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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.

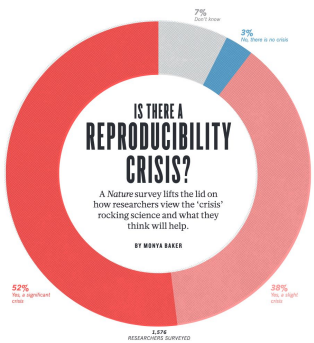
is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be postulated. Let us also consider, for computational simplicity, circumscribed 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 c 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 2×2 table, one gets PPV $= (1-\beta)R/(R$

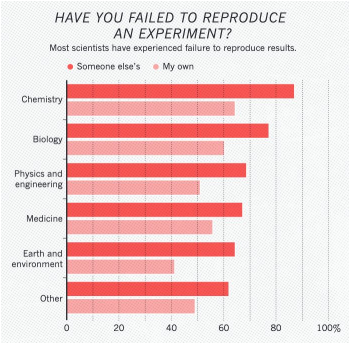
Crisis elements

- Highlighted around 2005
- Since 2010 more articles related to the non reproducibility
- Medecine is one of the most impacted discipline

Reproducibility crisis

2016





Baker, M. 1,500 scientists lift the lid on reproducibility. *Nature* **533,** 452–454 (**2016**). https://doi.org/10.1038/533452a

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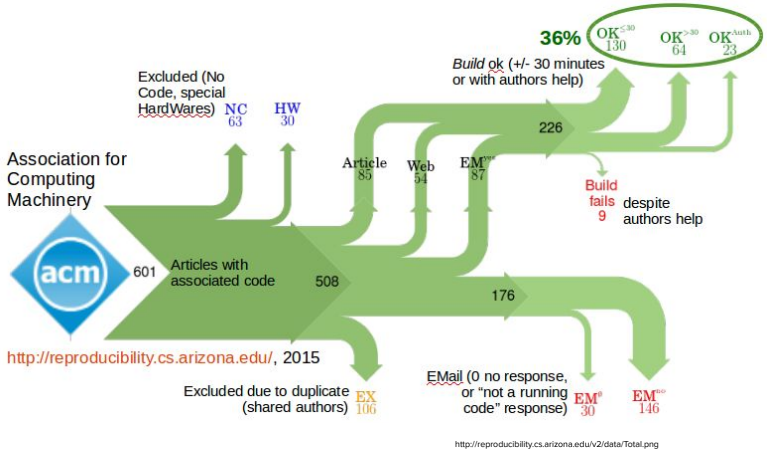
. https://doi.org/10.1038/533452a

Also in computer sciences



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. http://reproducibility.cs.arizona.edu/v2/data/Total.png

Long term negative impact of retracted papers

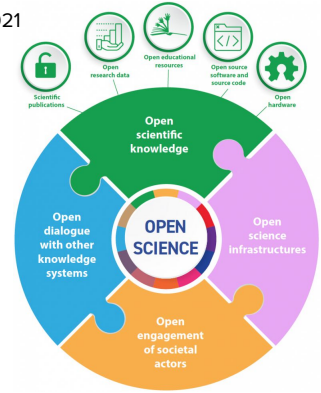
Article	Year of retraction	Citing Articles before retraction	Citing Articles after retraction	Total cites (journals indexed by Web of Science)
1. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. N ENGL J MED; APR **2013**. Estruch R, et al.	2018	1919	816	2735
2. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. LANCET; FEB 28 **1998**. Wakefield AJ, et al.	2010	642	867	1509
3. Visfatin: A protein secreted by visceral fat that mimics the effects of insulin. SCIENCE; JAN **2005**. Fukuhara A, et al.	2007	232	1192	1424
4. An enhanced transient expression system in plants based on suppression of gene silencing by the p19 protein of tomato bushy stunt virus. PLANT J; MAR **2003**. Voinnet O, et al.	2015	896	375	1271
5. Lysyl oxidase is essential for hypoxia-induced metastasis. NATURE; APR **2006**. Erler JT, et al.	2020	977	81	1058

Retraction Watch : Top 10 most highly cited retracted papers
https://retractionwatch.com/the-retraction-watch-leaderboard/top-10-most-highly-cited-retracted-papers/ 6

. https://retractionwatch.com/the-retraction-watch-leaderboard

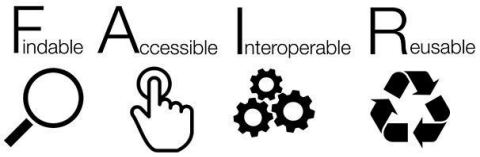
A way out: Open science and FAIR principles

2021



Graphic on page 11. UNESCO Recommendation on Open Science. CC BY IGO 3.0 C. Green

2016



Wilkinson, M., Dumontier, M., Aalbersberg, I. *et al.* The FAIR Guiding Principles for scientific data management and stewardship. *Sci Data* **3,** 160018 (2016). https://doi.org/10.1038/sdata.2016.18

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FAIR history

- Born in 2016 with *The FAIR Guiding Principles for scientific data management and stewardship*
- How to build, stock, share, use and publish data
- Make criteria to better use our data

. https://doi.org/10.1038/sdata.2016.18

www.nature.com/scientificdata

SCIENTIFIC DATA

Amended: Addendum

OPEN

SUBJECT CATEGORIES
» Research data
» Publication characteristics

Comment: The FAIR Guiding Principles for scientific data management and stewardship

Mark D. Wilkinson et al.#

Received: 10 December 2015
Accepted: 12 February 2016
Published: 15 March 2016

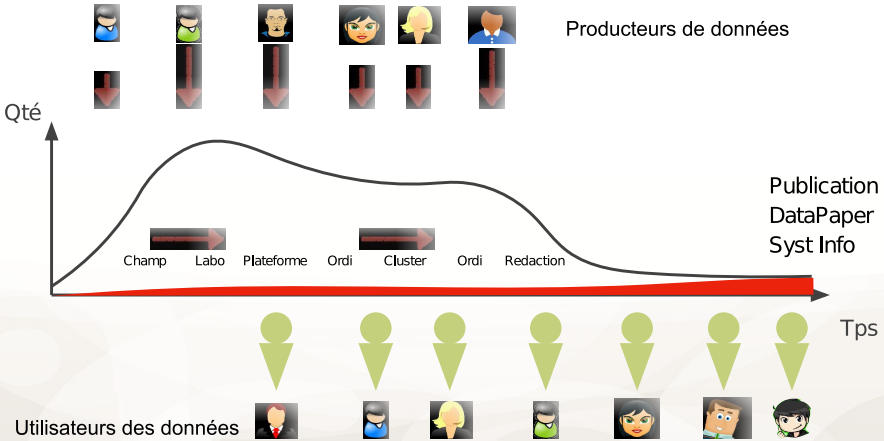
There is an urgent need to improve the infrastructure supporting the reuse of scholarly data. A diverse set of stakeholders—representing academia, industry, funding agencies, and scholarly publishers—have come together to design and jointly endorse a concise and measureable set of principles that we refer to as the FAIR Data Principles. The intent is that these may act as a guideline for those wishing to enhance the reusability of their data holdings. Distinct from peer initiatives that focus on the human scholar, the FAIR Principles put specific emphasis on enhancing the ability of machines to automatically find and use the data, in addition to supporting its reuse by individuals. This Comment is the first formal publication of the FAIR Principles, and includes the rationale behind them, and some exemplar implementations in the community.

. https://doi.org/10.1038/sdata.2016.18

Apply FAIR TO

- Your DATA
  - Data lifecycle
  - Data Management Plan (DMP)
  - Metadata
  - Data storage

Focus on the data lifecycle



Focus on the data lifecycle

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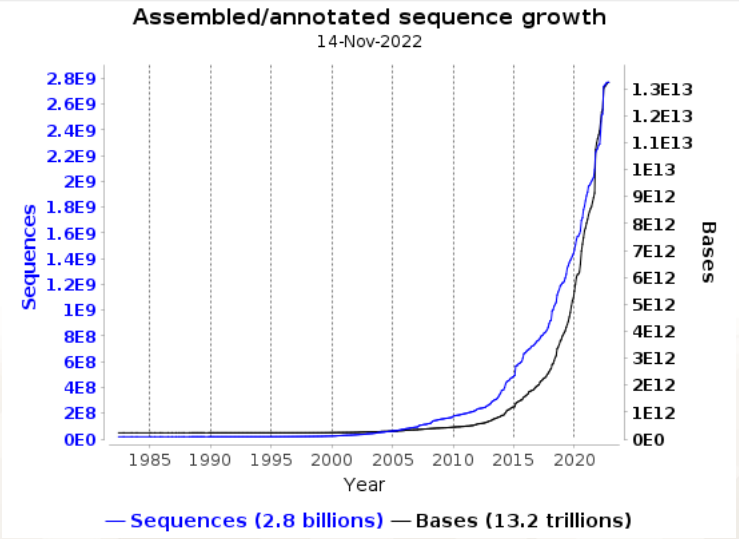
Focus on the data lifecycle



. https://www.ebi.ac.uk/ena/browser/about/statistics

Focus on the data exchange

Transfert de vos données de recherche

Comment transmettre vos données ?

Pas bien → Bien

Messagerie instantanée / **Email**

- Pas conçu pour le transfert de données
- Les communications peuvent être interceptées
- Localisation du stockage et durée de rétention inconnues

Envoi d'un disque / **Dropbox, Drive, etc**

- Risque de perte
- Risque d'accès non autorisés
- Acceptable si les données sont chiffrées

Cloud privé / **Service d'un consortium**

- Optimisé pour le transfert de données scientifiques
- Sécurisé
- Support gratuit

Cost of not having FAIR research data

Cost-Benefit analysis for FAIR research data

Apply FAIR TO

- Your DATA
  - Data lifecycle
  - Data Management Plan (DMP)
  - Metadata
  - Data storage
- Your scripts, environment...
  - Objective of this training

FAIR principles

Findable

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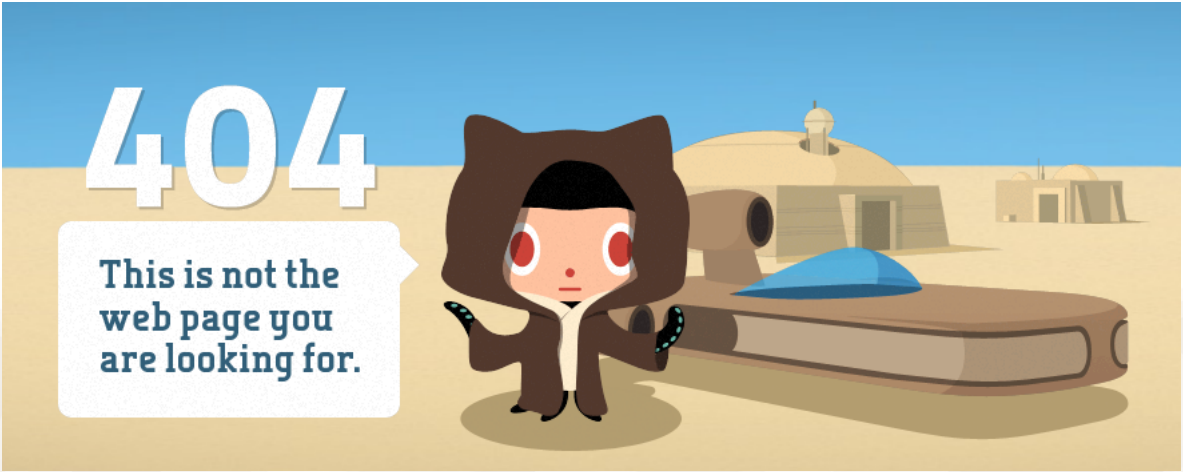
PID
Repository

8
https://doi.org/10.1038/sdata.2016.18


404
This is not the web page you are looking for.

To be Findable

- (meta)data are assigned a globally unique and persistent identifier
- data are described with rich metadata
- metadata clearly and explicitly include the identifier of the data it describes
- (meta)data are registered or indexed in a searchable ressource

FAIR principles

Findable

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PID
Repository

Accessible

https://nilsfirstworldproblems.tumblr.com/post/147555650875/i-cant-reach-the-top-shelves-of-the-kitchen

Protocols
(free, open, auth.)

https://doi.org/10.1038/sdata.2016.18

To be Accessible

- (meta)data are retrievable by their identifier using a standardized communication protocol
- the protocol is open, free, and universally implementable
- the protocol allows for an authentication and authorization procedure, where necessary
- metadata are accessible, even when the data are no longer available

FAIR principles

Findable

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Protocols
(free, open, auth.)

Interoperable

By Unknown author - Popular Science Monthly Volume 88, Public Domain, https://commons.wikimedia.org/w/index.php?curid=22614407

Standards
(format, vocabulary)

10
https://doi.org/10.1038/sdata.2016.18

To be Interoperable

- (meta)data use a formal, accessible, shared, and broadly applicable language for knowledge representation.
- (meta)data use vocabularies that follow FAIR principles
- (meta)data include qualified references to other (meta)data

FAIR principles

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Standards
(format, vocabulary)

Reusable

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Metadata
License
Origin

11
https://doi.org/10.1038/sdata.2016.18

To be Reusable

- meta(data) are richly described with a plurality of accurate and relevant attributes
- (meta)data are released with a clear and accessible data usage license
- (meta)data are associated with detailed provenance
- (meta)data meet domain-relevant community standard

To be Reusable

A point on the licences

- number different types of licences from proprietary to totally free AND open
- more than 50 different kinds
- No licence = authors' rights
- France = support for free and open data

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Recherche dans GitHub par type de licence

Vous pouvez filtrer les référentiels en fonction de leur licence ou famille de licences à l'aide du qualificateur `license` et du mot clé de licence exact :

Licence	Mot clé de licence
Academic Free License v3.0	`afl-3.0`
Licence Apache 2.0	`apache-2.0`
Licence Artistic 2.0	`artistic-2.0`
Licence logicielle Boost 1.0	`bsl-1.0`
Licence BSD « simplifiée » à 2 clauses	`bsd-2-clause`
Licence BSD « nouvelle» ou «révisée» à 3 clauses	`bsd-3-clause`

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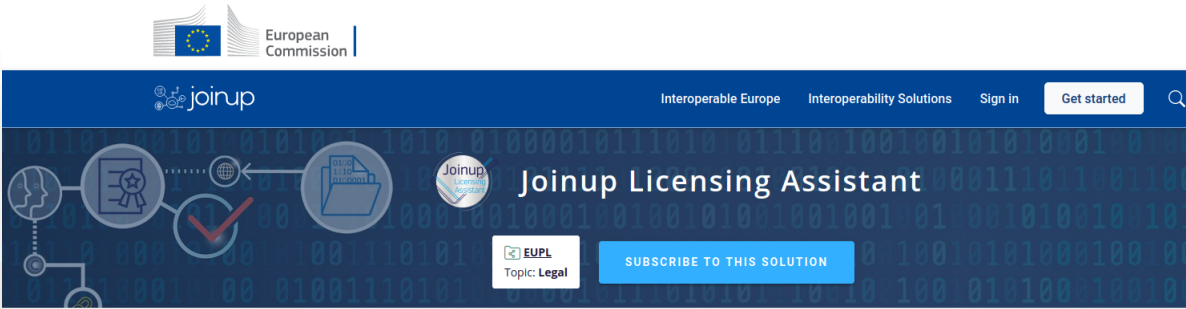

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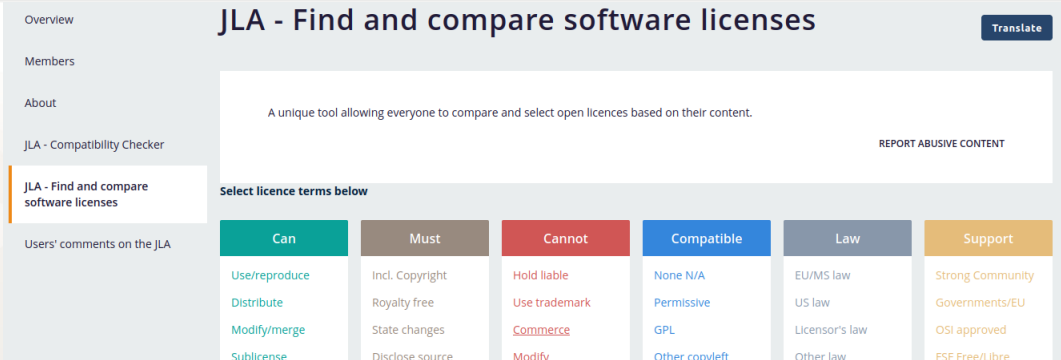

To be Reusable

A point on software archive

- Git-like (github, gitlab) are web services not archive
- Software are fragile

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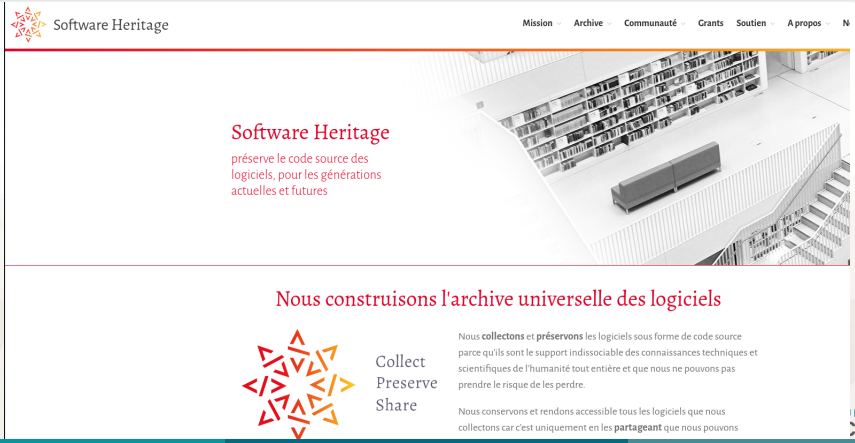

FAIR tools


Findable


Accessible


Interoperable


Reusable

Data

ENA
European Nucleotide Archive

FAIRsharing.org
standards, databases, policies

LibreOffice
The Document Foundation

DMP OPIDoR

Software and analyses

doi

HAL
open science

GitLab

CONDA

docker

jupyter

eLabFTW

snakemake

CeCILL

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A complete integrated FAIR environment

The Galaxy project

A complete integrated FAIR environment

The Galaxy project

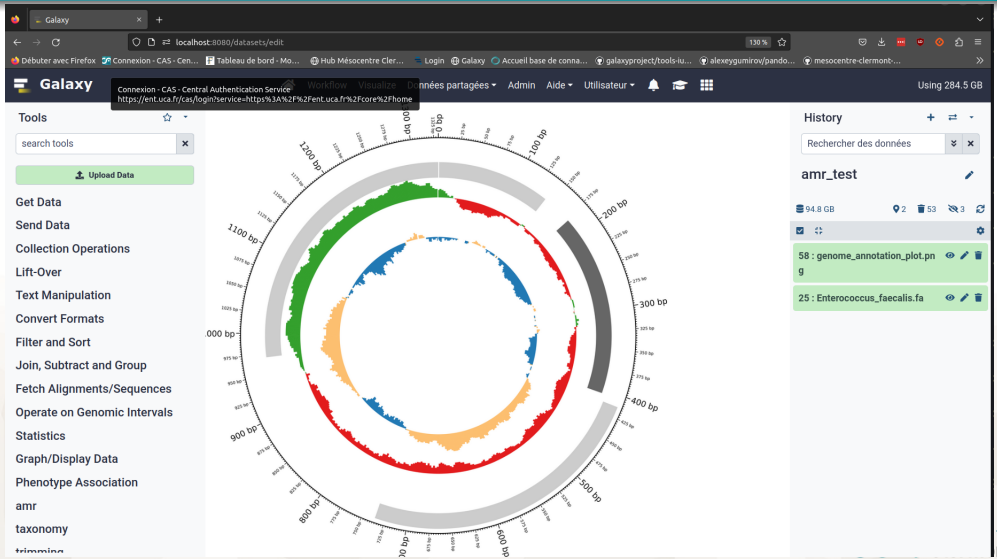
Galaxy

Galaxy is an open-source platform for FAIR data analysis that enables users to :

- Use tools from various domains (that can be plugged into workflows) through its graphical web interface.
- Run code in interactive environments (RStudio, Jupyter...) along with other tools or workflows.
- Manage data by sharing and publishing results, workflows, and visualizations.
- Ensure reproducibility by capturing the necessary information to repeat and understand data analyses.

A complete integrated FAIR environment

The Galaxy project



A complete integrated FAIR environment

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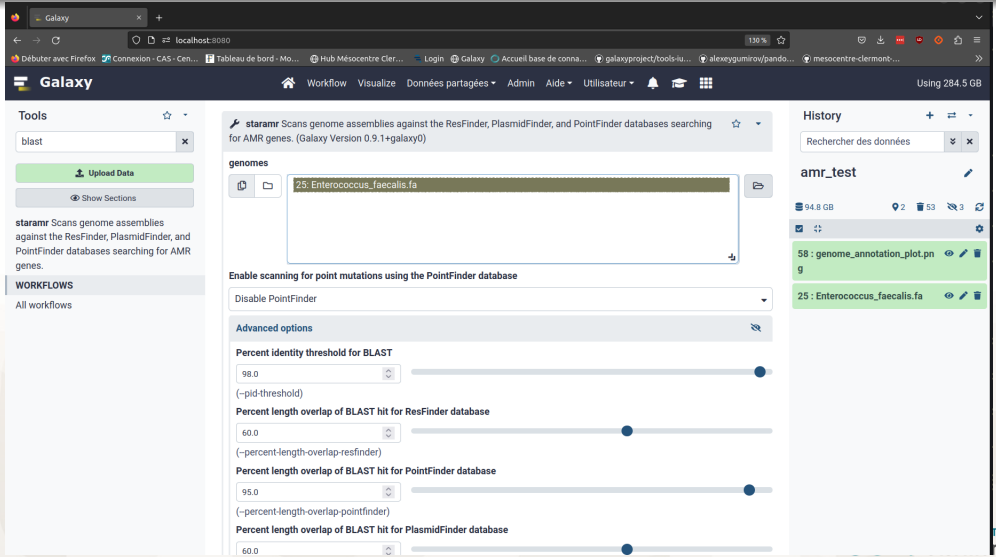
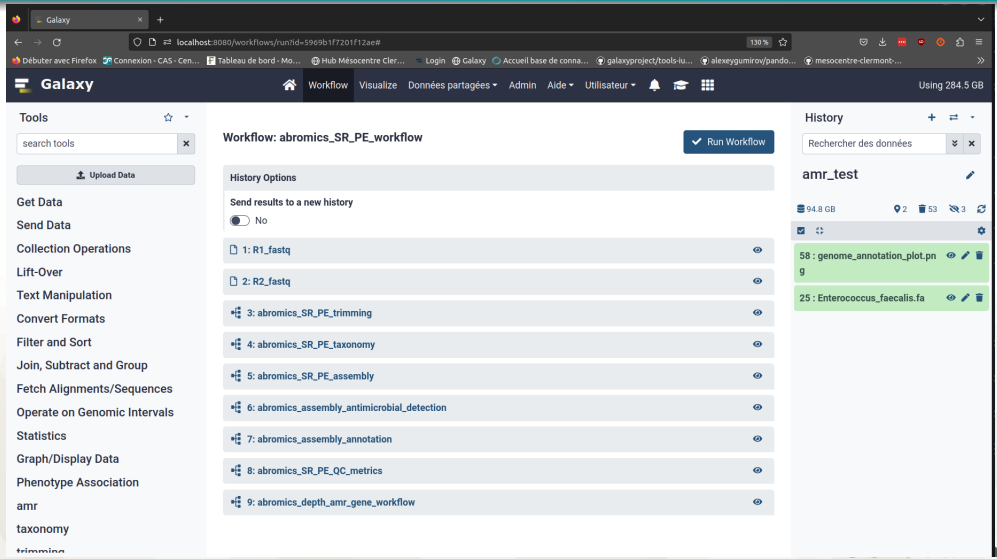


A complete integrated FAIR environment

The Galaxy project



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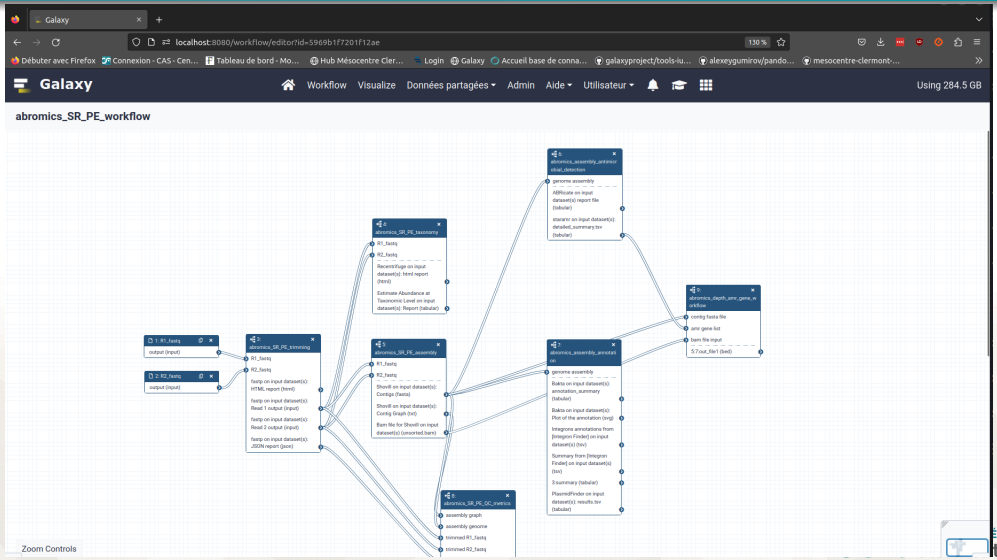

A FAIR approach at any level

"One practice to rule them all, One practice to find them, One practice to bring them all and in the FAIR bind them."

A FAIR approach at any level

"One practice to rule them all, One practice to find them, One practice to bring them all and in the FAIR bind them."

Improvement for who ?

At each level a good practice help you

- Long term efficiency to a bioinformatician
- stop wasting time for a beginner