting a paper published in a major journal can be the difference between heading a lab and facing unemployment. ***"Some fraction of people are starting to cheat,"*** he said.
- Better policing techniques, like plagiarism-detecting software, might help slow the rise in misconduct, Dr. Casadevall said, ***but the most important thing the scientific community can do is change its culture***.

Misconduct and reproductibility

- While it is true that there are some unethical individuals among scientists too, there is no massive fraud in academic research.
- Why so poor reproductibility?
- The problem we have is not a problem of scientific fraud, as some have suggested. ***It is not a failure of the scientific method***. Rather it is a consequence of the lack of rigorous application of the scientific principles in an intensely and increasingly competitive research environment in which scientists are scrambling to get their share of a national research budget that's shrinking. ***It is also the consequence of a system that currently turns a blind-eye to a lack of rigor.***

Why does the scientific community ascribe misconduct to individual behaviour rather than acknowledging that it is the tip of the iceberg of normal misbehaviour?



Harold Warmus NIH (Nobel Prize)

- ***What bothers me most is this sense of hypercompetition,***" Varmus says.
- Varmus also wants to address what he calls the "flawed values system" that the competitive atmosphere has spawned.
- And he thinks that easing the rush to publish in high impact journals might help address a much discussed problem: that many NIH-funded studies have proved difficult to reproduce
- Like HHMI awards, it will go to "people," not "projects." Varmus wants NCI to fund hundreds of these awards.

Sidney Brenner Nobel Prize

- Today the Americans have developed a new culture in science ***based on the slavery of graduate students.*** Now graduate students of American institutions are afraid. He just performs. He's got to perform. The post-doc is an indentured labourer. We now have labs that don't work in the same way as the early labs where people were independent, where they could have their own ideas and could pursue them.
- ***The most important thing today is for young people to take responsibility, to actually know how to formulate an idea and how to work on it***. Not to buy into the so-called apprenticeship. I think you can only foster that by having sort of deviant studies. That is, you go on and do something really different. Then I think you will be able to foster it
- But today there is no way to do this without money. ***The supporters now, the bureaucrats of science, do not wish to take any risks***. So in order to get it supported, they want to know from the start that it will work. This means you have to have preliminary information, which means that you are bound to follow the straight and narrow.

Sidney Brenner Nobel Prize

- "***A Fred Sanger would not survive today's world of science.*** With continuous reporting and appraisals, some committee would note that he published little of import between insulin in 1952 and his first paper on RNA sequencing in 1967 with another long gap until DNA sequencing in 1977.
- He would be labelled as unproductive, and his modest personal support would be denied. We no longer have a culture that allows individuals to embark on long-term—and what would be considered today extremely risky—projects.
- "I think one of the big things we had in the old LMB, which I don't think is the case now, was ***that we never let the committee assess individuals.*** We never let them; the individuals were our responsibility. ***We asked them to review the work of the group as a whole***. Because if they went down to individuals, they would say, this man is unproductive. He hasn't published anything for the last five years. So you've got to have institutions that can not only allow this, ***but also protect the people that are engaged on very long term, and to the funders, extremely risky work***

Sidney Brenner Nobel Prize

- ***Peer review is hindering science. In fact, I think it has become a completely corrupt system***. But I don't believe in peer review because I think it's very distorted and as I've said, i***t's simply a regression to the mean***.
- It's corrupt in many ways, in that scientists and academics have handed over to the editors of these journals the ability to make judgment on science and scientists. There are universities in America, and I've heard from many committees, ***that we won't consider people's publications in low impact factor journals.***
- Now I mean, people are trying to do something, but I think it's not publish or perish, it's publish in the okay places [or perish]. ***And this has assembled a most ridiculous group of people.***
- In one article, "Hard Cases", I campaigned against this [culture] because I think it is not only bad, it's corrupt. In other words it puts the judgment in the hands of people who really have no reason to exercise judgment at all. ***They just have to employ a lot of failed scientists, editors who are just like the people at Homeland Security, little power grabbers in their own sphere***. And that's all been done in the aid of commerce, because they are now giant organisations making money out of it.

Sidney Brenner Nobel Prize

- I think that this has now just become ridiculous and its one of the contaminating things that young people in particular have to actually now contend with. I know of many places in which they say they need this paper in Nature, or I need my paper in Science because I've got to get a post doc. But there is no judgment of its contribution as it is.
- Only the most successful academics can afford to challenge these norms by boycotting high impact journals. Until we win our Nobel Prizes, or grant and promotion structures change, we are shackled to this "publish or perish" culture. But together with leaders in science and academia such as Professor Brenner, we can start to change the structure of academic research and the language we use to judge quality.

How Luxury Brands are Damaging Science

- Randy Schekman (Nobel Prize) writes that he no longer wants to publish in Nature, Cell or Science.
- Schekman protested that these journals have distorted science through their publishing practices and that something has to change if the health of science is to improve.
- ***"mean the biggest rewards often follow the flashiest work, not the best".***
- He says that these ***journals have created commercial 'brands***' and they have used academic science to market them like "fashion designers who create limited-edition handbags or suits"because "they know scarcity stokes demand, so they artificially restrict the number of papers they accept".
- ***These "exclusive brands" have promoted themselves using the "gimmick called 'impact factor"***

How Luxury Brands are Damaging Science

- “somehow must be good without even looking at the research in question”**.**
- “The lure of the luxury journal can encourage the cutting of corners and contribute to the escalating number of papers that are retracted as flawed or fraudulent.
- To break the distorting influence of luxury journals he advocates a “new breed of Open Access journals that are free for anybody to read and have no expensive subscriptions to promote.
- ***“We need to reform the attitude of funders and universities: They must tell the committees that decide on grants and positions not to judge papers by where they are published. It is the quality of the science, not the journal’s brand, that matters.”***

Impact Factor Distortions

Bruce Alberts is Editorin-Chief of Science.

- To correct distortions in the evaluation of scientific research, DORA aims to stop the use of the “journal impact factor” in judging an individual scientist’s work.
- The Declaration states that the impact factor ***must not be used as “a surrogate measure of the quality of individual research articles***, to assess an individual scientist’scontributions, or in hiring, promotion, or funding decisions
- As frequently pointed out by leading scientists, this impact factor mania makes no sense.
- But perhaps the most destructive result of any automated scoring of a researcher’s quality is the “me-too science” that it encourages.
- ***Such metrics further block innovation*** because they encourage scientists to work in areas of science scientists to work in areas of science that are already highly populated

House of commons

- Peer review in scholarly publishing, in one form or another, is crucial to the reputation and reliability of scientific research.
  - *Drummond Rennie, deputy editor of the Journal of the American Medical Association, who once said **"'If peer review was a drug it would never be allowed onto the market »**. Dr Smith added: not only do scientists know little about the evidence on peer review but most continue to believe in peer review, thinking it essential for the progress of science. Ironically, a faith based rather than an evidence based process lies at the heart of science.*

- In order for current peer-review practices to be optimised and innovative approaches introduced, publishers, research funders and the users of research outputs (such as industry and government) must work together.
- We note that new innovations in pre-publication review are being introduced that have the potential to accelerate the pace of research communication and avoid duplication of effort by the research community, with the consequent drain on resources.

  Professor Ron Laskey indicated that a pre-print server would also not be suitable for biomedical sciences. He described two worries from the Academy of Medical Sciences submission to this inquiry:
  - ***One is that biomedical sciences are more prone to inaccurate interpretations** […] There is a worry that, if you extended the pre-publication model to the biomedical sciences without any attempt to peer review, a lot of half-truths*
  - ***The second problem is the appetite of the media for some aspects of biomedical science**. Without peer review we would get a storm, frankly, of incorrect headlines.*

House of commons

- The publication of peer-reviewed articles is not only important in terms of maintaining a robust scientific record, it also has an impact ***on the careers of researchers and the reputations of research institutions. We have been assured by research funders that they do not use journal Impact Factor as a proxy measure for the quality of research or of individual articles***. *We consider that research institutions should be cautious about this approach, because as we have previously noted, there is no substitute for reading the article itself in assessing the worth of a piece of research.*
- While pre-publication peer review continues to play an important role, the growth of post-publication peer review and commentary represents an enormous opportunity for experimentation with new media and social networking tools. Online communications allow the widespread sharing of links to articles, ensuring that interesting research is spread across the world, facilitating rapid commentary and review by the global audience. They also have a valuable role to play in alerting the community to deficiencies and problems with published work.

House of commons

- ***Oversight of research integrity in the UK is in need of revision***. Research Councils UK, Universities UK and the Government should revisit these recommendations and reassess how they can best be implemented.
- ***Employers must take responsibility for the integrity of their employees' research.*** However, we question who would oversee the employer and make sure that they are doing the right thing. In the same way that there is an external regulator overseeing health and safety, ***we consider that there should be an external regulator overseeing research integrity.***
- ***We also recommend that all UK research institutions have a specific member of staff leading on research integrity***. Such a person would be a first point of call in case of an ethical breach. Where an investigation subsequently takes place within a research institution, it is essential that the outcome be published.

NIH initiative

- Let's be clear: with rare exceptions, we have no evidence to suggest that irreproducibility is caused by scientific misconduct.

- Instead, a complex array of other factors seems to have contributed to the lack of reproducibility. ***Factors include poor training of researchers*** in experimental design; increased emphasis on making provocative statements rather than presenting technical details; and publications that do not report basic elements of experimental design.

- Exacerbating this situation are the policies and attitudes of funding agencies, academic centres and scientific publishers. ***Funding agencies often uncritically encourage the overvaluation of research published in high-profile journals***. Some academic centres also provide incentives for publications in such journals, including promotion and tenure, and in extreme circumstances, cash rewards

NIH initiative

- As a funding agency, the NIH is deeply concerned about this problem.
- ***The NIH is also exploring ways to provide greater transparency*** of the data that are the basis of published manuscripts.
- Clearly, reproducibility is not a problem that the NIH can tackle alone.
- The NIH is firmly committed to making systematic changes that should reduce the frequency and severity of this problem — but ***success will come only with the full engagement of the entire biomedical-research enterprise***

As seen in

- **Reproducibility Initiative Identifying and rewarding high-quality research**
- **Major projects :**
- **Cancer Biology Reproducibility Project**
- **Antibody Validation Project**

Scientific integrity

- A US National Academies report explained that, for the individual researcher, integrity embodies a range of good research practice and conduct, including:
  - intellectual honesty in proposing, performing, and reporting research;
  - accuracy in representing contributions to research proposals and reports; fairness in peer review;
  - collegiality in scientific interactions, including communications and sharing of resources;
  - transparency in conflicts of interest or potential conflicts of interest; protection of human subjects in the conduct of research;
  - humane care of animals in the conduct of research; and adherence to the mutual responsibilities between investigators and their research teams

- External watchdogs—be they the media or federal agencies—might therefore have the adverse effect of destroying trust in the informal networks of the communication system. A discursive “spiral of mistrust” (Weingart, 2005) might develop, triggered from the outside and then amplified within science.
- Regardless of whether this perception is justified, we can only speculate on the unintended consequences of short-term evaluations for the culture of science. ***They will probably be dramatic and irreversible, because the fragile balance of mutual trust and focused critique—a unique social invention—might be lost.***
- ***Institutional changes, rather than individual motivations, encourage misconduct.***

Thanks

- Wishful thinking or change in the scientific atmosphere?
- "If you want to bury a problem, appoint a commission," said Clemenceau
- "Une civilisation sans la Science, ce serait aussi absurde qu'un poisson sans bicyclette ». Pierre Desgraupes

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