Combining Tools for Reproducible Research with Snakemake

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Reproducibility is rarer than you think

The results of only 26% out of 204 randomly selected papers in the journal Science could be reproduced.[1]

[1] Stodden et. al (2018). "An empirical analysis of journal policy effectiveness for computational reproducibility". PNAS. 115 (11): 2584-2589

> Many journals are revising author guidelines to include data and code availability.
>
> (...) an improvement over no policy, but currently insufficient for reproducibility.

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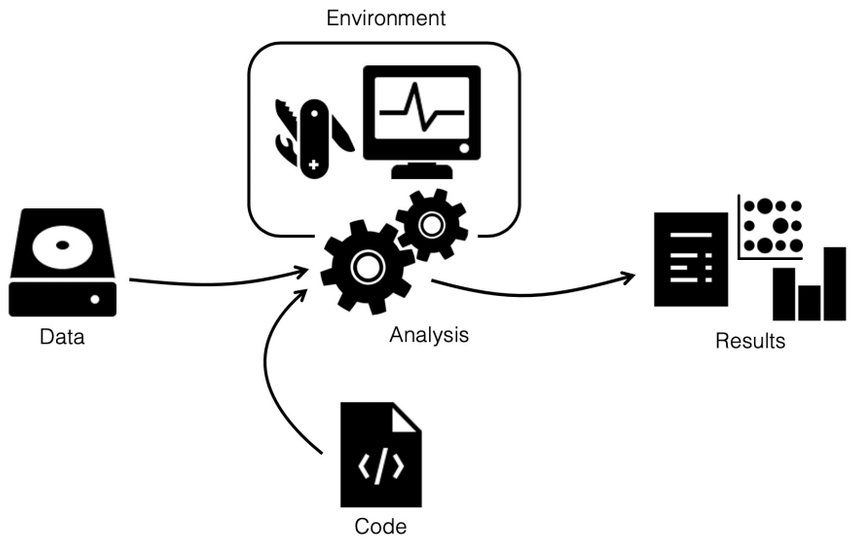
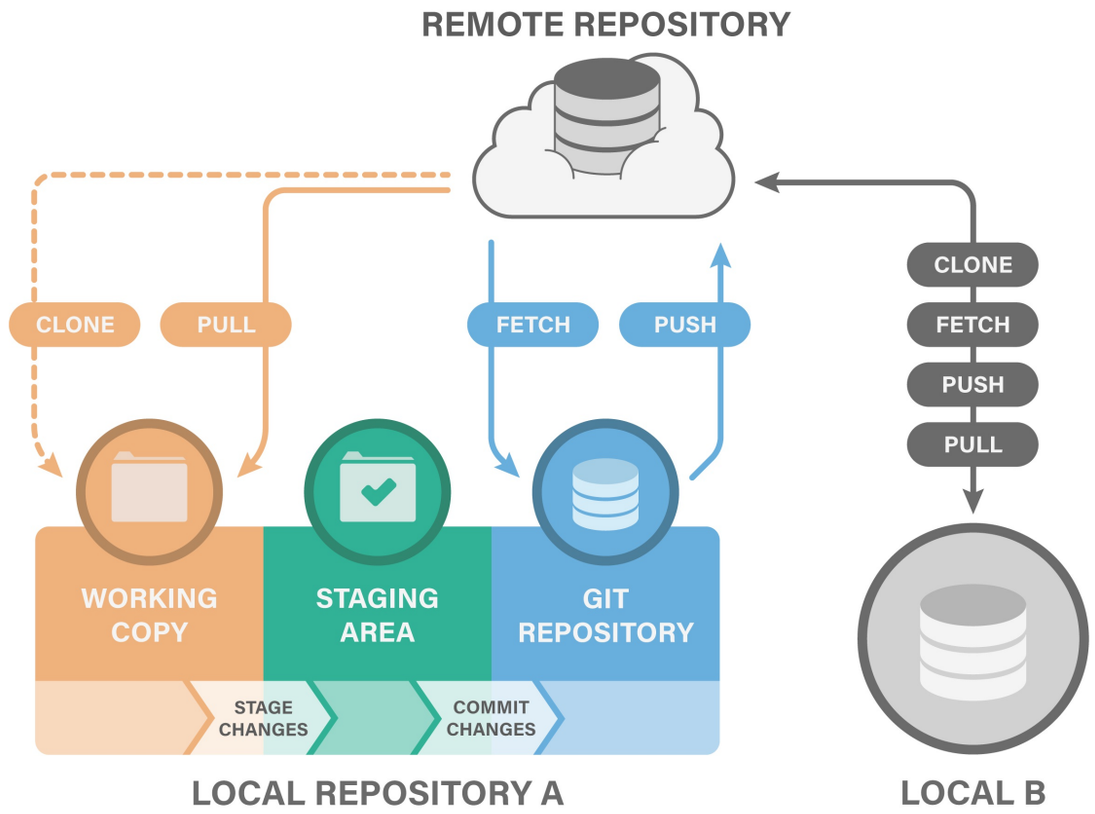


- Track your Snakemake code with Git and push it to a remote repository on GitHub or BitBucket to ensure that the different code versions are tracked and available
- Combine Snakemake with Conda and/or containers to make the compute environment and the code reproducible
- Integrate foreign workflow management systems such as Nextflow pipelines into your Snakemake workflow

Git

- A widely used system for distributed version control to version, backup and share your code and documents
- Keeps a complete history of the changes you make to your files that can be re-visited & compared
- Git tracks who contributed what to your code
- Git is mainly used for text files, not large or binary files, so ideal for Snakemake workflows

Git



1. Do some coding (i.e. add or change contents of files)
2. Stage the changes (i.e. specify which changes should be stored)
3. Commit the changes (storing them in the repository's history)
4. Push and pull regularly to/from your remote repository (on GitHub or Bitbucket) to collaborate, backup and share your code

Conda

- Is a package, dependency, and environment manager

  > packages: any type of program (e.g. bowtie2, snakemake etc.)
  >
  > dependency: other software required by a package
  >
  > environment: a distinct collection of packages

- Keeps track of the dependencies between packages in each environment

Conda

Running a Snakemake rule with a Conda environment

- Make sure you have Conda installed (Miniconda or Anaconda)
- Find your Conda package on http://anaconda.org
- Create a Conda environment file (`tePSI.yaml`)

```
name: tePSI
channels:
  - nanjiang
  - bioconda
dependencies:
  - transposonpsi=1.0.0
```

- A good location for the `yaml` file can be a directory for environments within your main Snakemake directory
- For reproducibility, it is important to keep track of software versions, so make sure to include package versions in your environment file
- Git is ideal to track changes in your Conda environment files

Conda

Running a Snakemake rule with a Conda environment

- Add the path to the Conda environment `yaml` file to your rule using the `conda` directive

```
rule transposonPSI:
    """Identify transposons in the UniProt/Swissprot protein dataset"""
    input:
        chunk = PROT_DIR + "split_result/" + PROT_NAME + "_chunk{nr}.fa"
    output:
        allHits = temp(PROT_DIR + "split_result/" + PROT_NAME + "_chunk{nr}.fa.TPSI.allHits"),
        topHits = temp(PROT_DIR + "split_result/" + PROT_NAME + "_chunk{nr}.fa.TPSI.topHits")
    params:
        dir = PROT_DIR + "split_result/"
    conda: "envs/tePSI.yaml"
    shell:
        """
        cd {params.dir}
        transposonPSI.pl {input.chunk} prot
        """
```

- Start your workflow on the command line with `--use-conda`

```
$ snakemake --use-conda
```

- This doesn't work if you use `run` instead of `shell` (or other directives)

Conda

Using a Conda environment for the entire workflow

- Write a Conda environment file that includes all tools used by the workflow, or those used by rules with `run` directives (e.g. `generode.yaml`)

```
name: generode
channels:
  - bioconda
  - conda-forge
dependencies:
  - python=3.7.6
  - snakemake=5.22.1
  - biopython=1.76
  - matplotlib=3.2.1
  - pandas=1.0.3
  - numpy=1.18.4
```

Conda

Using a Conda environment for the entire workflow

- Create the environment

```
$ conda env create -f generode.yml
```

- Use a terminal multiplexer to run the workflow in a shell instance in the background, e.g. tmux or screen

- Activate your Conda environment in the tmux or screen session

```
$ conda activate generode
```

- Start your Snakemake workflow

```
(generode) [...] $ snakemake
```

Docker & Singularity

What can I use Docker for?

- Run applications securely isolated in a container, packaged with all dependencies and libraries
- As advanced environment manager
- To package your code with the environment it needs
- To package a whole workflow (e.g. to accompany a manuscript)
- And much more

Singularity

- Is an open source container platform suitable for HPC clusters

Docker & Singularity

Docker nomenclature

- A Docker file is a recipe used to build a Docker image
- A Docker image is a standalone executable package of software
- A Docker container is a standard unit of software run on the Docker Engine
- DockerHub is an online service for sharing docker images
- Docker images can be converted into Singularity images

Docker & Singularity

Running Snakemake rules with Singularity

- Snakemake can run a rule isolated in a container, using Singularity
- Each Conda package is also available as Docker and Singularity images (e.g. check http://biocontainers.pro for Conda packages from the bioconda channel)
- Many other Docker images are also available on DockerHub (https://hub.docker.com/)
  - But be aware that Docker images in free accounts are automatically deleted after a certain time of inactivity

Docker & Singularity

Running Snakemake rules with Singularity

- Make sure your system has Singularity installed
- Find your Docker or Singularity image, e.g. on http://biocontainers.pro
- Add the link to the container image (or the path to a Singularity `*.sif` file) to your rule using the `container` directive

```
rule transposonPSI:
    """Identify transposons in the UniProt/Swissprot protein dataset"""
    input:
        chunk = PROT_DIR + "split_result/" + PROT_NAME + "_chunk{nr}.fa"
output:
    allHits = temp(PROT_DIR + "split_result/" + PROT_NAME + "_chunk{nr}.fa.TPSI.allHits"),
    topHits = temp(PROT_DIR + "split_result/" + PROT_NAME + "_chunk{nr}.fa.TPSI.topHits")
params:
    dir = PROT_DIR + "split_result/"
container: "docker://quay.io/biocontainers/transposonpsi:1.0.0--pl526_0"
shell:
    '''
    cd {params.dir}
    transposonPSI.pl {input.chunk} prot
    '''
```

- Start your workflow on the command line with `--use-singularity`

```
$ snakemake --use-singularity
```

Docker & Singularity

Packaging your Snakemake workflow in a Docker container

- Write a Docker file (`my_workflow`), e.g.
    - Start with the official Miniconda `base` image
    - Install the core packages of the workflow (e.g. Snakemake and dependencies such as pandas)
    - Include all rule-specific environments as separate Conda files (running your rules with Conda)
    - Include your workflow with `COPY <local-src> <container-destination>` into the Docker file
    - Include the required input data, e.g.
        - Mount the path with the data inside the container
        - Mount a sample list, specifying their data paths

Docker & Singularity

Packaging your Snakemake workflow in a Docker container

- Create a Docker image from your Docker file (e.g. called `my_workflow`)

```
$ docker build -t my_workflow .
```

- Run your container

```
$ docker run --name my_first_workflow_instance -i -t my_workflow
```

- Share your Docker file on GitHub or BitBucket, or your Docker image on DockerHub

Docker & Singularity

Containerization of Conda based workflows

- Snakemake can automatically generate a Docker container image that contains all Conda environments
- Some advantages:
    - More transparent to understand for others than a black box container image
    - The workflow can still be run without containers
    - Testing can be done without containers, thereby limiting the number of uploads of updated images

Docker & Singularity

Containerization of Conda based workflows

- Generate a Dockerfile with `--containerize`

```
snakemake --containerize > Dockerfile
```

- This Docker image can also be used in the workflow (globally or per rule) via the directive `containerized`

```
containerized: "docker://username/myTEworkflow:1.0.0"

rule transposonPSI:
    """Identify transposons in the UniProt/Swissprot protein dataset"""
input:
    chunk = PROT_DIR + "split_result/" + PROT_NAME + "_chunk{nr}.fa"
output:
    allHits = temp(PROT_DIR + "split_result/" + PROT_NAME + "_chunk{nr}.fa.TPSI.allHits"),
    topHits = temp(PROT_DIR + "split_result/" + PROT_NAME + "_chunk{nr}.fa.TPSI.topHits")
params:
    dir = PROT_DIR + "split_result/"
conda: "envs/tePSI.yaml"
shell:
    """
    cd {params.dir}
    transposonPSI.pl {input.chunk} prot
    """
```

Integrating foreign workflow management systems

- From version 6.2 on, Snakemake can run workflows written in other workflow management systems such as Nextflow
- The workflow is run in Snakemake until a rule to run the foreign workflow is reached
- In this rule, Snakemake hands over to the other workflow management system indicated by the directive `handover`

```
rule chipseq_pipeline:
    input:
        input="design.csv",
        fasta="data/genome.fasta",
        gtf="data/genome.gtf",
    output:
        "multiqc/broadPeaks/multiqc_report.html",
    params:
        pipeline="nf-core/chipseq",
        revision="1.2.1",
        profile=["conda"],
    handover: True
    wrapper:
        "0.74.0/utils/nextflow"
```

(example from Snakemake documentation)

Integrating foreign workflow management systems

- The handover rule is run locally
- Submission of jobs to the cluster or cloud system is handled by the other workflow management system
- Afterwards, Snakemake continues running rules that use the output files of the foreign workflow

Summary

There are many ways to use other tools for reproducible research together with Snakemake:

- Use Git to version control, backup and share your code
- Run rules or your entire workflow in Conda environments
- Run your rules in isolated Docker or Singularity containers using Singularity
- Package your entire workflow in a Docker container
- Run pipelines written in other workflow management systems in your Snakemake workflow

Questions?

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