THE UNIVERSITY OF UTAH

The Snakemake Workflow Manager

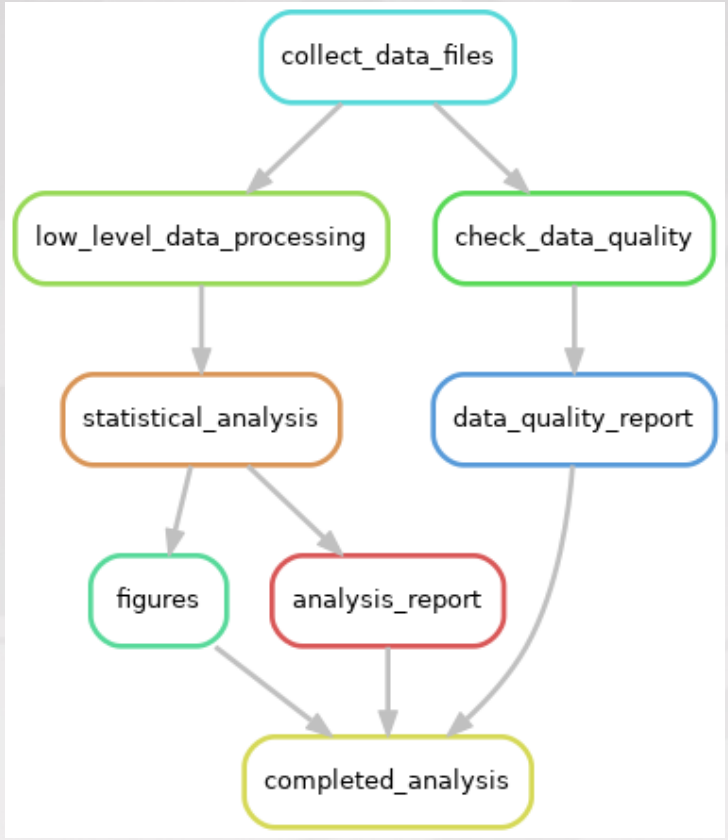
Brett Milash

Center for High Performance Computing

University of Utah

A workflow manager is software that:

- Conducts a complex workflow or analysis
- Follows dependencies from results back to configuration and input files
- Executes commands step-by-step to carry out workflow



https://snakemake.readthedocs.io/en/stable/

Why use a workflow manager?

- Human efficiency and convenience
- Computational efficiency – only the required steps are executed
  - Great when your workflow needs to be restarted
  - Handles parallel execution
  - Handles execution on a compute cluster
- Improved reproducibility
- Portability between clusters, institutions
- Modularity – re-use and standardization

Why choose snakemake?

Over 100 different workflow managers:
https://github.com/pditommaso/awesome-pipeline

Snakemake is:

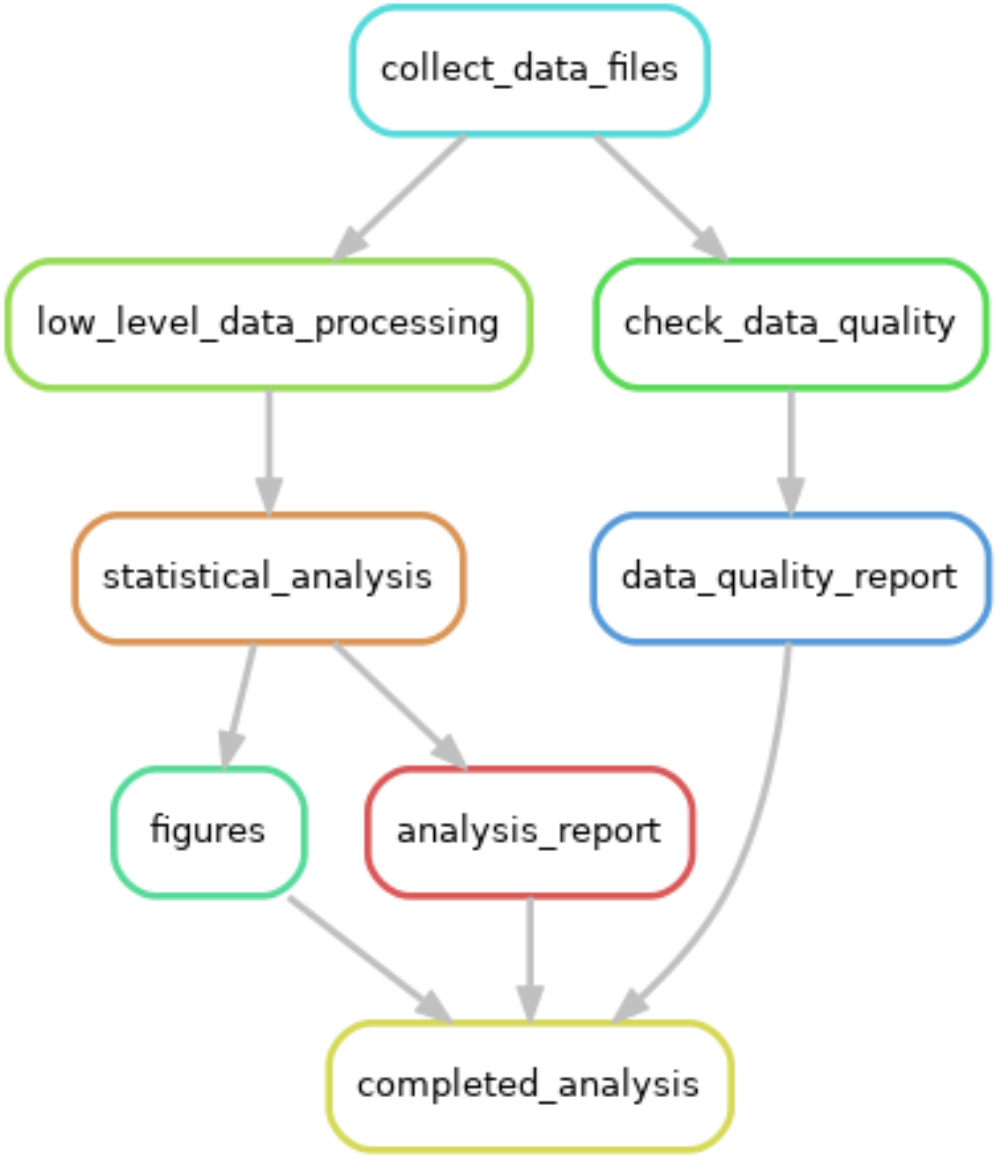
- ❑Actively used and developed
- ❑Can be configured for local and/or cluster execution
- ❑Native SLURM support
- ❑No significant system administration support required
- ❑General purpose (not just for bioinformatics, for example)
- ❑Significant functionality bang for your learning buck

Installation options

- Use the CHPC module:
  - `module load snakemake`
- Install your own using pip:
  - `pip install --user snakemake`
  - `export PATH=$HOME/.local/bin:$PATH`
- Install your own using anaconda:
  - `module load anaconda3`
  - `conda install –c bioconda –c conda-forge snakemake`

Snakemake principles

- Based on same ideas as Linux “make” utility
- Workflow broken into steps, each governed by a “rule”
- Each rule executes one or more commands to transform input file(s) into output file(s)
- Rules linked together into a directed acyclic graph (DAG) when output files of one rule match input files of another rule
- The “ultimate goal” is the output of the first rule in the workflow file
- Minimum work done to produce output of first rule
- Rule is triggered if:
  - its output file(s) missing or
  - *its input files have been updated since output created*



https://snakemake.readthedocs.io/en/stable/

Simple example

See the example at:

https://github.com/CHPC-UofU/workflows-with-snakemake/tree/main/Examples/HelloWorld

Snakemake workflows are built out of rules

```
rule link:
        input: "hello_world.o"
        output: "hello_world"
        message: "Rule {rule} linking .o file {input}"
        shell: "gcc -o {output} {input}"
```

Rules can have:

- names
- inputs
- outputs
- actions (shell or python)

Rules:

- are linked implicitly
- (or explicitly)
- can emit messages
- are executed in parallel if possible
- are executed locally or on a cluster

The first rule defines the default "target" for the workflow

Snakefile syntax

- Snakemake workflows (”snakefiles”) are python code
- All the python syntax rules apply:
  - Input and output file names in quotes
  - Shell commands in quotes
  - Whitespace / indentation is significant
  - Use either tabs or spaces (not both)
- Your snakefiles can include blocks of python code

Rule inputs

- Inputs are one or more file names, in quotes, comma-separated
- Inputs are optional
- Inputs can have “symbolic” names

```
rule align:
      input: index=“hg19”, data=“sample1.fastq”
      output: ”sample1.sam”
      shell: “bwa mem {input.index} {input.data} –o {output}”
      message: “Rule {rule} aligning input file {input.data}”
```

Rule outputs

- Just like inputs: one or more file names, in quotes, comma-separated
- Can have ”symbolic names”
- Outputs are optional - common in top-level rule that simply checks if inputs are present.

```
rule align:
        input: index=“hg19”, data=“sample1.fastq”
        output: samfile=”sample1.sam”
        shell: “bwa mem {input.index} {input.data} –o {output.samfile}”
        message: “Rule {rule} aligning input file {input.data}”
```

Rule actions: the “shell:” section

- This is where you encode the actual work of the workflow
- By default: /bin/bash in strict mode (set –euo pipefail)
- Multi-line shell statements: use triple-quotes
- Can load modules, only affects the current rule.

```
rule link:
        input: "hello_world.o"
        output: "hello_world"
        shell: """
                module load gcc/6.1.0
                gcc -o {output} {input}
                """
```

Rule “run:” section: action as python code

- Instead of bash, the action can be written in python
- Put this in the “run:” section of the rule
- Note there are no quotes around the python code

```
rule usercount:
        input: "userfile.txt"
        output: "users.count"
        run:
                users=set()
                with open(input[0]) as infile:
                        for line in infile:
                                unid=line.split()[0]
                                users.add(unid)
                with open(output[0],'w') as outfile:
                        print(f"There are {len(users)} users.",file=outfile)
```

Rule messages

- Rules can emit messages with the “message:” section
- Messages are optional
- Really useful for monitoring your workflow
- Can access the inputs, outputs with {input}, {output}
- Can access the rule name as {rule}

```
rule align:
      input: index=“hg19”, data=“sample1.fastq”
      output: ”sample1.sam”
      shell: “bwa mem {input.index} {input.data} –o {output}”
      message: “Rule {rule} processing input file {input.data}”
```

Snakemake command line arguments

First, need to load the module:

```
$ module load snakemake
```

Run snakemake using 1 core on default ”Snakefile”, default (i.e. first) rule:

```
$ snakemake --cores 1
```

Run snakemake using 1 core on non-default snakefile:

```
$ snakemake --cores 1 –s my_snakefile
```

Run snakemake using 1 core on non-default rule:

```
$ snakemake --cores 1 rule_name
```

Read the snakemake help:

```
$ snakemake --help
```

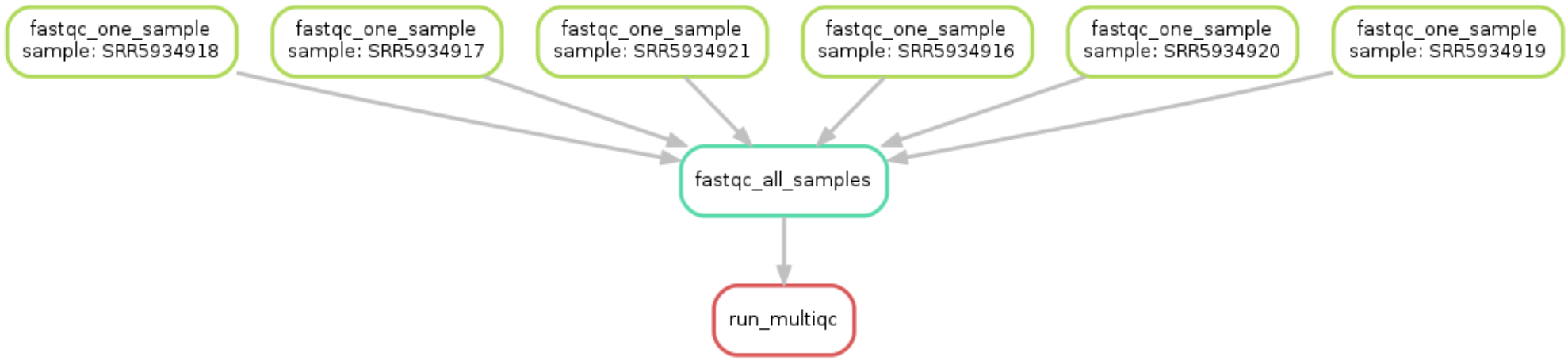
Exercise1 - Simple workflow

See the exercise 1 instructions here:

https://github.com/CHPC-UofU/workflows-with-snakemake/tree/main/Exercises/Exercise1

Graphical output

- Rule graph
  - Shows in general how rules depend on one another, but not the actual inputs/outputs
  - `snakemake [–s snakefile] --rulegraph | dot –Tpng > rulegraph.png`
- Directed Acyclic Graph (DAG)
  - all targets represented
  - Completed rules have dashed outline
  - `snakemake [–s snakefile] --dag | dot –Tpng > dag.png`



Directories as input or output

- In “modern” snakemake (version 5.0 or later):
  - Directories as input or output must be specified with directory()
    - input: directory(“data_directory”)
- In older versions of snakemake (pre version 5.0):
  - Directories as input or output are just named like regular files
    - input: “data_directory”

Wildcards: filename patterns

- These make rules reusable, not tied to specific files
- Rules with wildcards are candidates for parallel execution

How to do it:

- Create one rule that handles a single input -> output action using {variable} as a placeholder for the variable part of the input and output file name(s). This acts as a **template**.
  - Example: rule transforms input file “{sample}.data” to output file “{sample}_report.pdf”
- Create another rule whose **input** lists all the template rule’s output files.
  - Example:

    ```
    input: “A_report.pdf”, “B_report.pdf”, “C_report.pdf”
    ```
  - You can use the expand() function for this.

    ```
    input: expand(“{sample}_report.pdf”, sample=[“A”,”B”,”C”])
    ```
  - Python lists and list comprehension are useful here.
- Caveat: if you want to use {variable} in your shell section, you need to write it as “{wildcards.variable}”, for example “{wildcards.sample}”

Snakemake wildcard example

```
# Given data files A.txt, B.txt, …, F.txt, create a .md5 checksum file for
# each one, named A.md5, B.md5, …, F.md5 .
#
# Here are the sample names that are embedded in the file names:
samples=[ 'A', 'B', 'C', 'D', 'E', 'F' ]

# These two rules create the .md5 checksum file for each sample's .txt file.
rule all_checksums:
        input: expand("{sample}.md5", sample=samples)
        # expand() produces the list ["A.md5", "B.md5", ... "F.md5"]

# This is the template rule that transforms 1 input file into 1 output file:
rule one_checksum:
        message: "Creating checksum file {output} for data file {input}."
        input: "{sample}.txt"
        output: "{sample}.md5"
        shell: "md5sum {input} > {output}"
```

Exercise 2: Workflow with wildcards

See the exercise 2 instructions here:

https://github.com/CHPC-UofU/workflows-with-snakemake/tree/main/Exercises/Exercise2

Snakemake on a cluster

- Any snakemake workflow can run on a cluster:

```
snakemake --cluster-config cluster.yaml --jobs 20 …
```

- Cluster configuration file can be in JSON or YAML format
- The catch is that we must tell snakemake how to start a job:
  - --cluster “sbatch –A {cluster.account} –p {cluster.partition}”

Cluster configuration

- Basic cluster configuration file:

```
# cluster.yaml - cluster configuration for my snakemake job.
__default__:
    partition: slurm_partition
    account: slurm_account
    time: 1:00:00
    nodes: 1
```

- The __default__ config applies to all rules
- Can override default with rule-specific configurations

```
image_processing:
    partition: kingspeak_gpu
    account: kingspeak_gpu
```

Local rules

- When running on a cluster, you may want to specify some rules NOT run on the cluster
- localrules: rule1, rule2, rule3
- Snakemake knows to run rules without an action (e.g. “shell:”) locally.

Watching your workflow run on the cluster

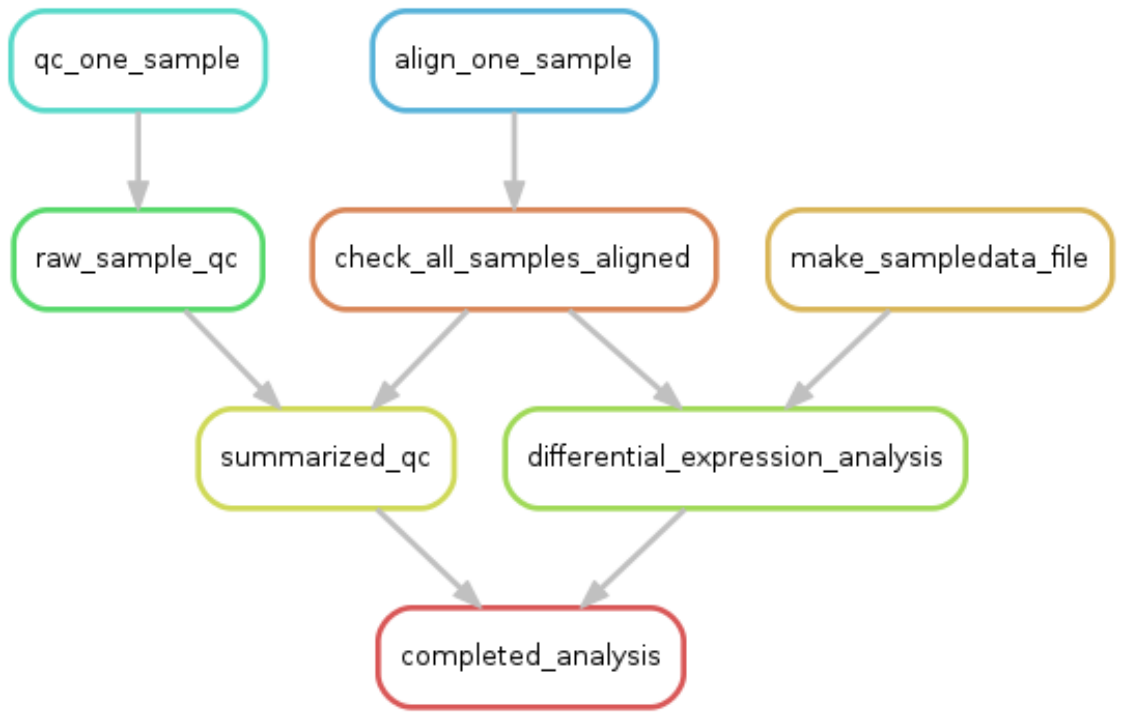
- Run the squeue command to see your SLURM jobs:
  - `watch –n 3 squeue -M all -u $USER  # Check jobs on all clusters every 3s.`
- You can get fancy with the output:
  - `watch –n 3 squeue -M all 3 -u $USER -o "%.6i %.10P %.7a %.20j %.2t %.6M %R"`

Snakemake exercise 3

See the exercise 3 instructions here:

https://github.com/CHPC-UofU/workflows-with-snakemake/tree/main/Exercises/Exercise3

Modular workflows




```
# Snakefile.qc
rule summarized_qc:
        input: …
        output: touch("qc.done")
        shell: …

rule qc_one_sample:
        input: …
        output: …
        shell: …

rule raw_sample_qc:
        input: …
        output: …
```

```
# In main Snakefile:
include: "Snakefile.qc"
```

Developing complex workflows

1. Define “skeleton” of workflow, link rules together using touch().
2. Start at beginning, implementing one rule at a time, testing as you go.
3. Use a small data set for testing, fast feedback
4. Implement the cluster configuration
5. Re-test
6. Run it with real data set

Granularity

- Fine-grained
  - Many rules, simple shell statements
  - Efficient for local rules, easy debugging
  - Inefficient for cluster jobs, as each rule requires submitting a job
- Coarse-grained
  - Few rules, complex shell statements
  - More efficient on clusters, but harder to debug

Handling batches

- On a cluster, the snakemake paradigm maps the execution of one rule to one SLURM job – this may not fit your workflow well
  - Rule execution may be too small to fully occupy a node
  - Wait time in the SLURM queue on a busy cluster
- Solutions:
  - Write rules that process batches of samples or values
  - Use shared partitions in SLURM

Snakemake is container-friendly

- Snakemake supports running code in containers using singularity
- See: https://snakemake.readthedocs.io/...#running-jobs-in-containers

Snakemake may not be right for you

- What if your inputs and outputs aren't files?
- What if your cluster doesn't use SLURM or LSF?
  - For example: HTCondor (Open Science Grid: > 1.2 billion core hours last year)
- nextflow: https://www.nextflow.io/
  - non-file inputs and outputs
  - support for HTCondor (OSG) and many other schedulers