

THREAT TO RESEARCH INTEGRITY: PUBLISH (WHATEVER) OR PERISH

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HOW REPRODUCIBLE ARE THE PUBLISHED SCIENTIFIC DATA?

- ▶ There is a growing concern about reproducibility of research results.
- ▶ This problem is highlighted in pre-clinical experiments, that cannot be reproduced by pharmaceutical industry
- ▶ It has been published a study in which only 20-25% of the relevant data of 67 pre-clinical reports could be reproduced by a pharmaceutical company (Nature Rev. Drug Disc. 10:720, 2011).
- ▶ Evidence exists that similar phenomena also occurs in other fields of knowledge.

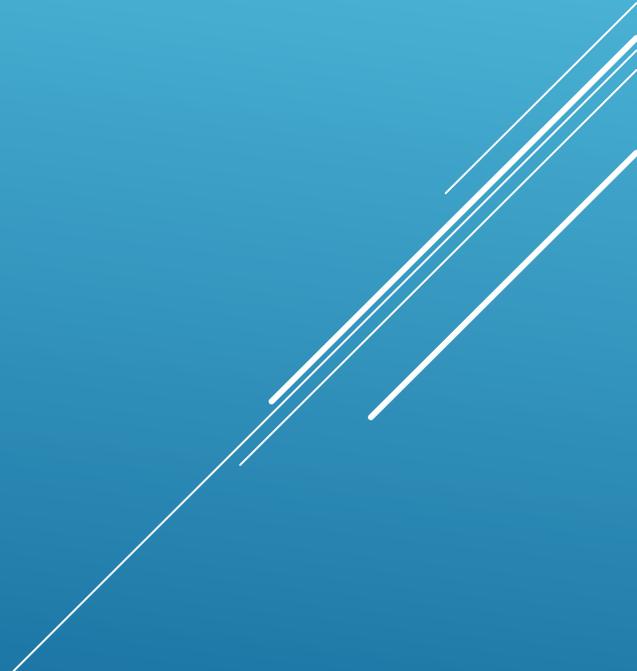
Irreproducibility does not mean necessarily wrongdoing

IN PRE-CLINICAL STUDIES, WHICH ONE IS MORE LIKELY TO BE CORRECT: ACADEMIA OR INDUSTRY?

- ▶ Academia – more rigor may lead to delayed publication or even no publication (few journals publish negative results)
- ▶ Industry – more rigor may avoid waste of money (... but after having a new product, industry tends to overlook adverse effects and overestimate positive effects)

Is there such a thing as “excessive rigor”?

CAUSES OF FAILURE TO REPRODUCE PUBLISHED DATA

- ▶ Fabrication/falsification of the data
 - ▶ Uncontrolled (unpredictable) variability
 - ▶ Honest experimental errors or differences in procedures
- 
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In the early 1960, there was a serious dispute among muscle physiologists, whether Ca^{2+} was important for the activity of the contractile proteins. Different groups had contradictory and irreconcilable results.

Ebashi realized that depending on details of the purification of the contractile proteins, all experiments could be reproduced.

He discovered a protein (troponin) that plays a crucial role in the control of contraction. Its presence or absence in the assay depends on the temperature of purification of actin, and determines the need for Ca^{2+} .

EXAMPLE OF EXPERIMENTAL DIFFERENCES

CAUSES OF FAILURE TO REPRODUCE PUBLISHED DATA

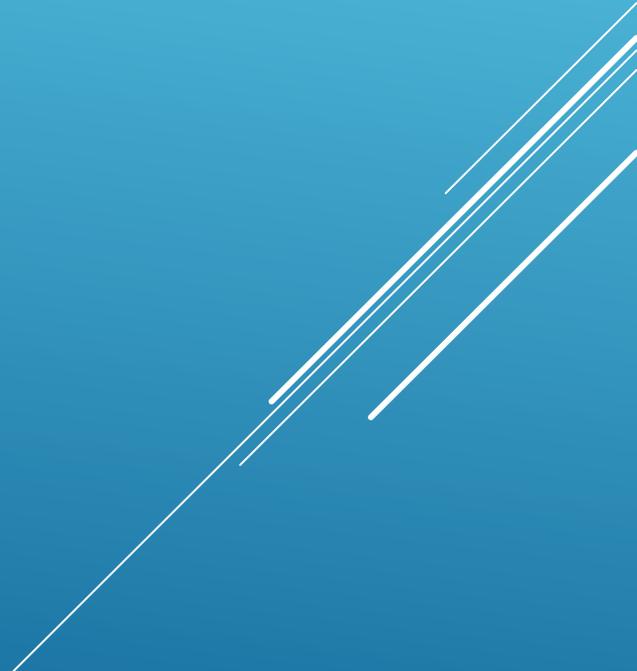
THE SINGAPORE STATEMENT

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3- *Research Methods*: Researchers should employ appropriate research methods, base conclusions on critical analysis of the evidence and report findings and interpretations fully and objectively.

.....

NON-RESPONSIBLE CONDUCT OF SCIENCE AS CAUSE OF IRREPRODUCIBLE RESULTS

- ▶ Bad practices – Lack of experimental rigor
 - ▶ Bad interpretation of the data (including bad use of statistics)
 - ▶ Bias towards positive results (selective report)
 - ▶ Lack of detailed description of experimental methodology
 - ▶ Negligent or hasty manuscript elaboration
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BIAS TOWARD POSITIVE RESULTS: THE CASE OF MEMORY OF WATER

In 1988, a group of researchers claimed that after many sequential dilutions of a solution of antibody, to the point that no single molecule of antibody could remain, the product of dilution retained the properties of the original solution.

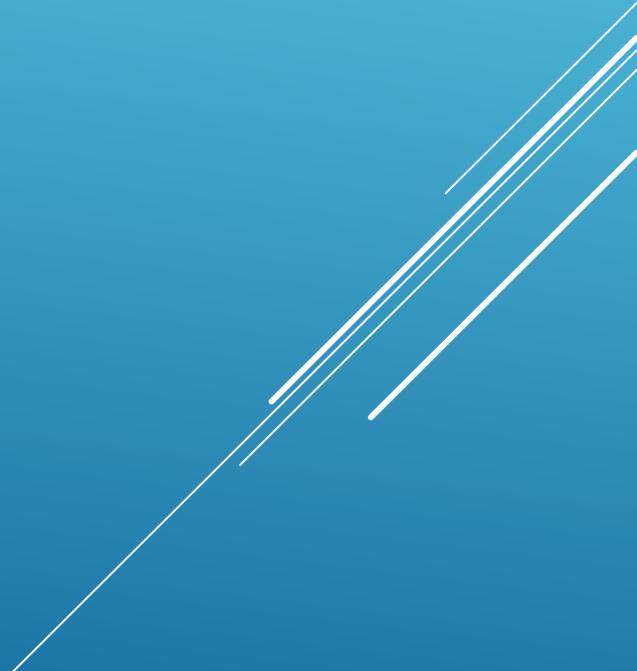
The paper was published in June (Nature 333: 816, 1988), with a warning from the editor stating that the manuscript seemed to contain no flaw, but lacked a reasonable explanation.

In July a group of experts, including a magician, accompanied the execution of the experiments, and the results confirmed what was published.

The group of experts required that the researchers performed the experiments without knowing the experimental and control flasks (blind experiment). All following results contradicted the publication.

The group of experts published a note in Nature 334: 287, 1988.

CAUSES OF FAILURE TO REPRODUCE PUBLISHED DATA

- ▶ Fabrication/falsification of the data
 - ▶ Uncontrolled (unpredictable) variability
 - ▶ Honest experimental errors or differences in procedures
 - ▶ Non-responsible conduct of research
 - ▶ Negligence on manuscript assessment
- 
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NEGLIGENCE ON MANUSCRIPT ASSESSMENT – ONE EXAMPLE

- ▶ Fake manuscripts “with such grave errors that a competent peer reviewer should easily identify it as flawed and unpublishable” were submitted to 304 open access journals.
- ▶ Out of the 255 editorial decisions received within the time of the investigation, only 98 (38.4%) were rejections. Bohannon. Science 342: 60, 2013.
- ▶ Although not investigated, it is expected that this editorial negligence is not restricted to open access journals, but the enormous growth of the number of this type publication is a matter of concern.
- ▶ It is fair to conclude that nowadays anything can be published in a “scientific” publication

On time - I think open access publication is a great idea: it is a pity that this idea has also been appropriated by several predatory publishers!

HOW TO AVOID THESE
PROBLEMS?
HOW TO MAKE SCIENTIFIC
PUBLICATIONS MORE
RELIABLE?

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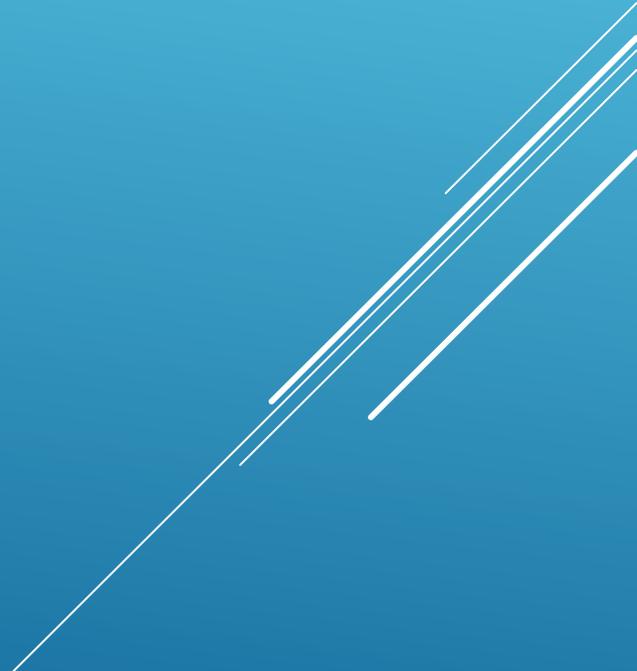
- ▶ Publish (and follow) guidelines of the quality requirements
- ▶ Improve the mechanisms of peer review
- ▶ When appropriate, use qualified statisticians for manuscript review
- ▶ Reject manuscripts with evidence of careless handling (orthography, truncated sentences, figure errors)
- ▶ Stimulate publication of relevant data that underlies one's work or support one's reasoning (including negative results)
- ▶ Allow contradicting and/or supporting comments or publication of refutation papers (subject to review)
- ▶ Open access strategies (signed reviews and post publication review)
- ▶ Open data

POSSIBLE CONTRIBUTION FROM THE PUBLISHERS

- ▶ Periodically instruct researchers on good practices
- ▶ Redesign reward system – emphasis on assessment of quality and reward reproducible research
- ▶ Recognize signed reviews of manuscripts on papers on internal assessments and promotions
- ▶ Use good practices records in recruiting processes
- ▶ Pre-register clinical trials
- ▶ Have fair, timely and rigorous mechanisms for handling malpractice allegations

ROLE OF RESEARCH INSTITUTIONS

POSSIBLE ACTIONS FROM THE FUNDING AGENCIES





Created in May 2012 aiming at favoring international cooperation among world research funding agencies and provide basis for creating global research policies.





“While researchers and institutions themselves remain ultimately responsible for undertaking research with integrity, research funding agencies have an obligation to ensure that the research they support is conducted in accordance with the highest standards possible.”

STATEMENT OF PRINCIPLES FOR RESEARCH INTEGRITY



Leadership

Promotion

Education

Transparent Processes

Response to Allegations of Misconduct

Conditions for Research Support

International Cooperation

STATEMENT OF PRINCIPLES FOR RESEARCH INTEGRITY



Leadership

Research funding agencies must lead by example in the responsible management of research programs.

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Research funding agencies should encourage institutions to develop and implement policies and systems to promote integrity in all aspects of the research enterprise.

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Research funding agencies should promote continual training in research integrity, and develop initiatives to educate all researchers and students on the importance of research integrity.

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STATEMENT OF PRINCIPLES FOR RESEARCH INTEGRITY



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Research funding agencies should, within the scope of their mandate, publish policies and procedures to promote research integrity and to address allegations of research misconduct.

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During any investigation of misconduct, research funding agencies should support a process that values accountability, timeliness and fairness.

Conditions for Research Support

International Cooperation

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Conditions for Research Support

Research funding agencies should incorporate integrity in research as a condition for obtaining and maintaining funding by researchers and institutions.

International Cooperation

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Conditions for Research Support

International Cooperation

Research funding agencies will work cooperatively with partners to support and facilitate research integrity worldwide.

- ▶ Stimulate workshops and seminars on responsible conduct of research
- ▶ Transparency and guidelines on publications
- ▶ Peer review improvements – emphasis on quality
- ▶ Other mechanisms of CV assessment – reward one's effective contribution to science and/or technology
- ▶ Strengthen Open Access strategies

HOW FUNDING AGENCIES CAN
ACCOMPLISH THIS GOAL?

- ▶ Promote activities on research integrity and good practices
- ▶ Promote training strategies for responsible conduct and best practices with emphasis on its field of knowledge
- ▶ Publish guidelines of best practices in the respective field
- ▶ Contribute in the identification of predatory publications
- ▶ Stimulate the verification of published results and report of negative results
- ▶ Help implement policies on conflicting interest

ROLE OF SCIENTIFIC SOCIETIES

NO STAKEHOLDER ALONE
CAN SOLVE THE PROBLEM:
THERE IS A NEED FOR A JOINT
EFFORT!

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THANK YOU!

The image features a solid blue background with a gradient from light blue at the top to a darker blue at the bottom. In the bottom right corner, there are several white, parallel diagonal lines of varying lengths and positions, creating a sense of motion or a stylized graphic element.