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Reproducibility & replicability in MRI

Gaëlle Leroux

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Submitted on 22 Jun 2023

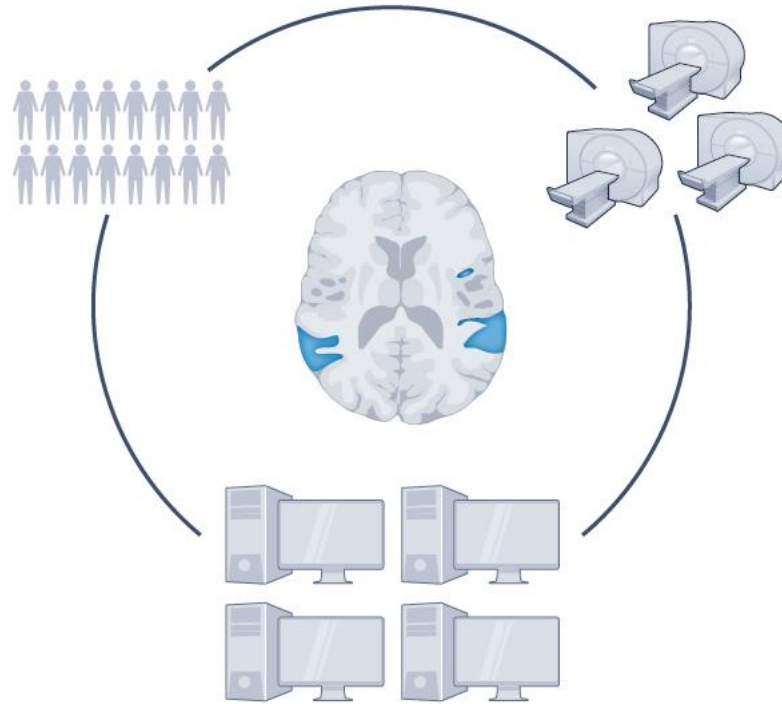
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Reproducibility & replicability in MRI



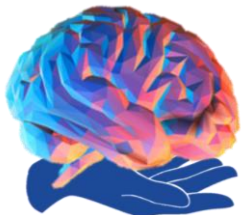
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Illustration from Vogt. Reproducibility in MRI. *Nat Methods* (2023)



Soutien
Méthodologique
aux projets
d'imagerie



Research data College

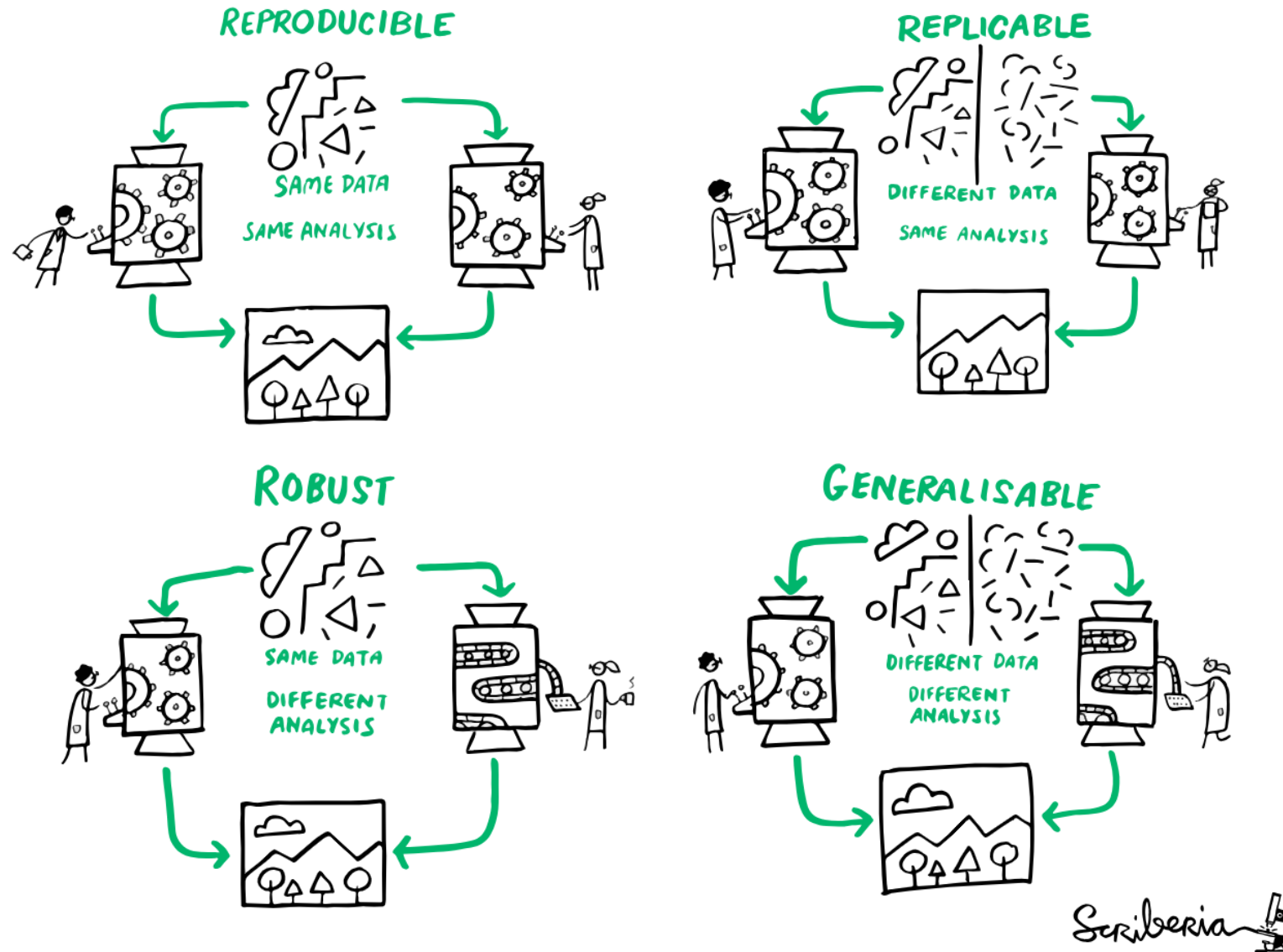
Generalisable
Replicable
Reproducible
Robust

		Data	
		Same	Different
Code	Same	1	2
	Different	3	4

From Kirstie Whitaker 2017, doi: <https://dx.doi.org/10.6084/m9.figshare.4244996>

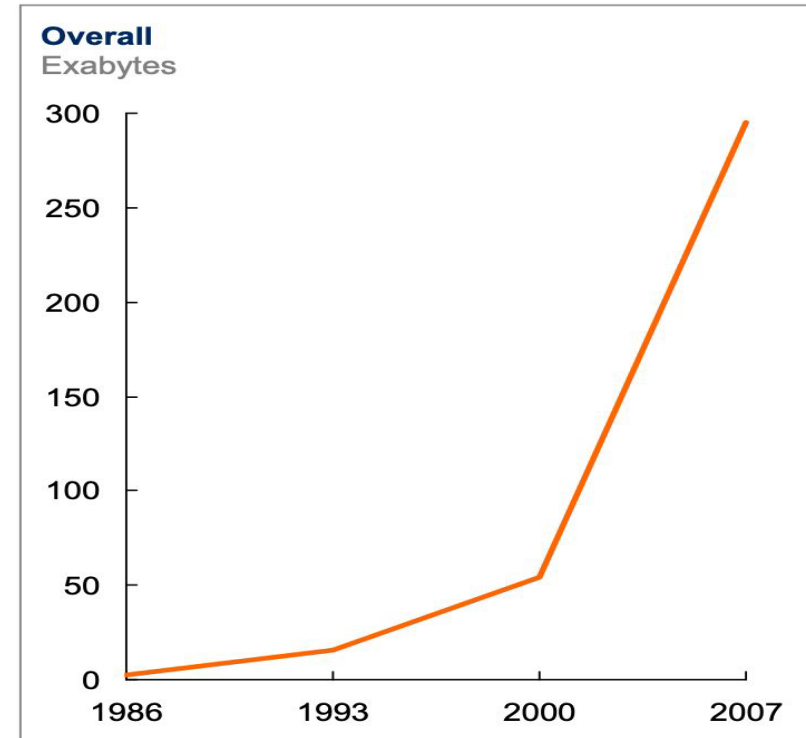
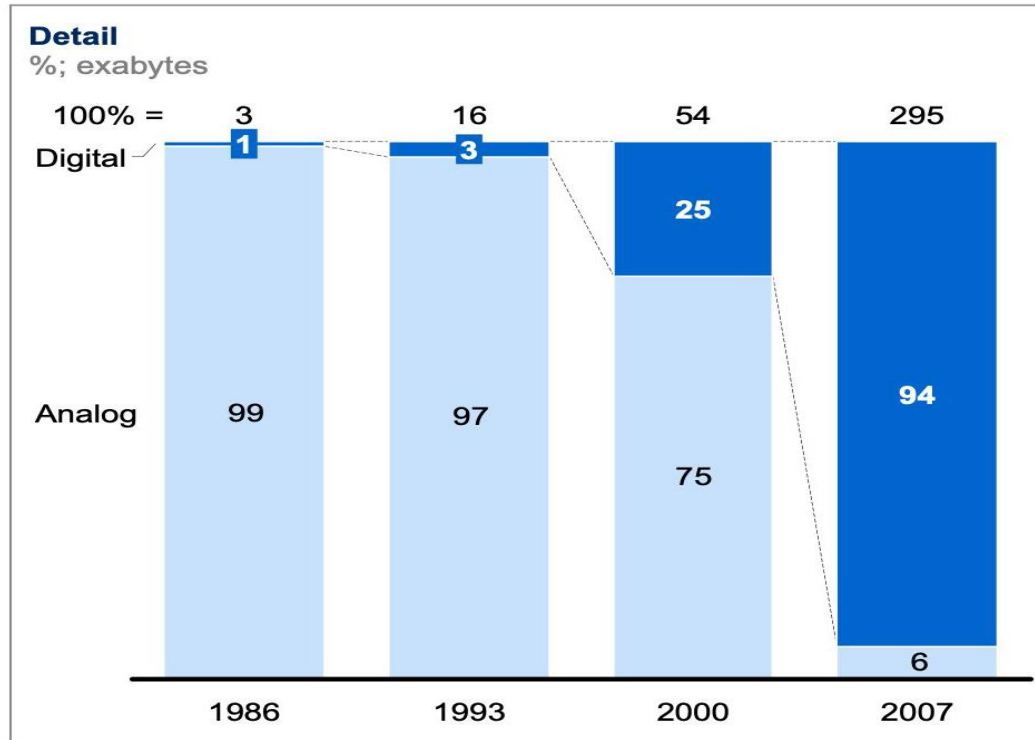
		Data	
		Same	Different
Code	Same	Reproducible	Replicable
	Different	Robust	Generalisable

From Kirstie Whitaker 2017, doi: <https://dx.doi.org/10.6084/m9.figshare.4244996>



The Turing Way project illustration by Scriberia. DOI: [10.5281/zenodo.3332807](https://doi.org/10.5281/zenodo.3332807)

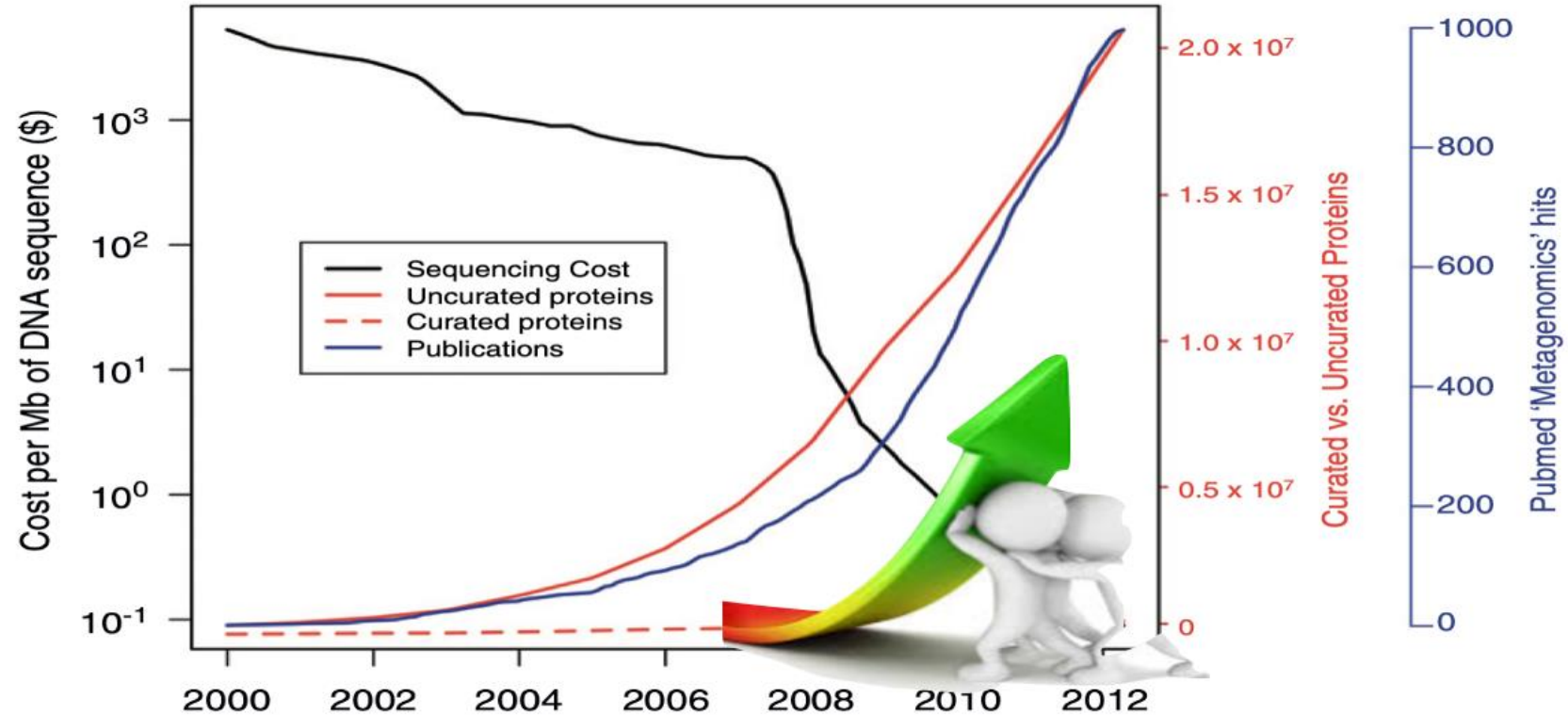
1. An overview of the “reproducibility crisis”: origins



[Source](#)

1. An overview of the “reproducibility crisis”: origins

Human genome:
in 1990 = 13 years & \$3 billion
in 2015 = a few hours & \$1,000



- ➔ The amount of data to be stored & to be analysed, explodes
- ➔ Analysis performance dramatically falls

[Source](#)

1. An overview of the “reproducibility crisis”: research tasks have moved

Before

1. Design the experiment
2. Collect data
3. Analyze results

Now

A change of paradigm

1. Massive data production / reuse
2. Organize (store, document, annotate)
3. Analyze (extract information)
4. Share information

1. An overview of the “reproducibility crisis”: alarm in 2005

Open access, freely available online

Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

Summary

There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power and bias, the number of other studies on the same question, and, importantly, the ratio of true to no relationships among the relationships probed in each scientific field. In this framework, a research finding is less likely to be true when the studies conducted in a field are smaller; when effect sizes are smaller; when there is a greater number and lesser preselection of tested relationships; where there is greater flexibility in designs, definitions, outcomes, and analytical modes; when there is greater financial and other interest and prejudice; and when more teams are involved in a scientific field in chase of statistical significance. Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true. Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias. In this essay, I discuss the implications of these problems for the conduct and interpretation of research.

factors that influence this problem and some corollaries thereof.

Modeling the Framework for False Positive Findings

Several methodologists have pointed out [9–11] that the high rate of nonreplication (lack of confirmation) of research discoveries is a consequence of the convenient, yet ill-founded strategy of claiming conclusive research findings solely on the basis of a single study assessed by formal statistical significance, typically for a p -value less than 0.05. Research is not most appropriately represented and summarized by p -values, but, unfortunately, there is a widespread notion that medical research articles

It can be proven that most claimed research findings are false.

should be interpreted based only on p -values. Research findings are defined here as any relationship reaching formal statistical significance, e.g., effective interventions, informative predictors, risk factors, or associations. “Negative” research is also very useful.

is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be postulated. Let us also consider, for computational simplicity, circumscribed fields where either there is only one true relationship (among many that can be hypothesized) or the power is similar to find any of the several existing true relationships. The pre-study probability of a relationship being true is $R/(R+1)$. The probability of a study finding a true relationship reflects the power $1 - \beta$ (one minus the Type II error rate). The probability of claiming a relationship when none truly exists reflects the Type I error rate, α . Assuming that r relationships are being probed in the field, the expected values of the 2×2 table are given in Table 1. After a research finding has been claimed based on achieving formal statistical significance, the post-study probability that it is true is the positive predictive value, PPV. The PPV is also the complementary probability of what Wacholder et al. have called the false positive report probability [10]. According to the 2

74,946 Save	7,388 Citation
3,001,940 View	9,576 Share

Inadequate methodologies

A result is all the more likely to be false when:

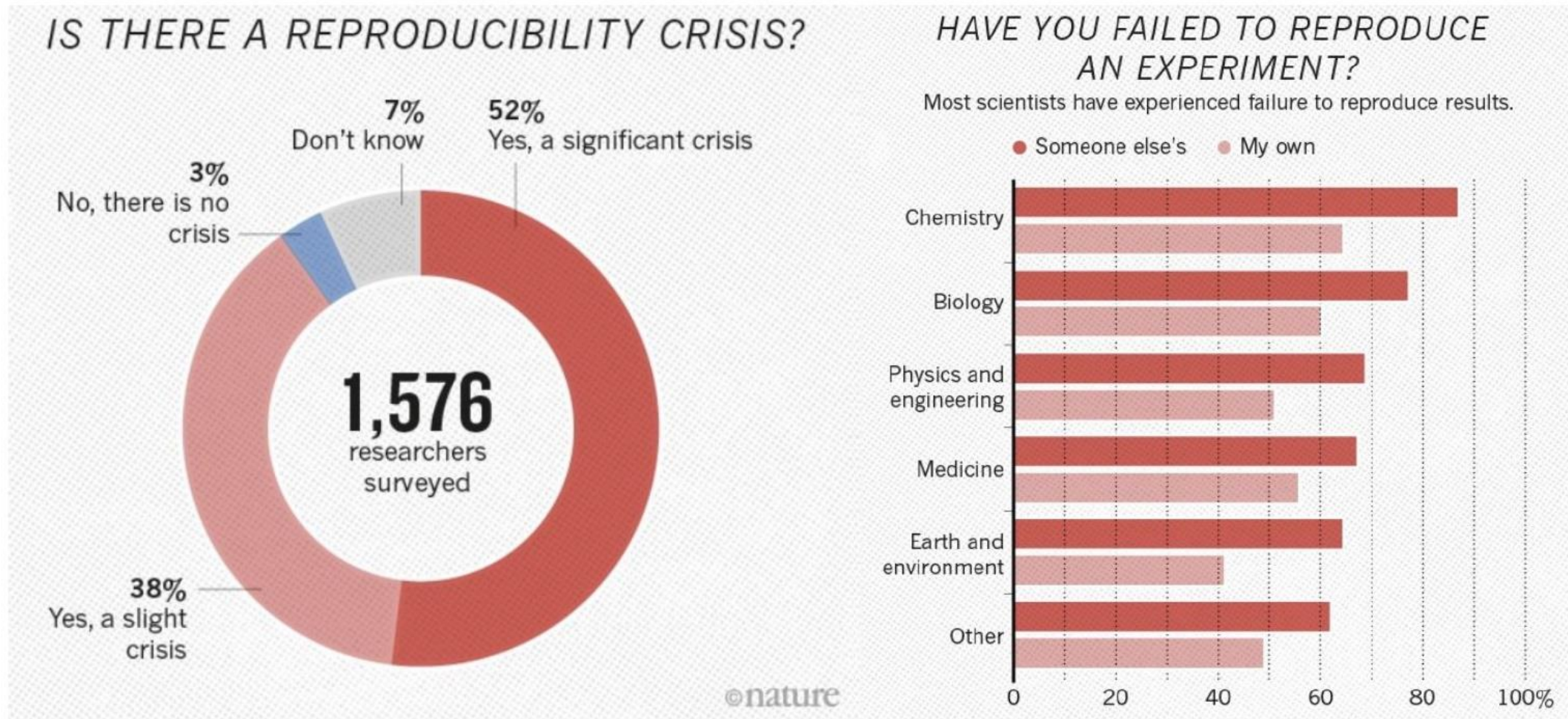
- **effect sizes** are small
- there is a **greater number and lesser preselection** of tested relationships
- there is **greater flexibility** in designs, definitions, outcomes, and analytical modes
- there is greater **financial and other interest** and prejudice

+ the propensity of **journals to publish only positive results**

+ the **"publish or perish"** culture for researchers

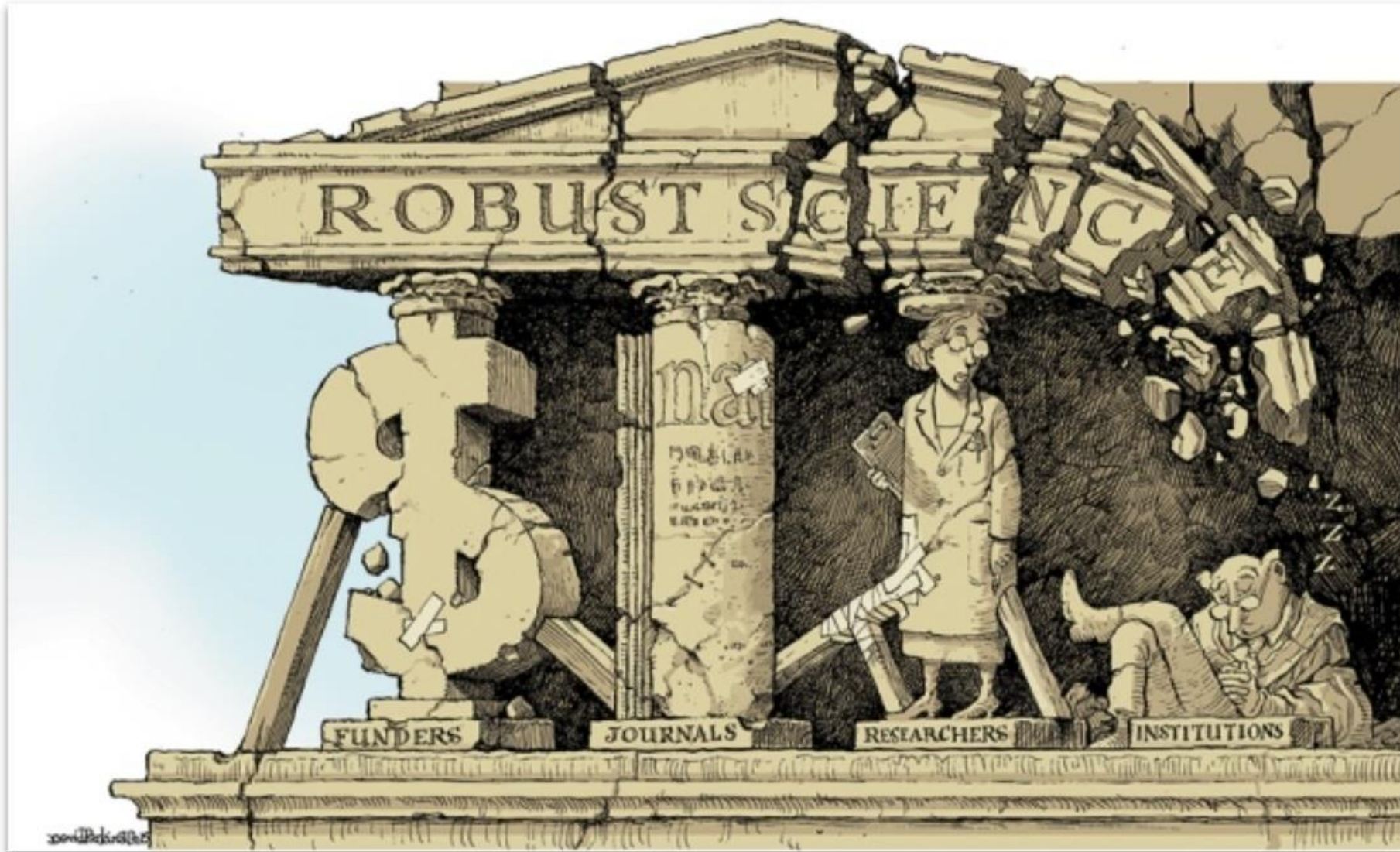
Ioannidis (2005) Why most published research findings are false. *PLoS Med* 2(8): e124 DOI: 10.1371/journal.pmed.0020124

1. An overview of the “reproducibility crisis”: awareness in 2016



"1,500 scientists lift the lid on reproducibility". Nature. 533: 452–454 - 2016

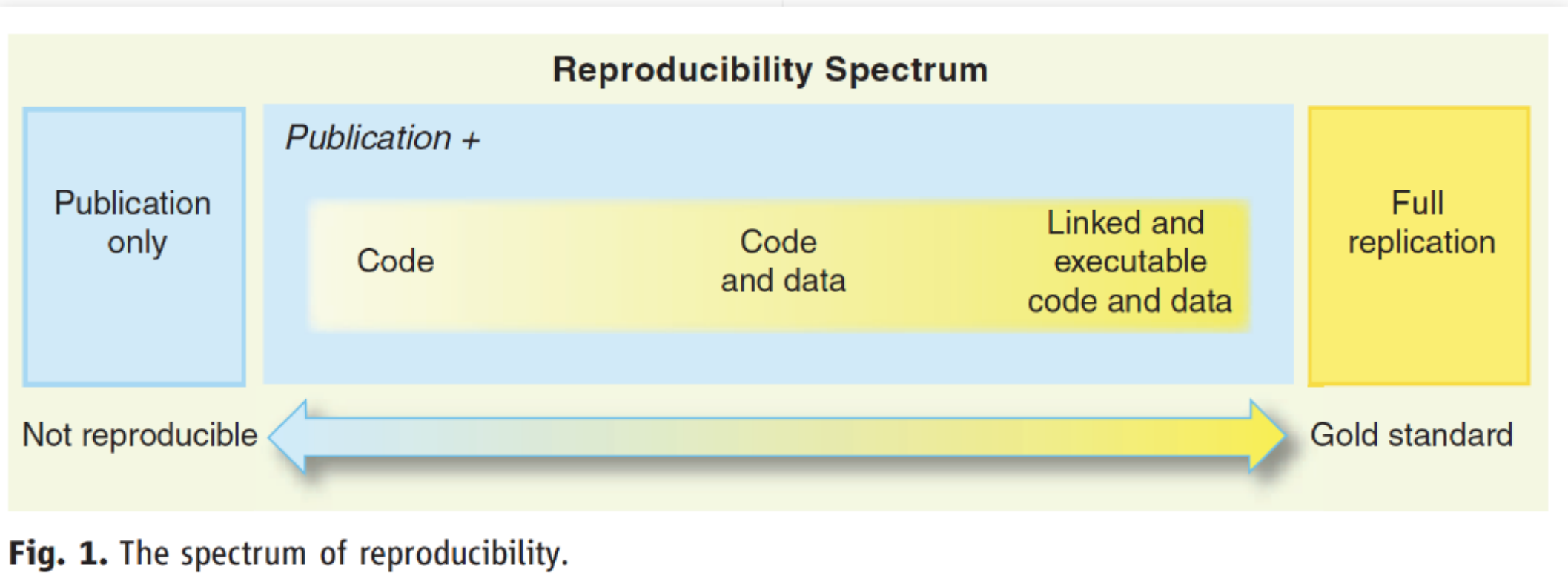
1. An overview of the “reproducibility crisis”: awareness in 2016



[Source](#)

1. An overview of the “reproducibility crisis”: not a binary phenomenon

Reproducibility is not black an white, but rather a continuum



Peng, Science, 2011

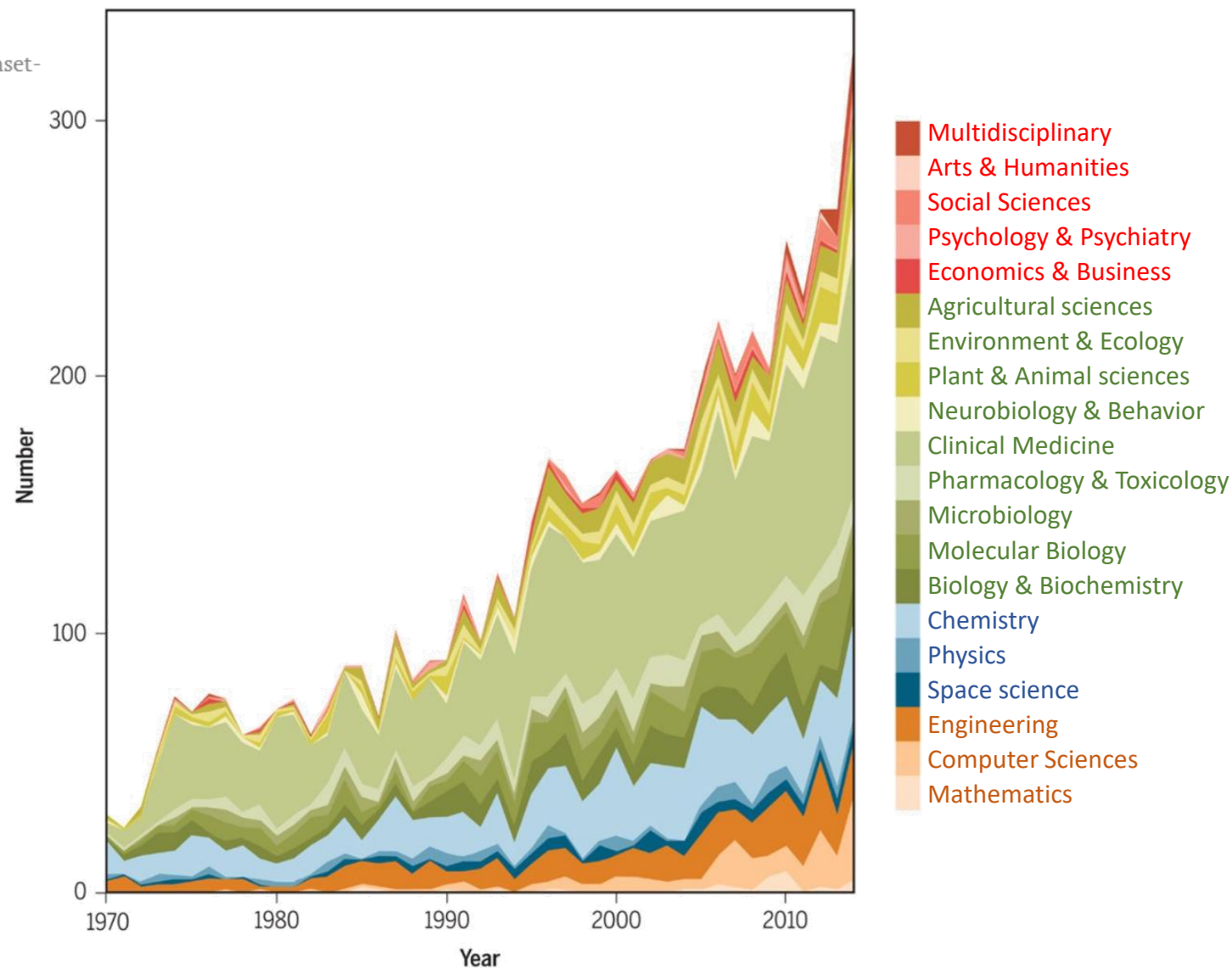
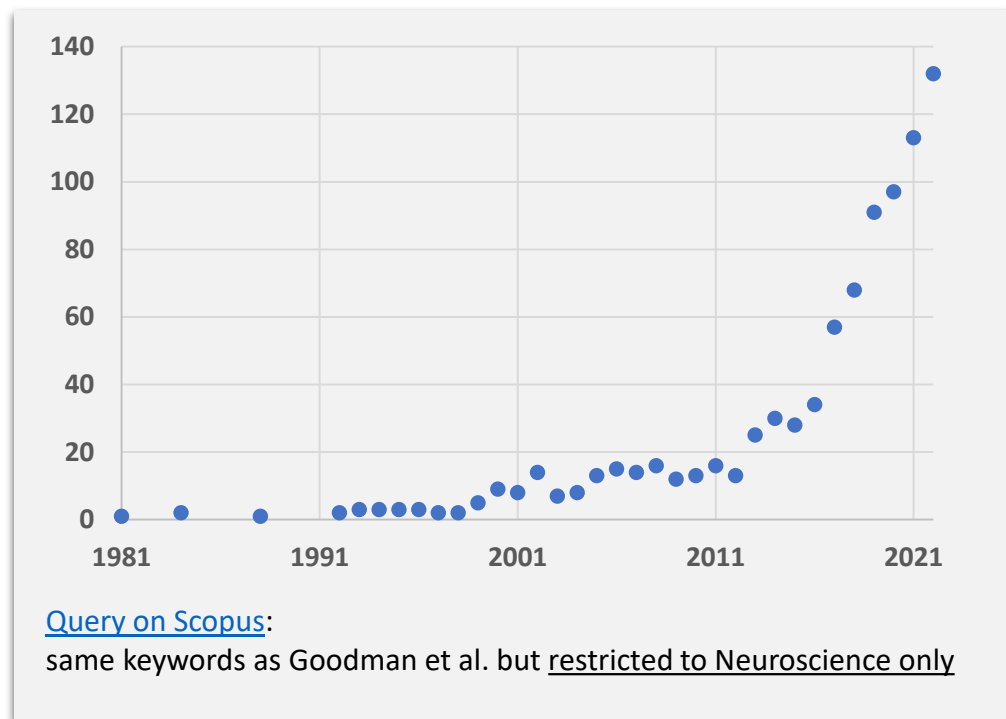
What does research reproducibility mean?

The language and conceptual framework of “research reproducibility” are nonstandard and unsettled across the sciences.

STEVEN N. GOODMAN, DANIELE FANELLI, AND JOHN P. A. IOANNIDIS [Authors Info & Affiliations](#)

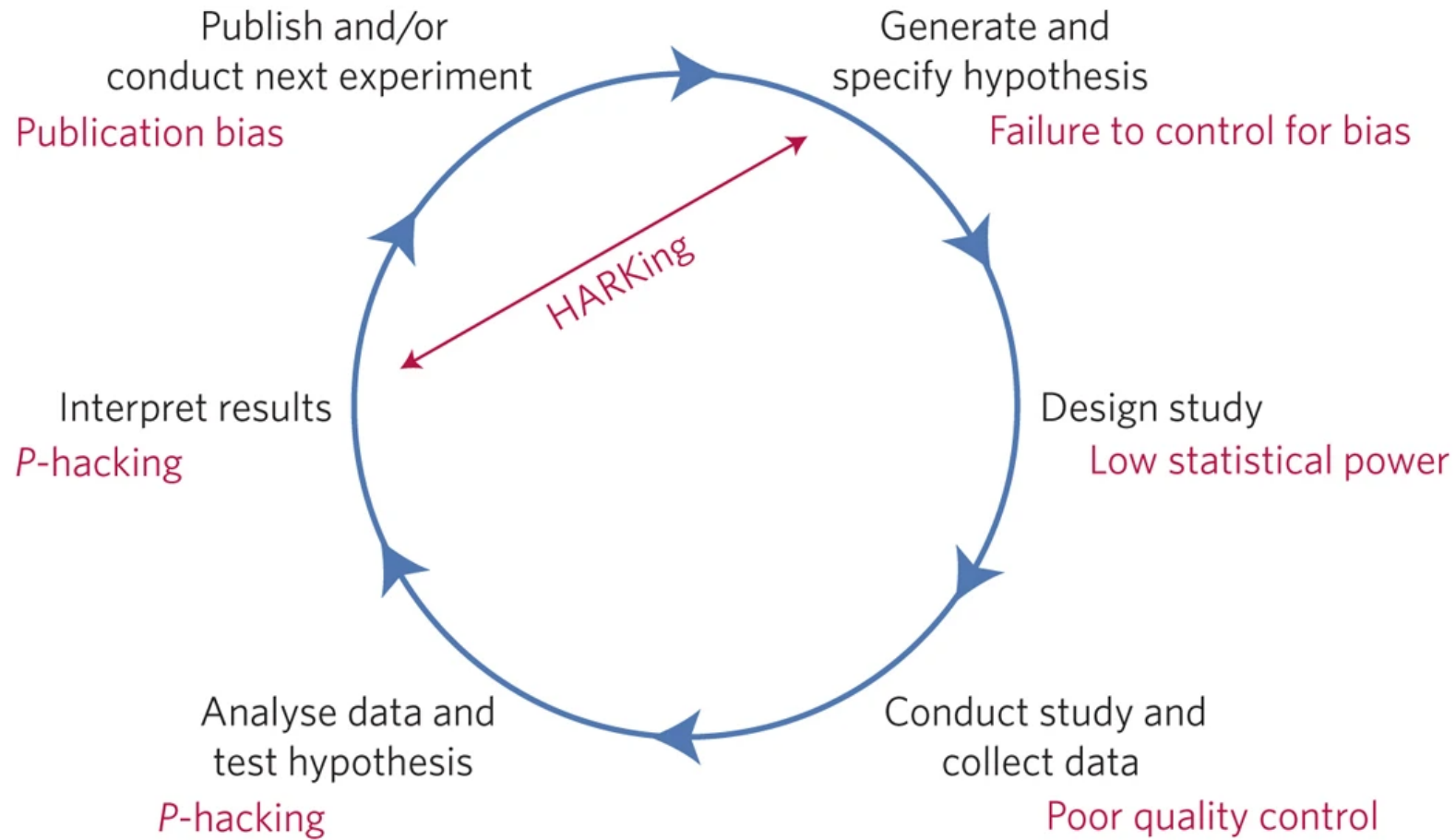
SCIENCE TRANSLATIONAL MEDICINE • 1 Jun 2016 • Vol 8, Issue 341 • p. 341ps12 • DOI: 10.1126/scitranslmed.aaf5027

2859 554



Keywords (at least 1 of the following expressions): research reproducibility, reproducibility of research, reproducibility of results, results reproducibility, reproducibility of study, study reproducibility, reproducible research, reproducible finding, or reproducible result

2. General tips to help with reproducibility: methods



Legend

Blue: An idealized version of the hypothetico-deductive model of the scientific method

Pink: threats to this model

Munafò *et al.* A manifesto for reproducible science. *Nat Hum Behav* 1, 0021 (2017). <https://doi-org.insb.bib.cnrs.fr/10.1038/s41562-016-0021>

2. General tips to help with reproducibility: methods

Table 1 | A manifesto for reproducible science.

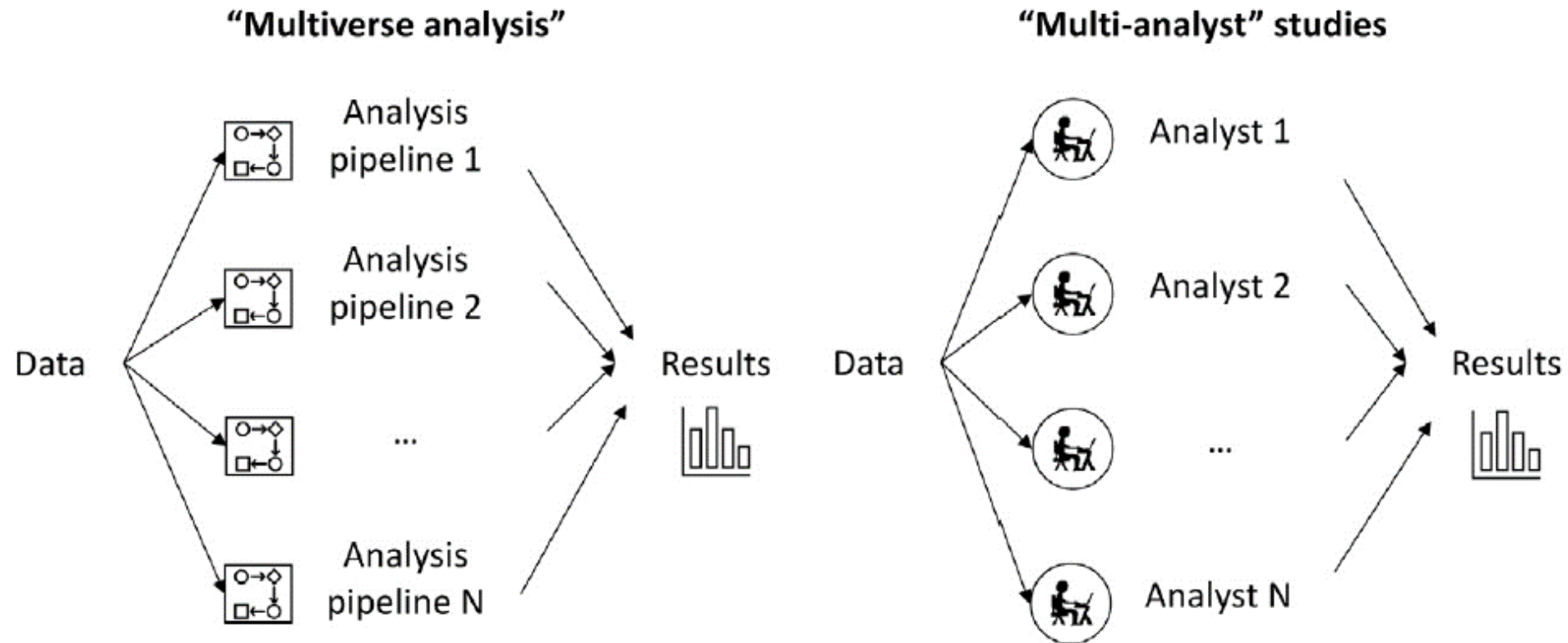
Theme	Proposal	Examples of initiatives/potential solutions (extent of current adoption)	Stakeholder(s)
Methods	Protecting against cognitive biases	All of the initiatives listed below (* to ****) Blinding (**)	J, F
	Improving methodological training	Rigorous training in statistics and research methods for future researchers (*) Rigorous continuing education in statistics and methods for researchers (*)	I, F
	Independent methodological support	Involvement of methodologists in research (**) Independent oversight (*)	F
	Collaboration and team science	Multi-site studies/distributed data collection (*) Team-science consortia (*)	I, F
Reporting and dissemination	Promoting study pre-registration	Registered Reports (*) Open Science Framework (*)	J, F
	Improving the quality of reporting	Use of reporting checklists (**) Protocol checklists (*)	J
	Protecting against conflicts of interest	Disclosure of conflicts of interest (***) Exclusion/containment of financial and non-financial conflicts of interest (*)	J
Reproducibility	Encouraging transparency and open science	Open data, materials, software and so on (* to **) Pre-registration (**** for clinical trials, * for other studies)	J, F, R
Evaluation	Diversifying peer review	Preprints (* in biomedical/behavioural sciences, **** in physical sciences) Pre- and post-publication peer review, for example, Publons, PubMed Commons (*)	J
Incentives	Rewarding open and reproducible practices	Badges (*) Registered Reports (*) Transparency and Openness Promotion guidelines (*) Funding replication studies (*) Open science practices in hiring and promotion (*)	J, I, F

Estimated extent of current adoption: *, <5%; **, 5-30%; ***, 30-60%; ****, >60%. Abbreviations for key stakeholders: J, journals/publishers; F, funders; I, institutions; R, regulators.

[Source](#)



2. General tips to help with reproducibility: methods



Botvinik-Nezer & Wager. Reproducibility in Neuroimaging Analysis: Challenges and Solutions. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* (2022) <https://doi.org/10.1016/j.bpsc.2022.12.006>

2. General tips to help with reproducibility: methods

Organizational principles:

1. Put each project in its own project directory
2. Keep together what needs to be kept together
3. Keep the **source data**
4. Make file names **human-readable**
5. Make file names **machine-readable**
6. Make file names **easy to sort**
7. **Back up your data**

[Source](#)

2. General tips to help with reproducibility: methods

XNAT @ CRNL (see wiki for details)



Bienvenue sur le XNAT du CRNL dédié au stockage des données source de tous les protocoles du CRNL !

TOUS les types de données peuvent être déposés.

Les pré-traitements, les données générées et les analyses statistiques doivent être réalisés dans les espaces disques des équipes, comme d'habitude.

Une question sur l'identification ? > merci d'ouvrir un ticket info (<https://extranet.crn1.fr/ticket>)

Une question sur les projets ? > merci d'envoyer un email à gaelle.leroux@cnrs.fr

Welcome to the CRNL XNAT dedicated to the storage of the source data of all CRNL protocols!

ALL data types can be uploaded.

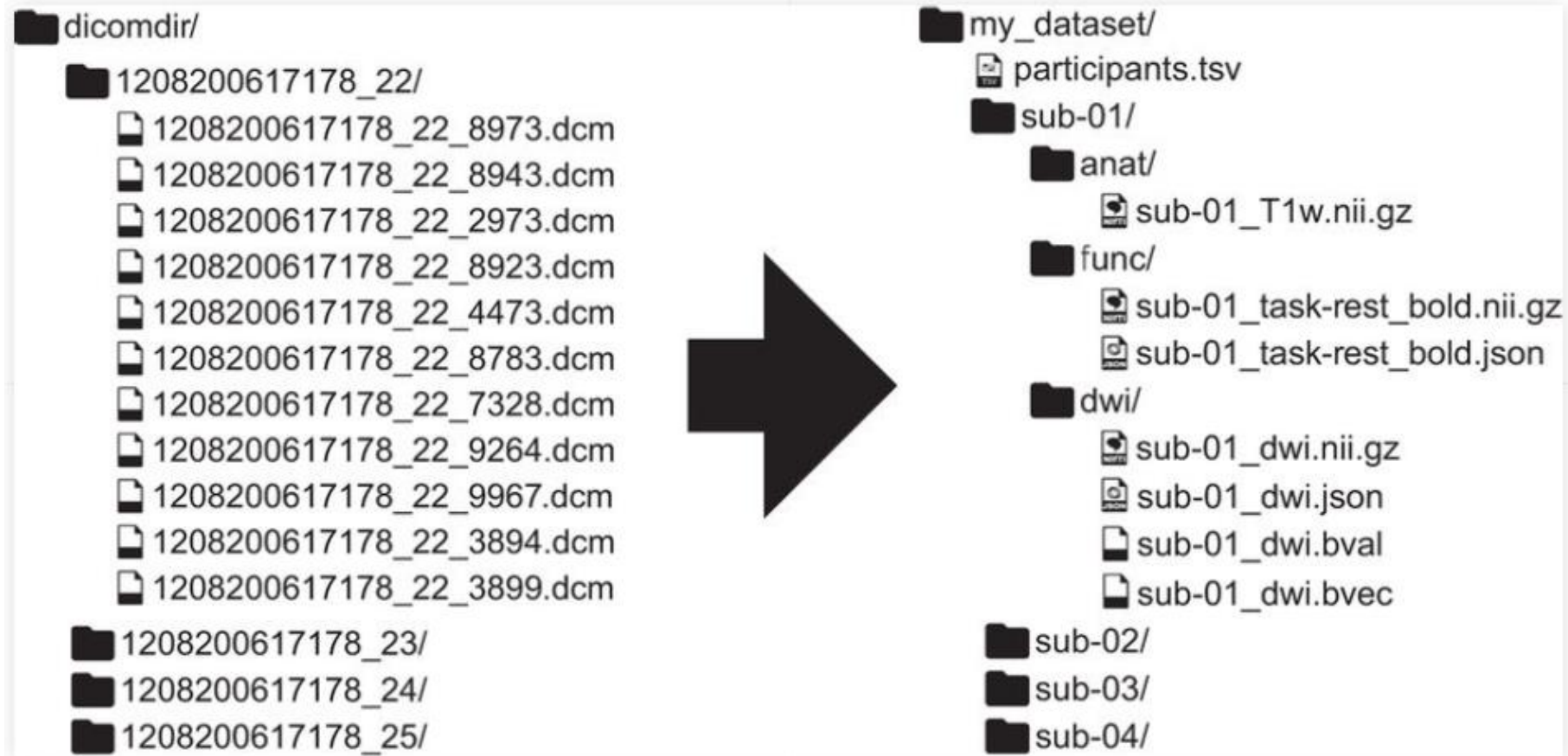
The pre-processing, derived data and statistical analyses are performed on the team disk space, as usual.

Any question about xnat login? > please, open a ticket to the IT service at the CRNL (<https://extranet.crn1.fr/ticket>).

Any question about the projects? > please, send an email to gaelle.leroux@cnrs.fr

A screenshot of the XNAT login interface. It features a 'LOGIN' dropdown menu with 'ldap1' selected. Below it is a 'USER' text input field with a small icon on the right. Underneath is a 'PASSWORD' text input field. At the bottom left, there is a link for 'Forgot login or password?'. At the bottom right, there is a blue 'Login' button.

2. General tips to help with reproducibility: methods

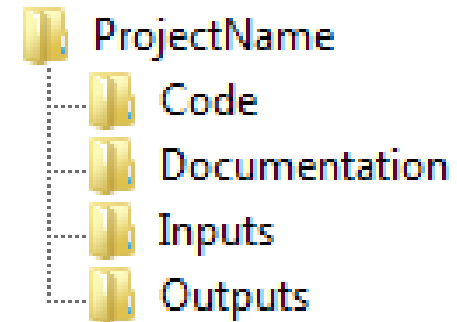


Source & further reading: Gorgolewski et al. *Sci Data*, 2016, <http://bids.neuroimaging.io>

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[Source](#)

Documentation principles:

8. Create an **overview** of your project
9. Make software **dependencies** explicit
10. Describe variables in a **codebook**
11. **Document** your code and its use
12. Give **meaningful names** to functions and variables
13. **Keep track** of how each result was produced

► Pour le code : nom explicite, indication du workflow, (version)

Usual

```
prog1.do  
prog2.do  
test.R  
final.R
```

Better

```
01_preparing_data.do  
02_stat_desc.do  
03_model1.R  
03_model2.R
```

[Source](#)

2. General tips to help with reproducibility: methods



GitLab

GitLab @ CRNL (see wiki for details)

or <https://gitlab.in2p3.fr/>



2. General tips to help with reproducibility: methods

Variable Name	Description	Type	Values or Characteristics
patientid	Patient ID	Numeric	Integers
sex	Patient Gender	Numeric	1=Female, 2=Male
proceduredate	Date of Procedure	Date, M/D/YYYY	
dob	Date of Birth	Date, M/D/YYYY	
patientrace	Patient Race	Numeric	0=Not Latino, 1=Latino,
tx	Treatment Group	Numeric	1-Tx 1, 2=Tx 2, 3=Tx 3
dischargeppt	Ppt at Discharge	Numeric	2 decimal places
notes	Notes	Character	
location	Location	Numeric	1=local, 2=regional, 3=distant
patientdied	Patient is Dead	Numeric	0=No, 1=Yes
deathdate	Date of Death	Date, M/D/YYYY	
clinicaloutcome	Clinical Outcome	Character	
outcomecomments	Outcome Comments	Character	

Source: <http://domstat.med.ucla.edu/pages/codebook2>

Further reading: Codebook cookbook - A guide to writing a good codebook for data analysis projects in medicine, Creating a codebook - Document, Discover, and Interoperate alliance

Tools: codebook generator for R: memisc

[Source](#)

2. General tips to help with reproducibility: methods

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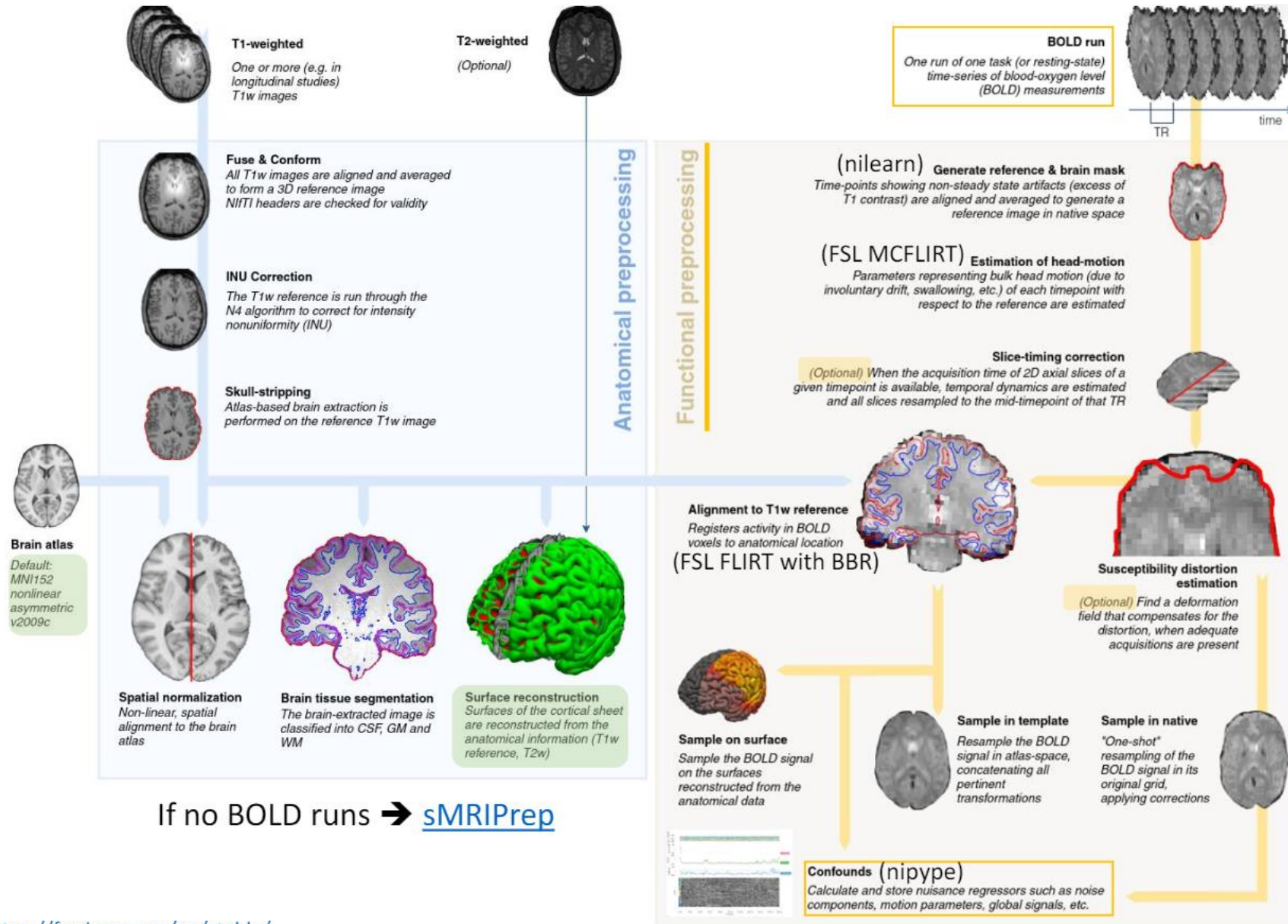
Principles of automation :

14. **Avoid manual** data manipulation steps
15. **Modularize code** rather than copy and paste
16. **Reuse code** rather than rewrite it
17. Don't comment or uncomment code sections to control program behavior
18. **Add assertions** to programs to check their operation
19. Save the random number generator seed
20. Record all intermediate results

[Source](#)

2. General tips to help with reproducibility: methods

fMRIPrep workflow



Source: <https://fmriprep.org/en/stable/>

2. General tips to help with reproducibility: methods

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18. Add assertions to programs to check their operation
19. Save the random number generator seed
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Distribution principles:

21. Store data in **open formats**
22. Process data with **open software**
23. Eliminate hard-coded paths in your code
24. Link text statements to underlying results
25. Submit code and data to a **DOI-issuing repository** and reference it in your article
26. Make the **license** of code and data explicit

[Source](#)

File format	Recommendation	Avoid
Document texte	PDF, TXT, ODT	MS Word, RTF
Feuille de calcul	ODS, CSV	MS Excel, PDF, OOXML
Base de données	SQL, SIARD, DB tables (.CSV)	MS Access, dBase (.dbf), HDF5
Données statistiques	SPSS Portable, STATA, XML, CSV, TXT	SAS et R
Images	JPEG, TIFF, PNG	DICOM
Audio	BWF, MXF, Matroska (.mka), FLAC, OPUS	<u>WAVE</u> , <u>MP3</u> , <u>AAC</u> , <u>AIFF</u> , <u>OGG</u>
Video	MXF, MKV	MPEG-4, MPEG-2, AVI, QuickTime (.mov, .qt)
Information géographique	GML, MIF/MID	ESRI Shapefiles, MapInfo, KML
Images géoréférencées	GeoTIFF (.tif, .tiff)	TIFF World File
Raster	ASCII GRID (.asc, .txt)	ESRI GRID

<https://facile.cines.fr/> service de validation des formats

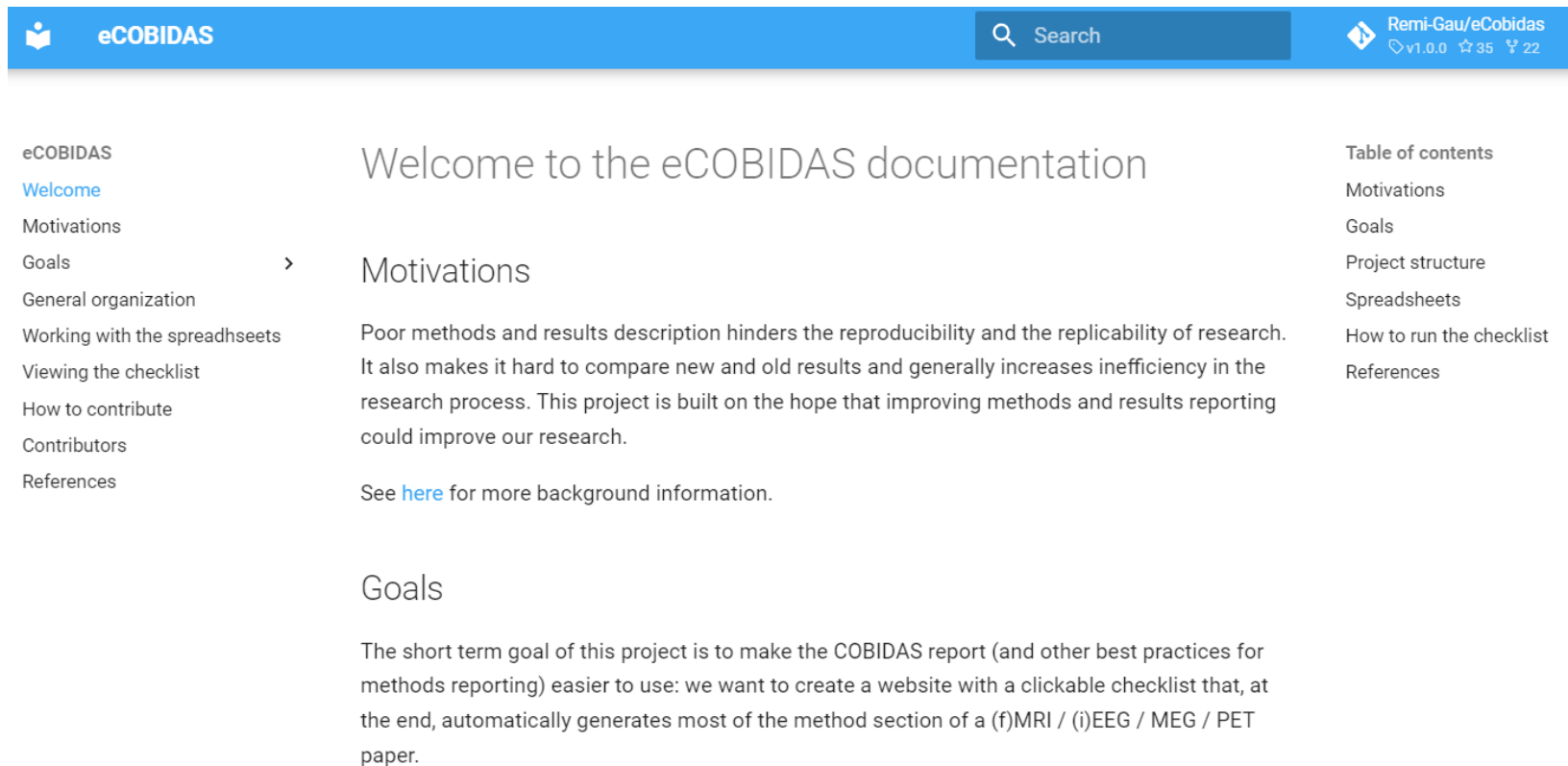
In practice, you can often work with a popular closed format and convert it to an open format. But you need to check whether the conversion alters the information, and take compensatory measures if necessary. Example: XLSX -> CSV conversion loses formatting.

[Source](#)

eCOBIDAS checklist

1. experimental design reporting,
2. image acquisition reporting,
3. preprocessing reporting,
4. statistical modeling,
5. results reporting,
6. data sharing,
7. reproducibility

For each of 7 areas of a study, a tabular listing of over 100 items to help plan, execute, report, and share research in the most transparent fashion is provided.



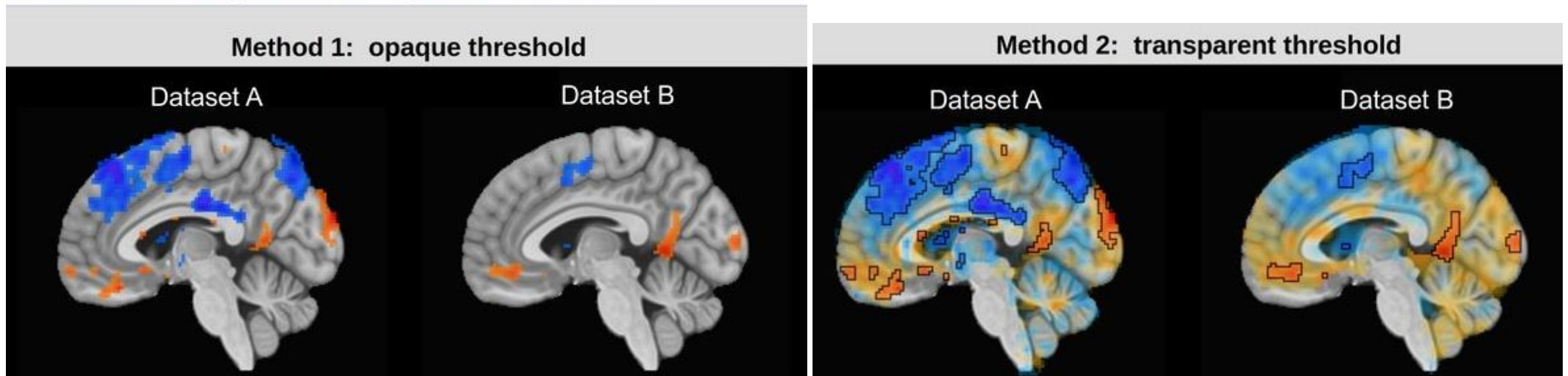
The screenshot shows the eCOBIDAS website documentation page. The header is blue with the eCOBIDAS logo on the left, a search bar in the center, and the repository name 'Remi-Gau/eCobidas' with version 'v1.0.0', stars '35', and forks '22' on the right. The main content area is white. On the left is a navigation menu with links: eCOBIDAS, Welcome, Motivations, Goals, General organization, Working with the spreadsheets, Viewing the checklist, How to contribute, Contributors, and References. The 'Motivations' link is highlighted with a right-pointing chevron. The main content area has a heading 'Welcome to the eCOBIDAS documentation' and a sub-heading 'Motivations'. Below this, it states: 'Poor methods and results description hinders the reproducibility and the replicability of research. It also makes it hard to compare new and old results and generally increases inefficiency in the research process. This project is built on the hope that improving methods and results reporting could improve our research.' A link 'here' is provided for more background information. Below this is a sub-heading 'Goals' and a paragraph: 'The short term goal of this project is to make the COBIDAS report (and other best practices for methods reporting) easier to use: we want to create a website with a clickable checklist that, at the end, automatically generates most of the method section of a (f)MRI / (i)EEG / MEG / PET paper.' On the right side of the page is a 'Table of contents' section with links to: Motivations, Goals, Project structure, Spreadsheets, How to run the checklist, and References.

<https://remi-gau.github.io/eCobidas/>

2. General tips to help with reproducibility: results of fMRI data

- Most studies do not present all results of their analysis, **hiding subthreshold ones.**
- **Hiding results negatively affects the interpretation and understanding of the study.**
- **Neuroimagers should present all results of their study, highlighting key**

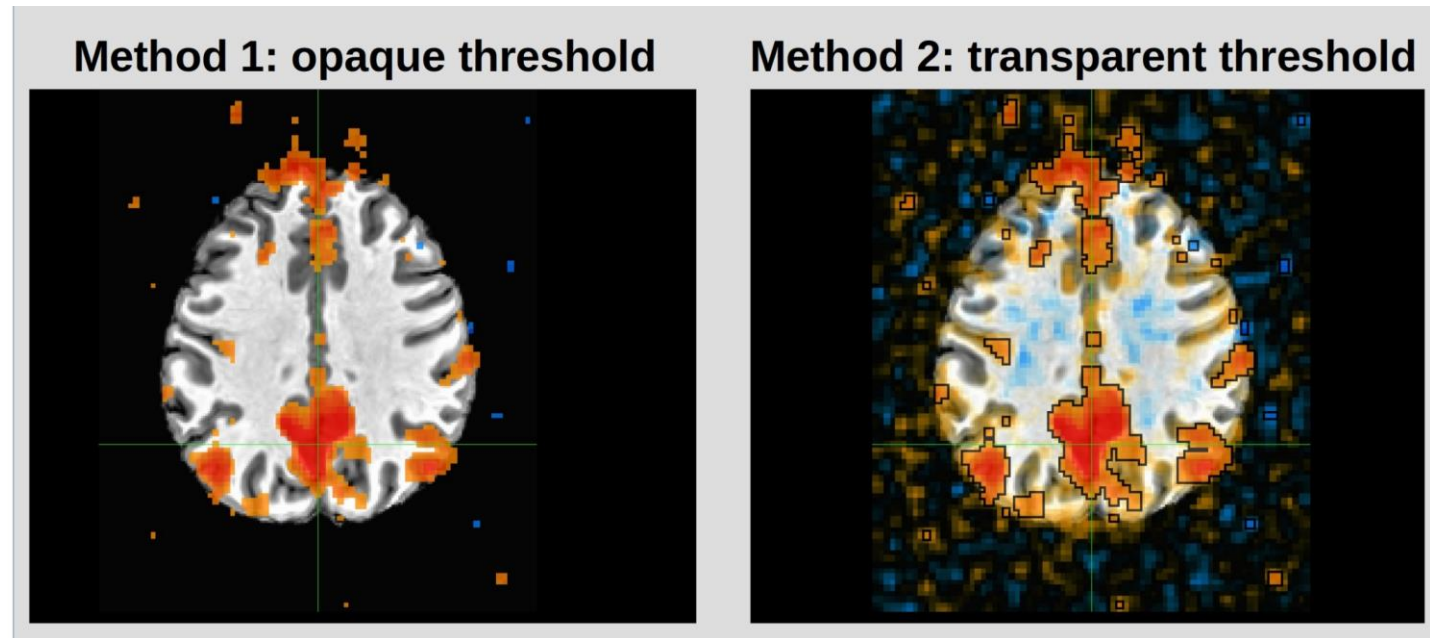
Q: Which method for viewing fMRI data makes it easier to understand the results, and to interpret how they might be similar and/or different? How would your description of the “reproducibility” of the results change when moving from the 1st to the 2nd?



Thresholds hide interesting effects!

Taylor & al. Highlight results, don't hide them: Enhance interpretation, reduce biases and improve reproducibility. *NeuroImage* (2023)

2. General tips to help with reproducibility: results of fMRI data



& other times, thresholds hide artifacts and badness.

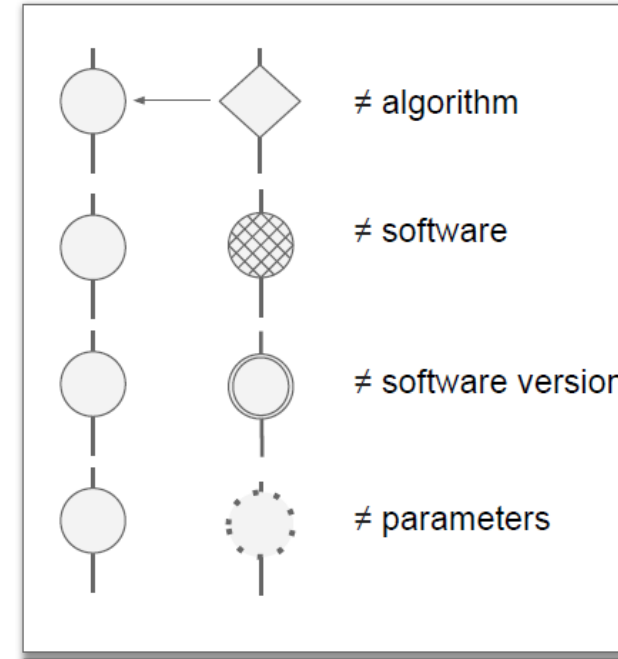
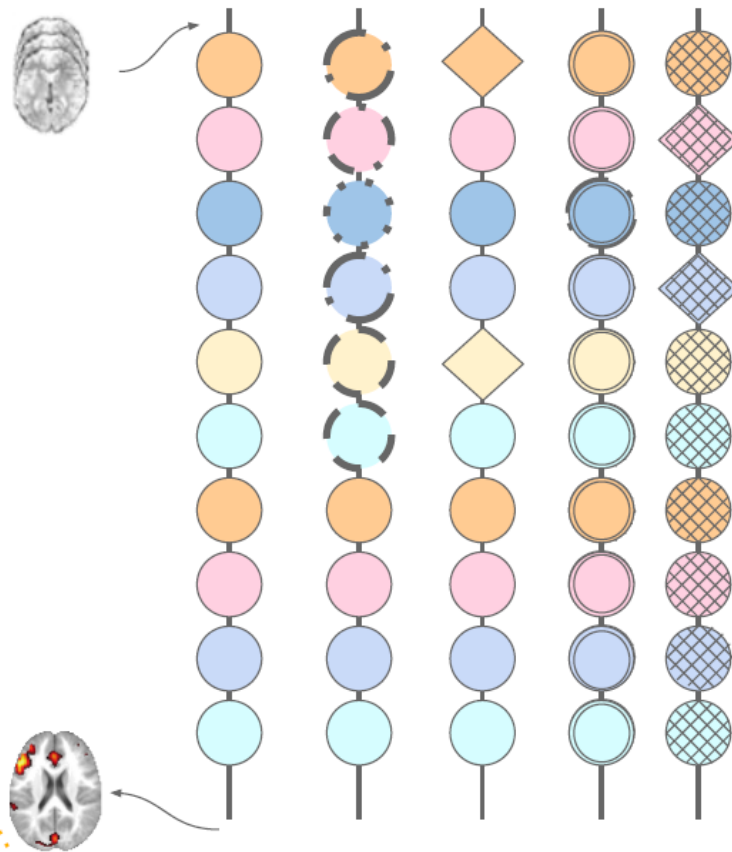
“We need to see each. Showing more results helps with quality control (QC) evaluation.

Become more confident in (or appropriately worried about!) your data.” [Paul Taylor](#)

Taylor & al. Highlight results, don't hide them: Enhance interpretation, reduce biases and improve reproducibility. *NeuroImage* (2023)

2. General tips to help with reproducibility: results of fMRI data

Analytical pipelines

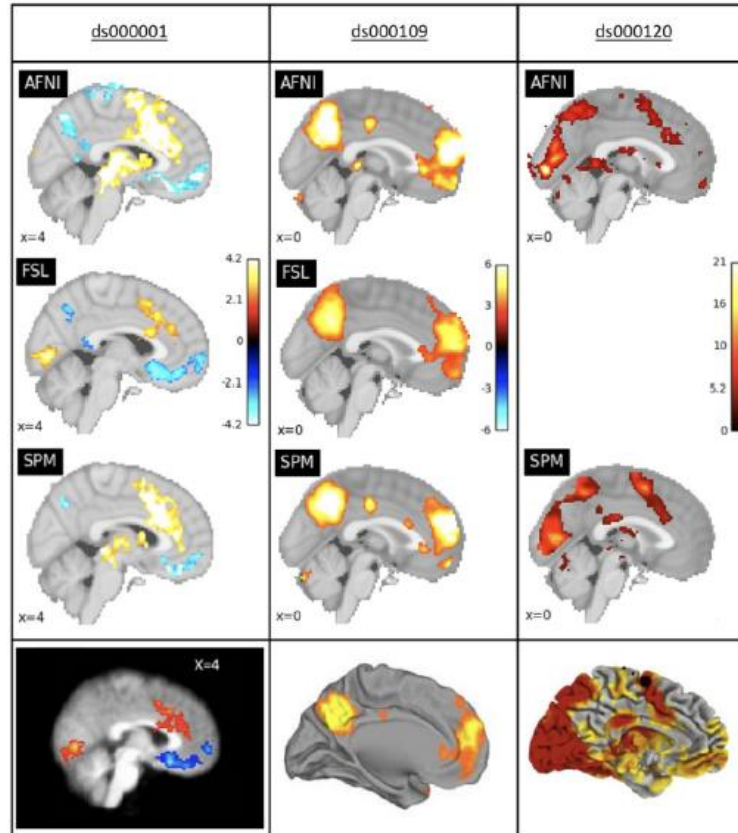


A family of "acceptable" pipelines
over 10^{30} combinations...

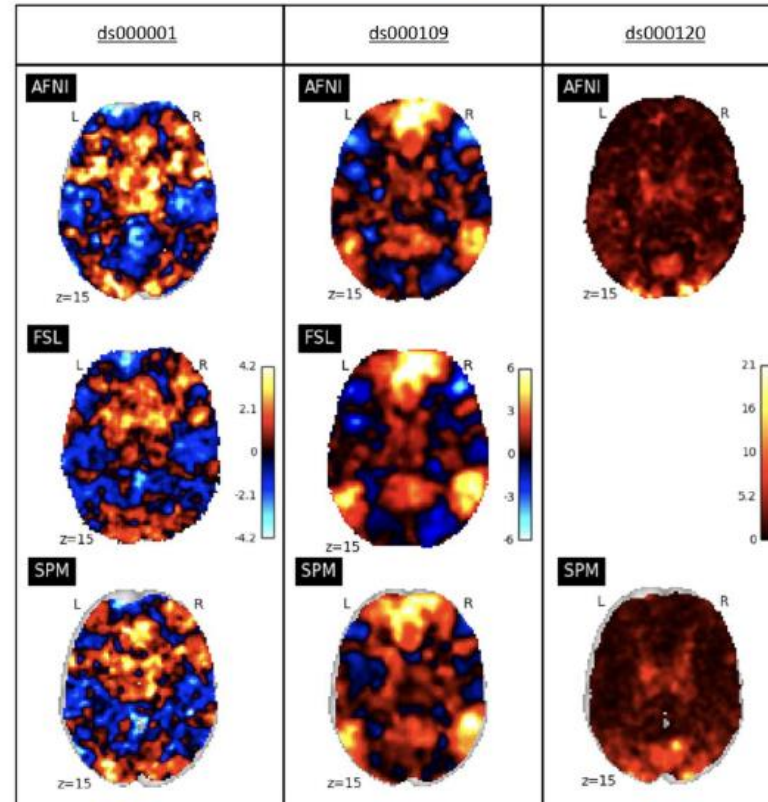
Maumet. Different analysis pipelines, different results... How to deal with analytical variability? 20th IEEE International Symposium on Biomedical Imaging (ISBI 2023), Cartagena (Colombia). ffhal-04073419f

2. General tips to help with reproducibility: results of fMRI data

Software Comparison Project



Comparison of the final results



Comparison of the statistic maps

Maumet. Different analysis pipelines, different results... How to deal with analytical variability? 20th IEEE International Symposium on Biomedical Imaging (ISBI 2023), Cartagena (Colombia). ffhal-04073419f

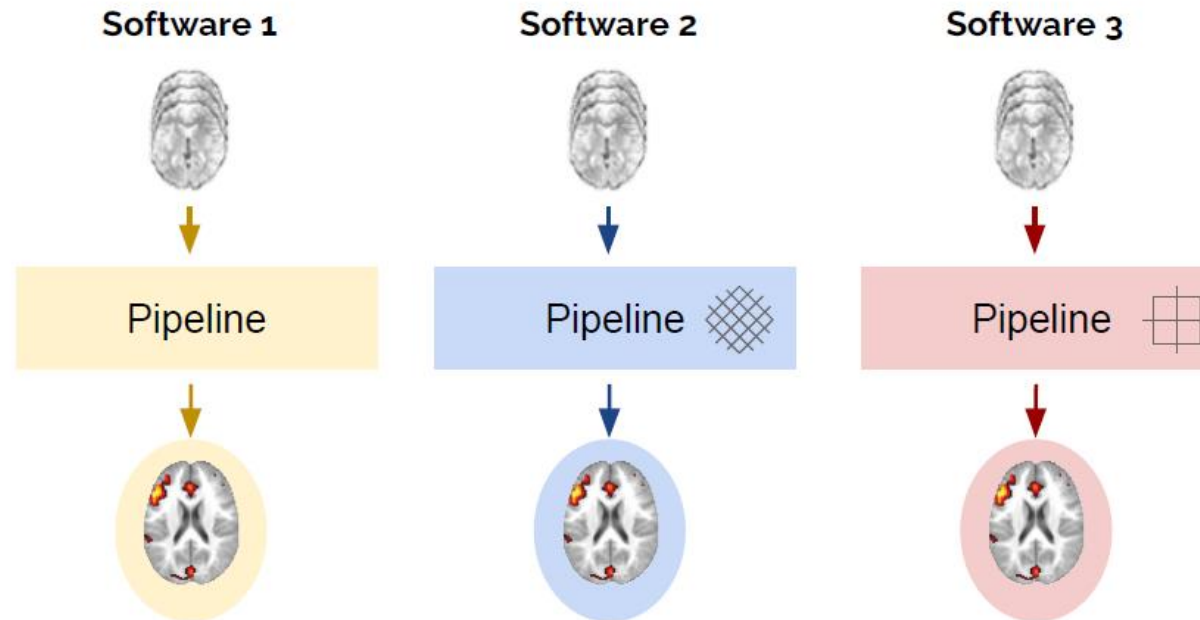
2. General tips to help with reproducibility: results of fMRI data

Variability across software

- Reproduced 3 published functional MRI studies
 - ds001, ds109, ds120 (from [Openneuro](#))
- Using 3 different software packages
 - AFNI, FSL, SPM



Alex Bowring Tom Nichols



Maumet. Different analysis pipelines, different results... How to deal with analytical variability? 20th IEEE International Symposium on Biomedical Imaging (ISBI 2023), Cartagena (Colombia). ffhal-04073419f

2. General tips to help with reproducibility: effect of analytical choices on fMRI findings

The **N**euroimaging **A**nalysis **R**eplication and **P**rediction **S**tudy

What happens when
70 independent groups of researchers
analyze the same fMRI dataset?

www.narps.info

2. General tips to help with reproducibility: results of fMRI data

Conclusions of the study:

The strongest factors in explaining the differences between results:

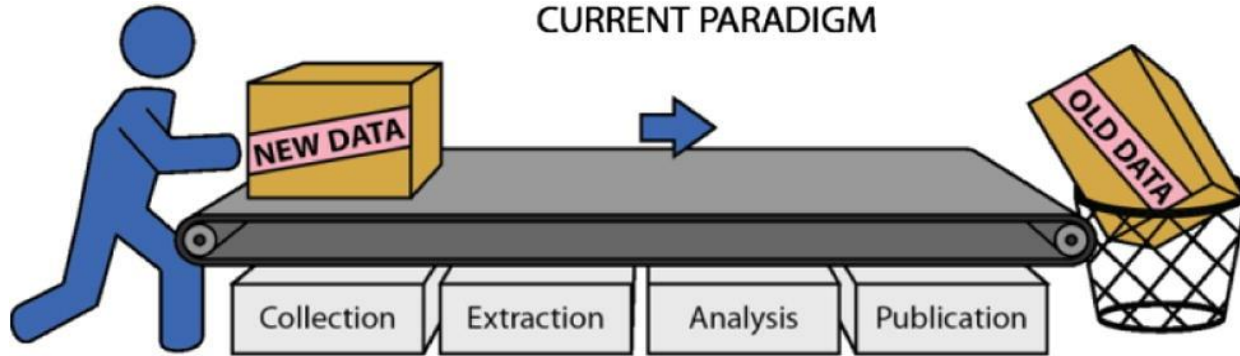
1. **Spatial smoothness** : higher FWHM lead to a higher likelihood of significant outcomes
2. **FSL vs other softs**: FSL has higher likelihood of significant results across all hypotheses
3. **Multiple correction method**
4. **No significant effect of standardized** vs customized preprocessing pipelines

Recommendations to:

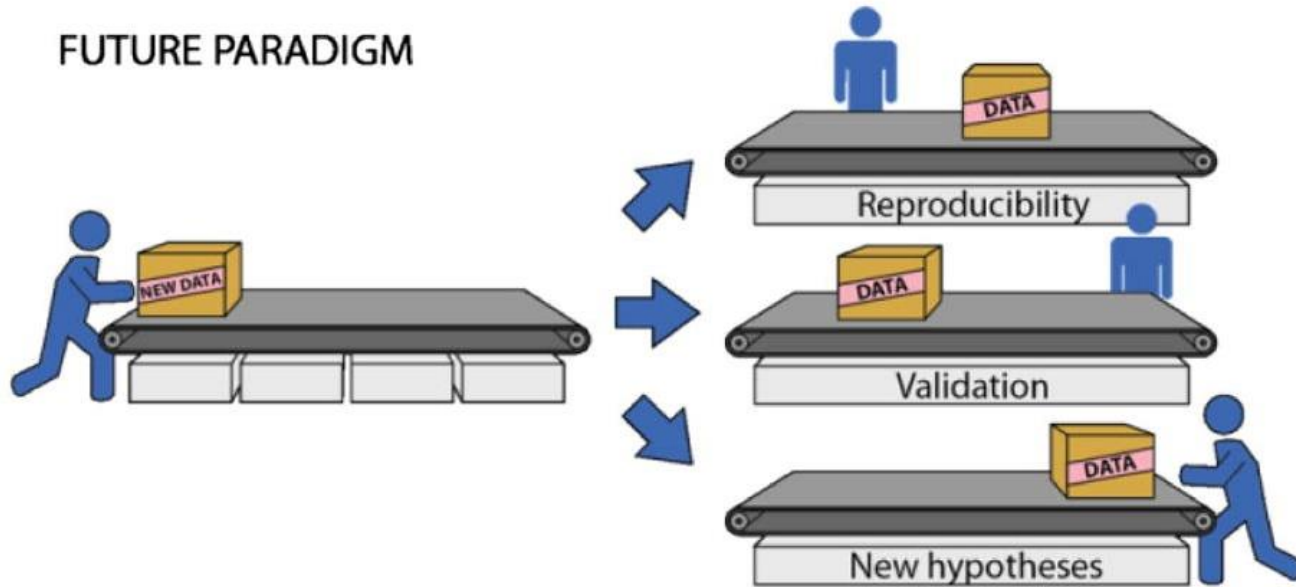
1. **Pre-register** the study, hypotheses, methods
2. **Share the pipeline, data and code** because the Mat & Methods section is never enough
3. **Share un- and thresholded maps** to allow image-based meta-analyses (e.g. on [NeuroVault](#))
4. **Use multiple pipelines** to analyse the data (“multiverse analysis”), several teams
5. Report them and **find the consensus using a meta-analysis**, not the “best” one.
6. Use **pipeline-optimization tools** to reduce analysis flexibility (e.g. [FitLins](#) & [LaConte](#) article)
7. Use **sensitivity analyses** to evaluate the effects of pipeline decisions

Botvinik-Nezer *et al.* Variability in the analysis of a single neuroimaging dataset by many teams. *Nature* **582**, 84–88 (2020).
<https://doi-org.insb.bib.cnrs.fr/10.1038/s41586-020-2314-9>

CURRENT PARADIGM



FUTURE PARADIGM



“My hope is that others will be able to reproduce some of our core findings and extend them in interesting new directions.”
–Pr. James R. Booth

Open science in the doctoral school <https://nsco.universite-lyon.fr/science-ouverte/>

French network on reproducible science: <https://www.recherche-reproductible.fr/>

UK Reproducibility Network <https://www.ukrn.org/>

[OSIRIS](#): OPEN SCIENCE TO INCREASE REPRODUCIBILITY IN SCIENCE



“Scientific integrity” Club(CRNL): <https://project.crnl.fr/IntegriteScientifique/>

NeuroImaging club meetings: <https://osf.io/sxkgq/>

Additional tools to the ones cited in the slides:

Electronic labbooks <https://dataacc.elab.one/login.php> & https://cle.inserm.fr/users/sign_in

Research Data Plan <https://dmp.opidor.fr/>

Support to data management & sharing <https://doranum.fr/>