Promoting reproducibility in bioinformatics with Reprohackathons

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In experimental sciences, variability of the results is mainly due to:

- **Biological variations**
  - Random nature of measured phenomena;
  - Different subjects, organisms, samples.

- **Technical variations**
  - Small changes in experimental conditions;
  - Noise of measurement tool;
  - Sample preparation.

Even with all things equal otherwise
1 Bioinformatics and reproducibility

Experimental variability: Conséquences?

- The same experiment gives different results
- The same experiment leads to the same scientific interpretation (hopefully)

Hypothesis $\rightarrow$ Experiment $\rightarrow$ Observation

Experiment $\rightarrow$ Observation

Experiment $\rightarrow$ Observation

Experiment $\rightarrow$ Observation

Same conclusion?
2 Computational reproducibility

**Computational variability**

In data analysis: computers and programs are supposed to be exact!
⇒ perfect reproducibility? (Hint: No)

- Different versions of operating system;
- Different versions of tools used;
- Different hardware;
- Random nature of some algorithms (simulations, etc.);
- Numerical instability;
- Parallel algorithms;
- Poor method description;
- etc.
Computational reproducibility

We define several *levels* of reproducibility (Cohen-Boulakia et al., FGCS, 2017):

- **Repeat:** The data analysis experiment is performed in the exact same computational setting as the original experiment. In that case, results should be exactly the same without any variation. This necessitate to gather as many information as possible about the initial experiment, i.e. all tools versions, all operating system library versions, the state of the random number generator, etc.;

- **Replicate:** The data analysis experiment can be performed in a slightly different environment (different tool versions, different library versions, different random seeds, etc.), but the general protocol remains the same. In that case, results are not exactly the same, but scientific interpretation should be identical;

- **Reproduce:** The data analysis experiment aims at validating the scientific hypothesis, and can be performed in a different environment and with a different protocol (different tools, different workflow, etc.). This level of reproducibility gives us the best level of confidence about the quality of the results.
2 Computational reproducibility

Available tools

Input Data --> Environment layer

Environment layer:
- Env 1: Tools
- Env 2: Tools
- Env 3: Tools
- Env 4: Tools

Workflow layer:
- nextflow
- CONDA

Execution layer:
- Cloud
- Cluster
- Local

Versioning:
- git

Data layer:
- Data

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2 Computational reproducibility

Actual usage?

Number of mentions of "Snakemake" or "Nextflow" in Nature or Science:

More and more data intensive biology + more and more adoption of workflow systems. But : Not there yet!!!
3 Promoting good practices

How to promote better practices for data analysis?

- Trainings for biologists & bioinformaticians practitioners (CNRS courses, Pasteur course, etc.)
- Workshops, Hackathons
- Dedicated Master’s programs!
4 Reprohackathons: hackathons for colleagues

**First reprohackathons (GDR MADICS)**

https://ifb-elixirfr.github.io/ReproHackathon/

Goal: To test the capacity of current workflows to reproduce a published scientific experiment, in **2 days**.

- 2017 - Gif sur Yvette: RNA-Seq data analysis workflow;
- 2018 - Lyon: Comparison of phylogenetic tree inference programs;

Workflows: Snakemake, Nextflow, CWL, Galaxy, etc.
Reprohackathon: hackathons for students

Reprohackathons: program for Master’s students

Master Program since 2020
Reprohackathon

- 3-4 months program (Sept-Dec)
- 1st part: Theoretical courses + Practicals (Containers, Workflows, versioning, etc.)
- 2nd part: Intense project (Reprohackathon)
Reprohackathon: hackathons for students

Theory + practicals
We give an article analyzing large sequencing dataset (RNA-Seq)

Students need to read and understand the article and the data analysis

Then in autonomy and in small groups, they have to:
- Re-implement it as a reproducible workflow using the ecosystem (Containers, HPC, Nextflow/Snakemake, git, etc.)
- Run it on a cloud infrastructure (IFB Cloud)
- Interpret and compare their results

Evaluation is based on:
- Code readability
- Our ability to run the data analysis without issue
- Final defense
Interesting findings

At a first look, students results were poorly reproducible:
5 Reprohackathon: hackathons for students

Interesting findings

But if we take the final statistical analysis apart (a lot of decisions to take here):
Thank you for your attention

GitHub

nextflow

Docker Hub

quay.io

Singularity

TARS

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