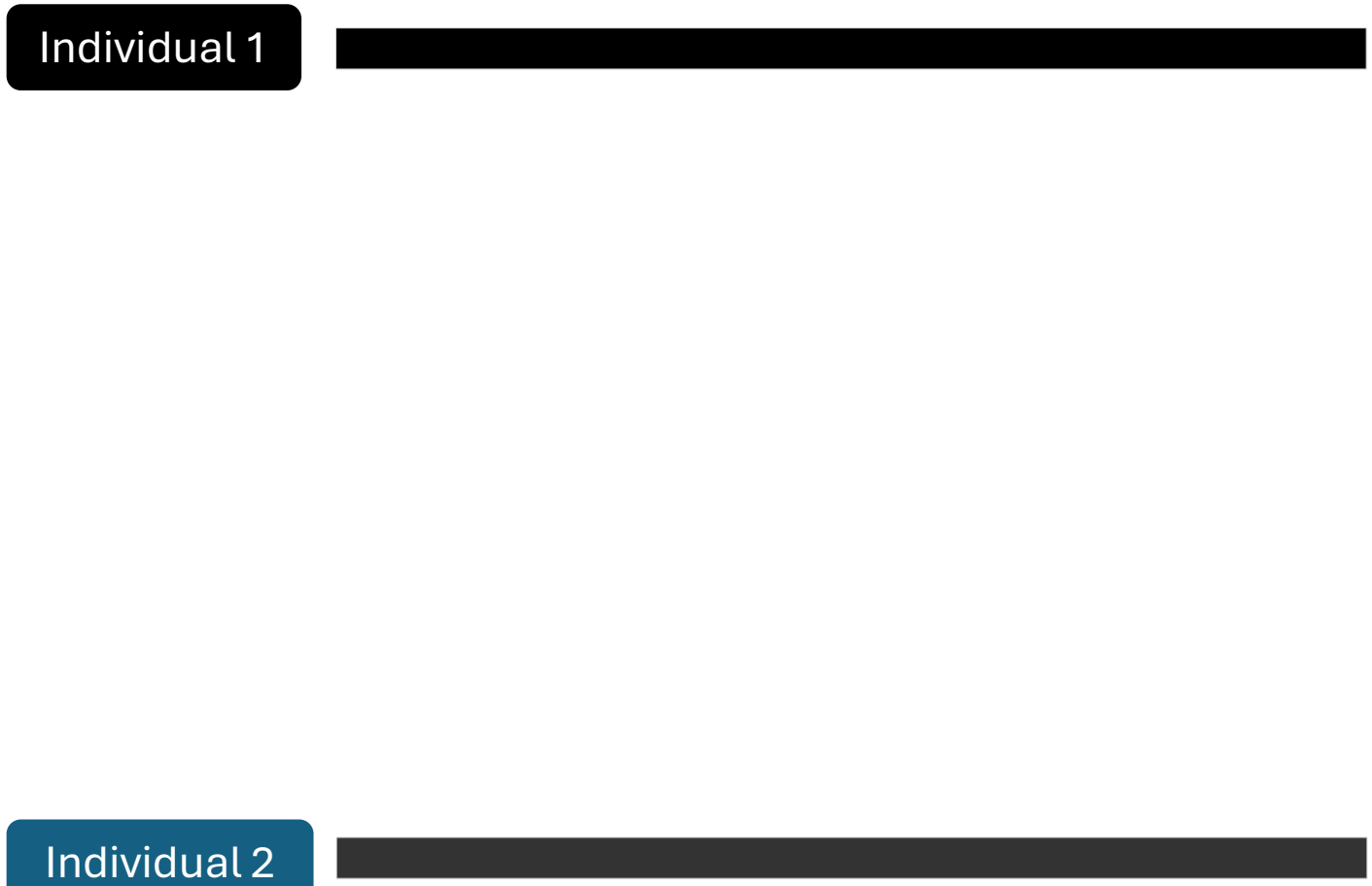
Population genomics with snpArcher

https://informatics.fas.harvard.edu/

Workshop December 2025

https://snparcher.readthedocs.io/

SNP calling is a cornerstone of population genomics



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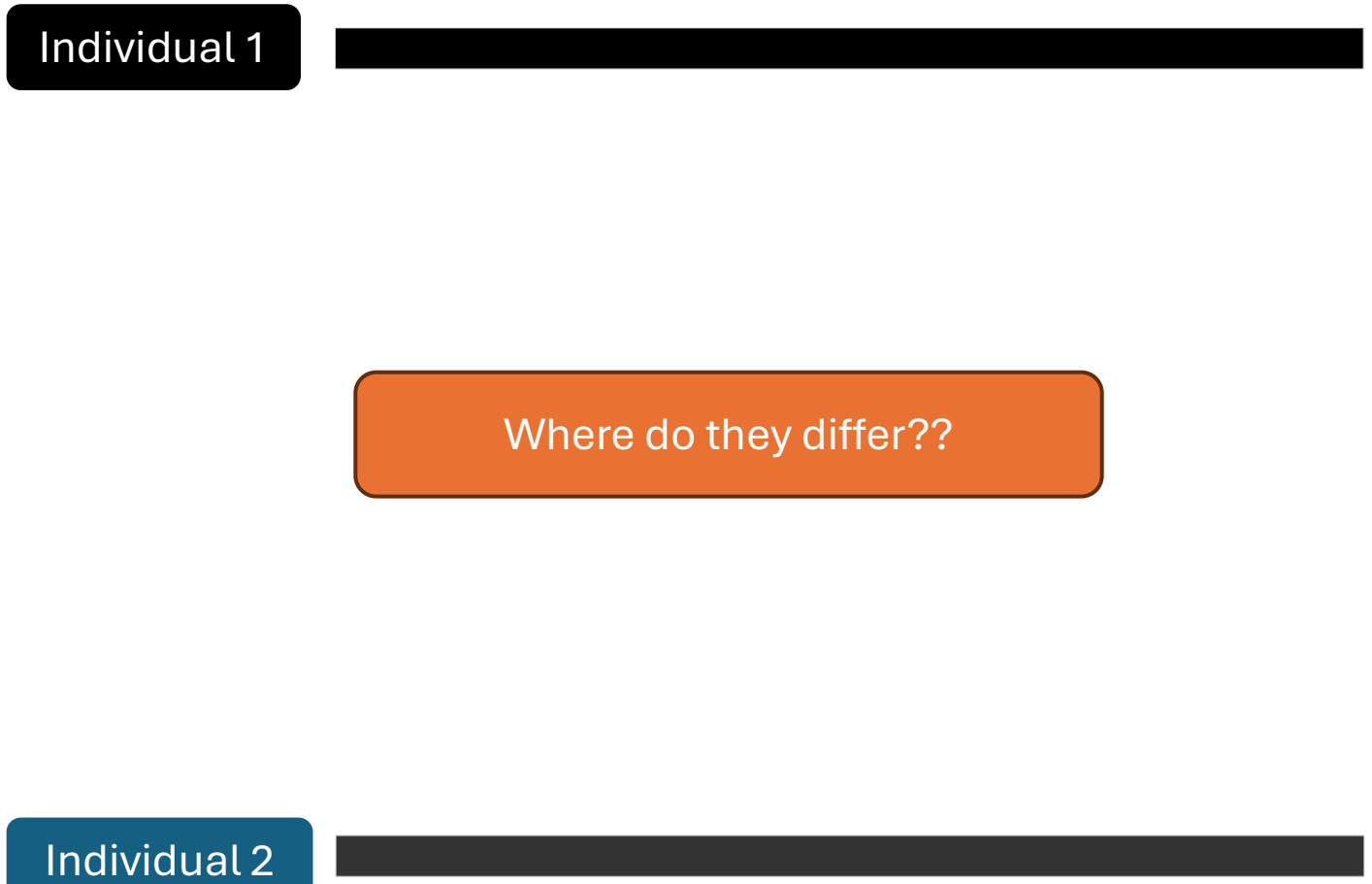

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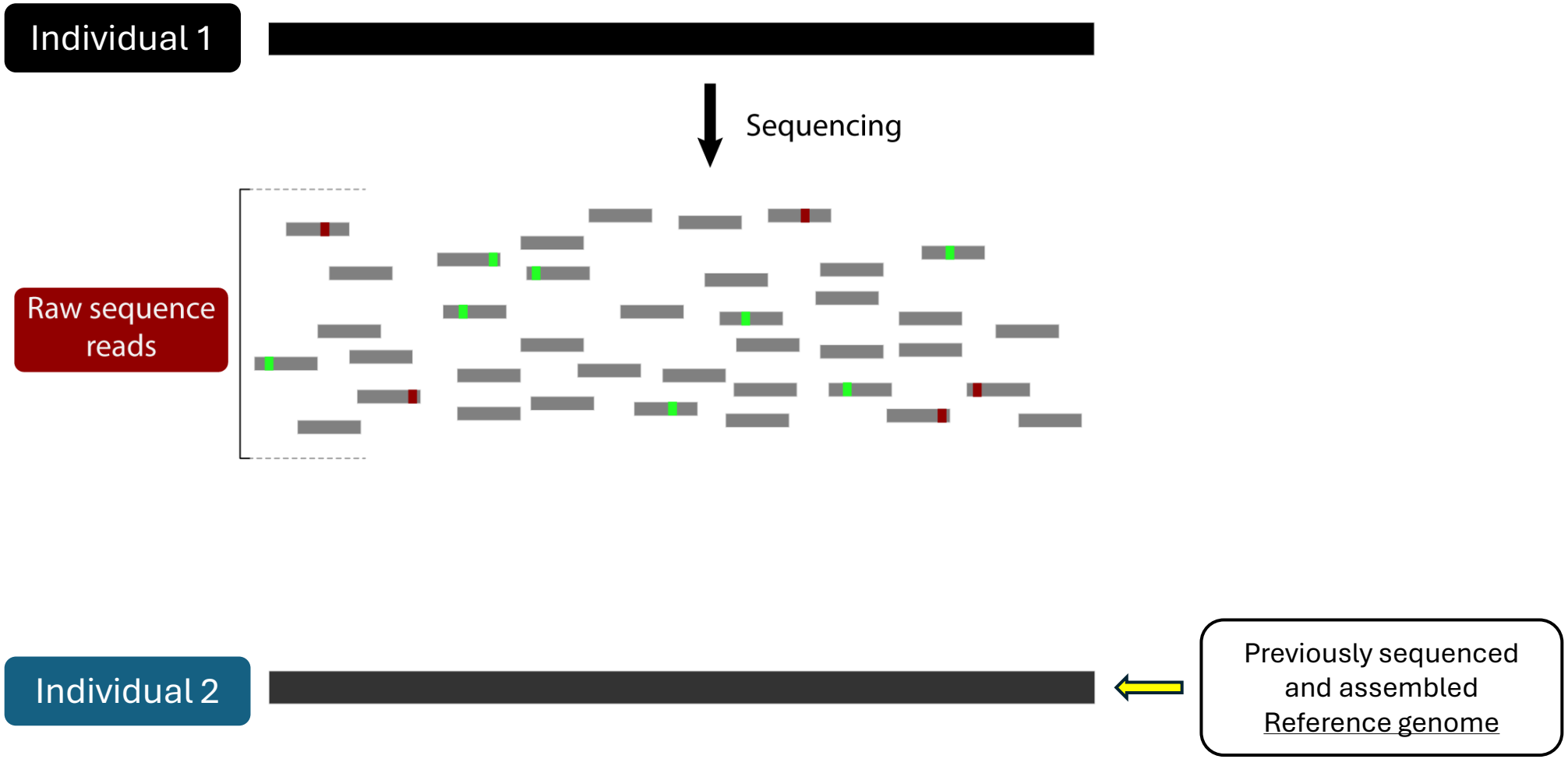

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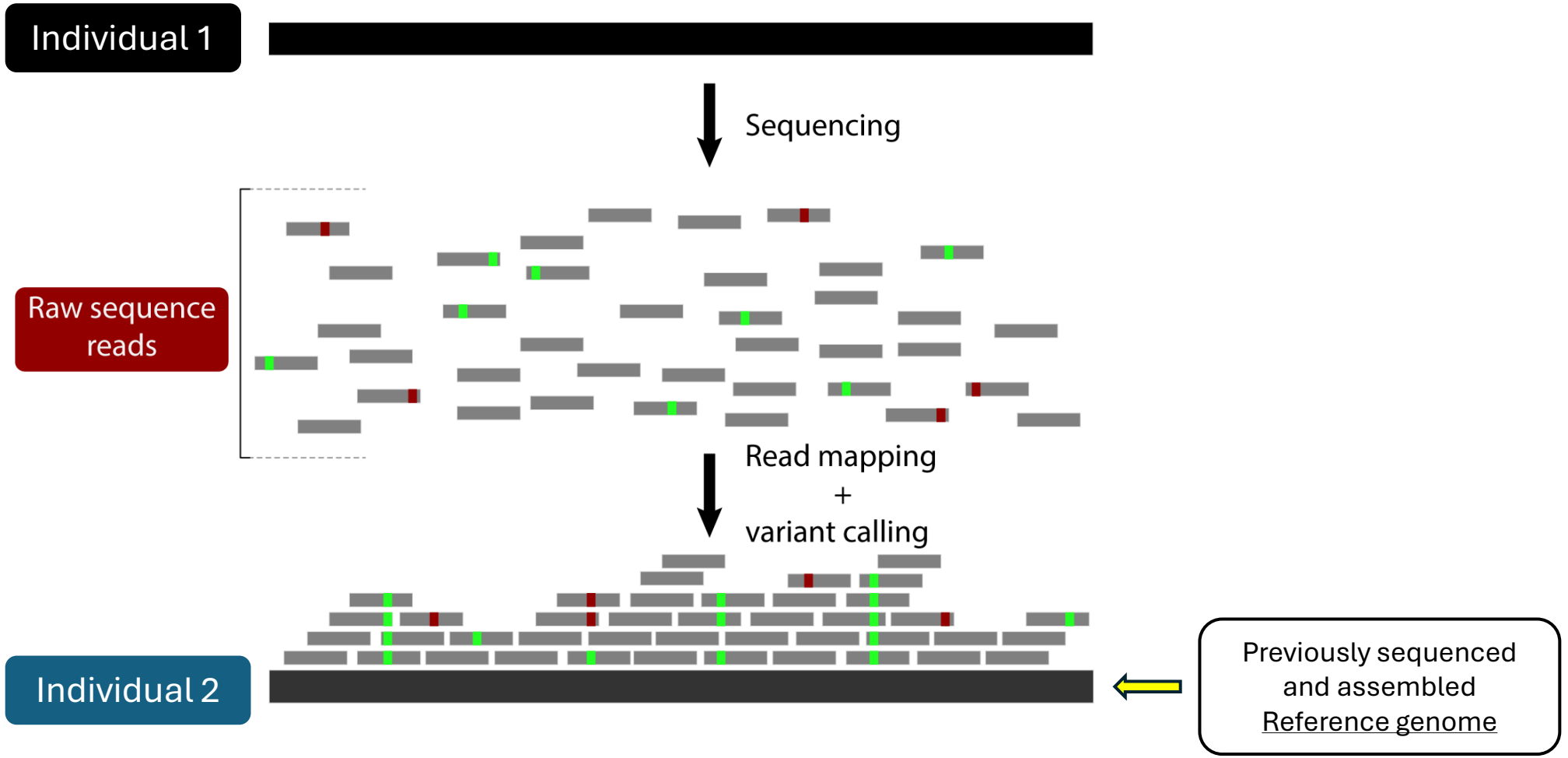
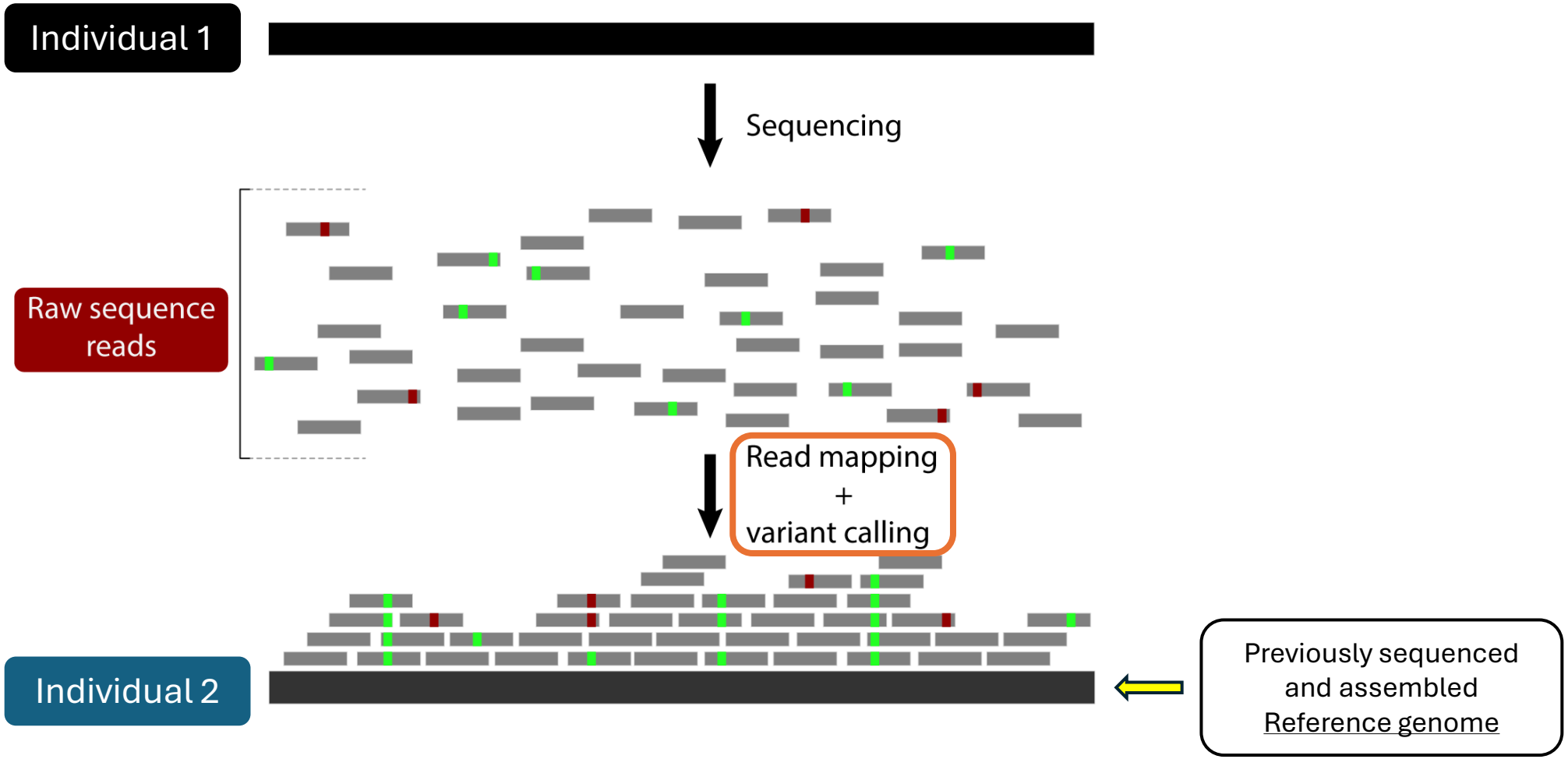
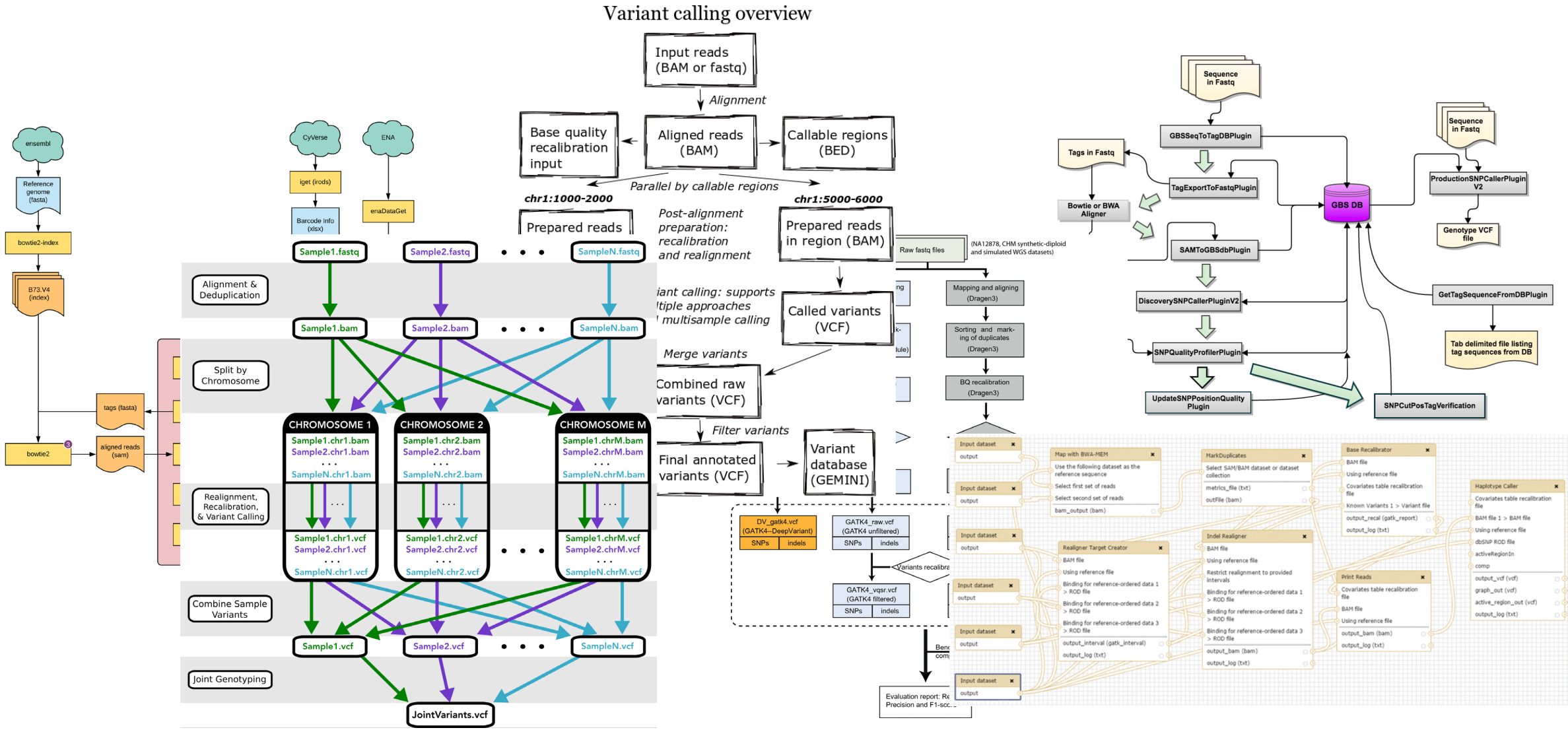


SNP calling is a cornerstone of population genomics



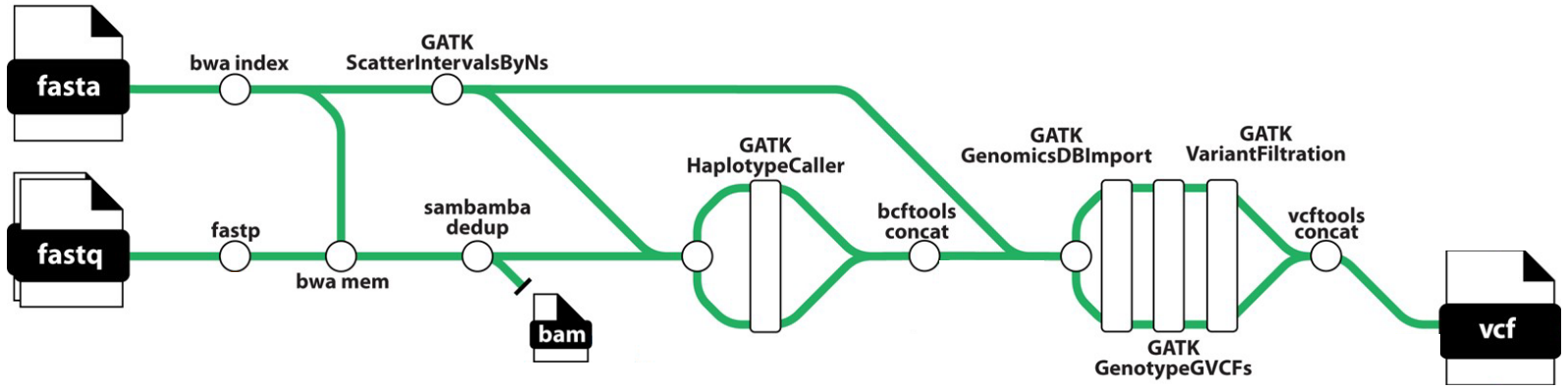
SNP calling is technically challenging



SNP calling is technically challenging

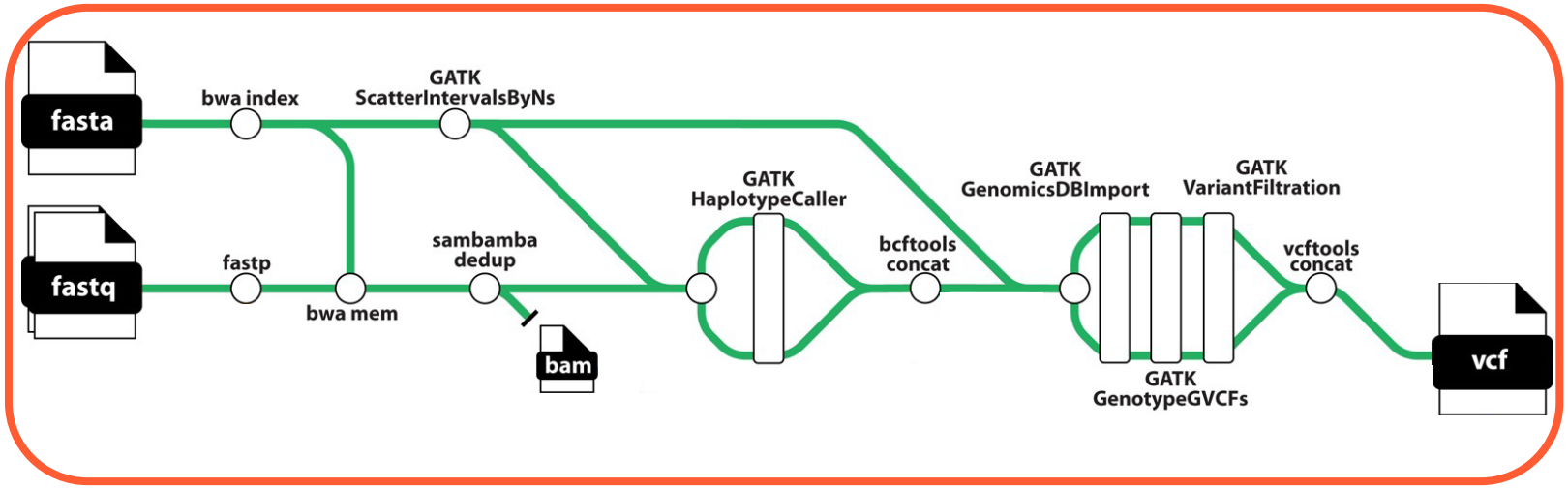
snpArcher is a Snakemake workflow that handles every step of the mapping and variant calling process for multiple samples

YAVCWI: Yet another variant calling workflow image

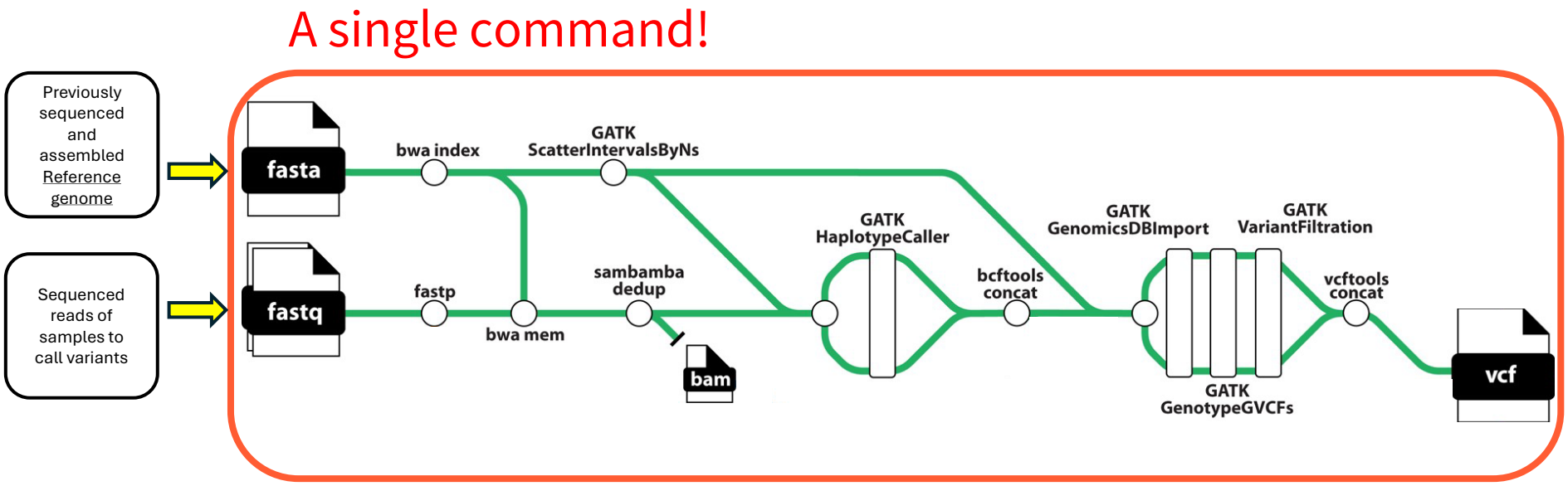


https://snparcher.readthedocs.io/

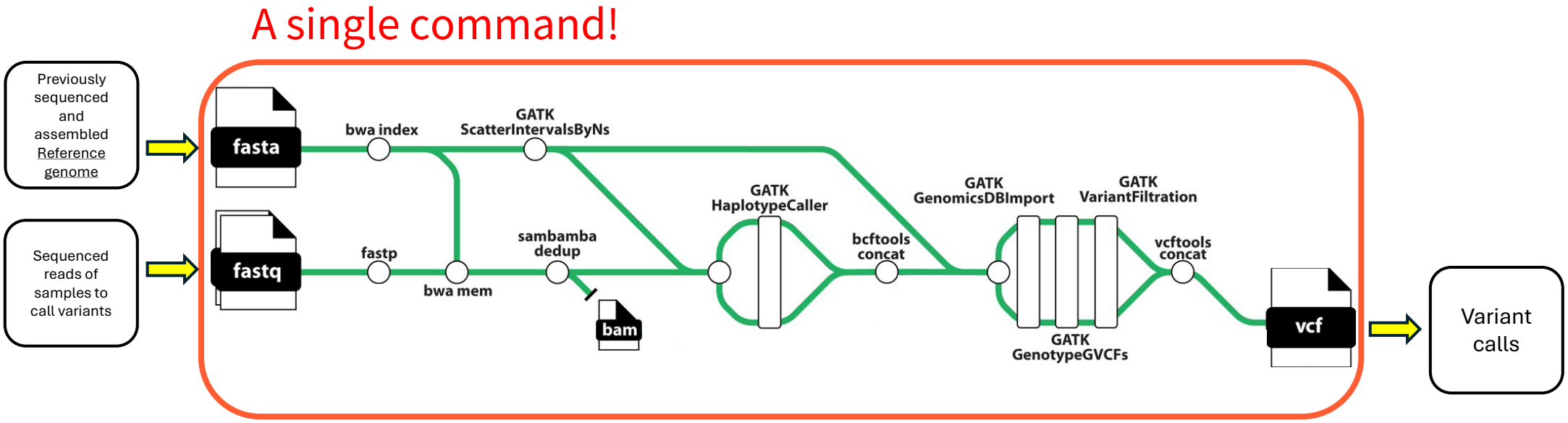
A single command!



A reference genome and samples with sequenced reads are the only inputs

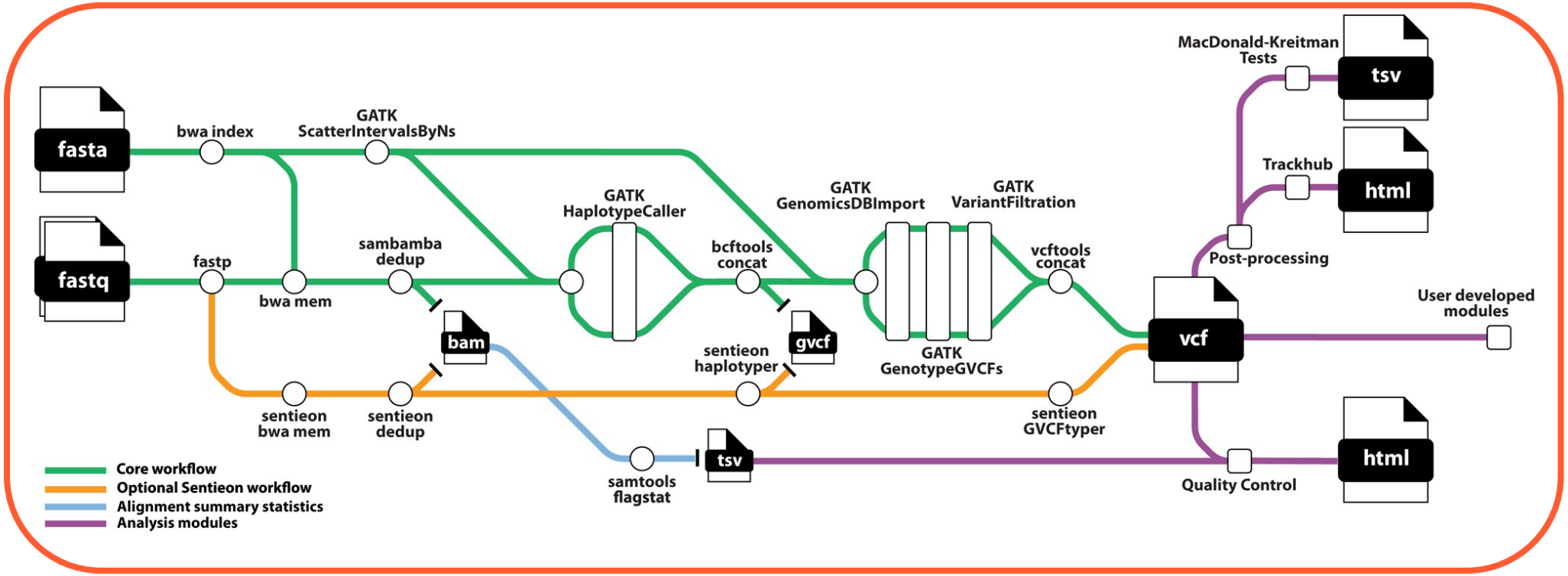


A variant call format (VCF) file is the main output



snpArcher has a range of other features

A single command!



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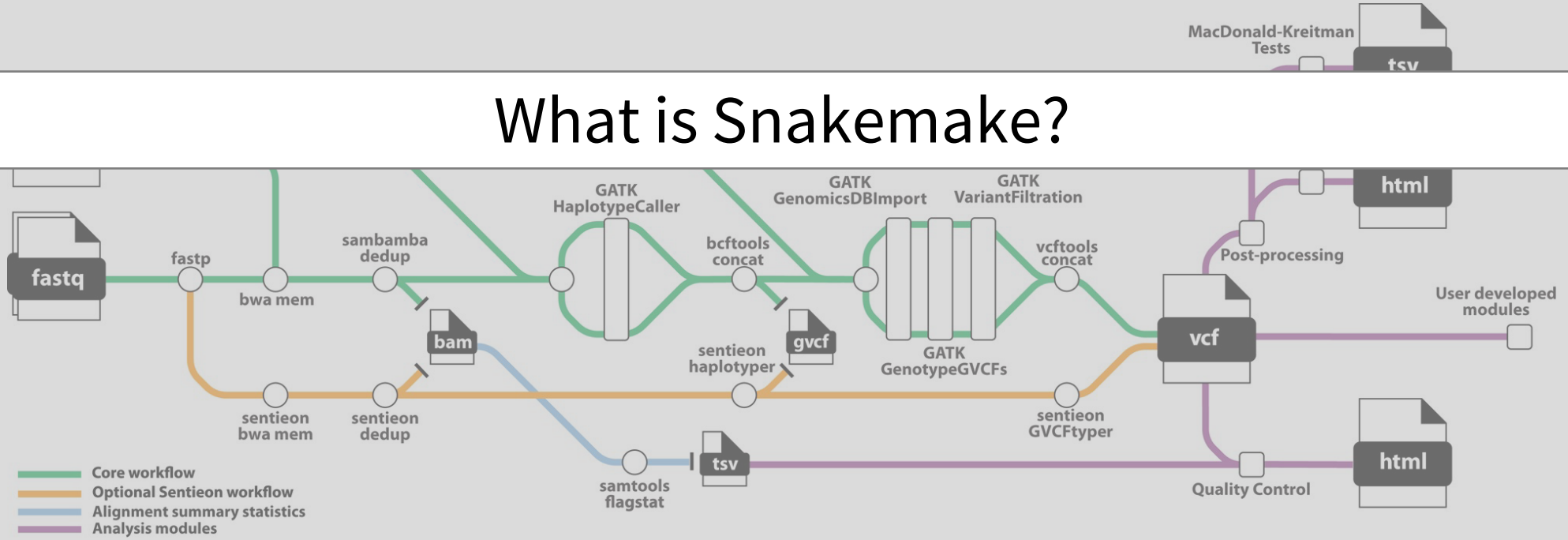
What is Snakemake?



Snakemake is a Python-based workflow management language

- Snakemake is based on rules – each rule is a step in the workflow (e.g. read mapping or variant filtering)
  - The output of one rule is the input for the next rule in the workflow

- Wildcards allow rules to be run on multiple files

- Snakemake integrates with SLURM and automatically submits each step in a rule as a single job

Installing Snakemake

Installing Snakemake

1. Install the package manager mamba

https://github.com/conda-forge/miniforge

If you already have mamba installed (type `mamba` to check) you should skip this step.

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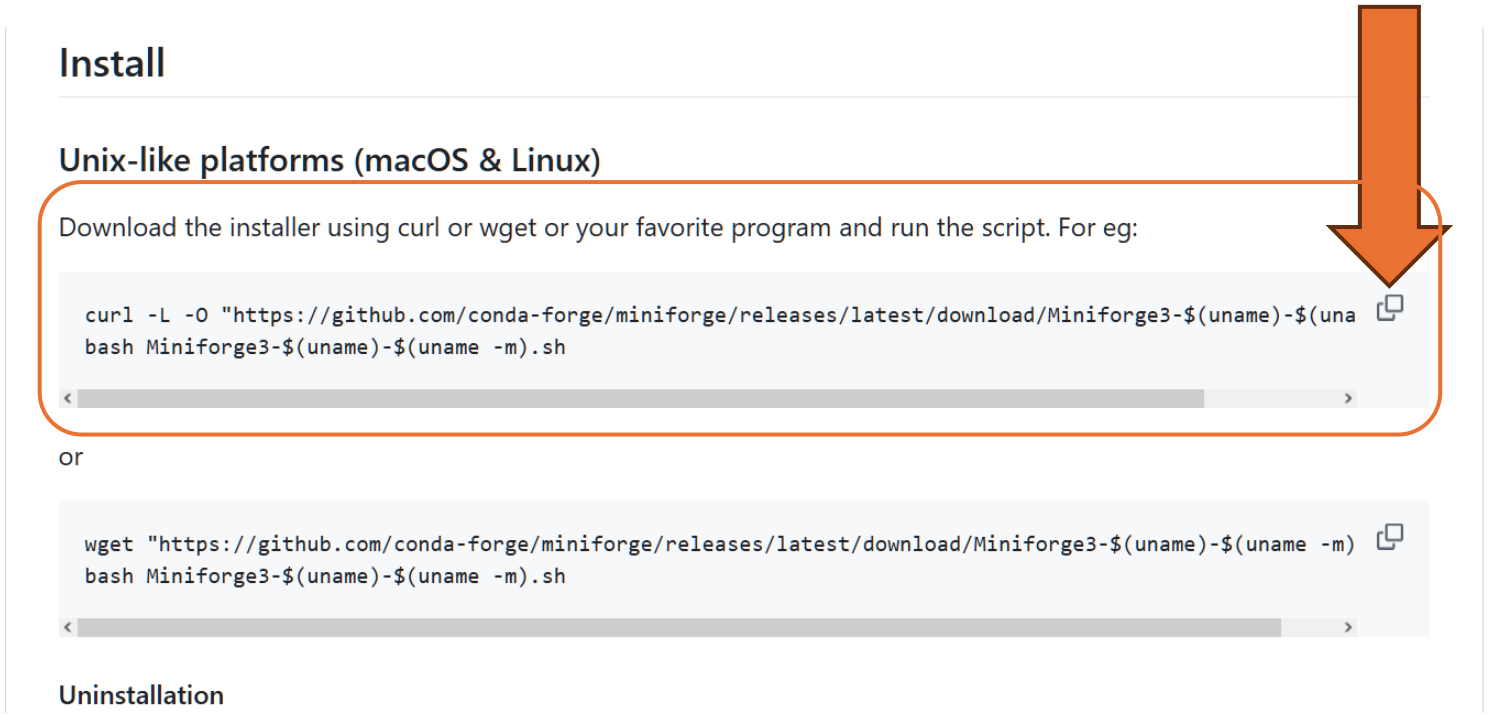
If you have conda installed or want to use the system module (`module load python`) and don't wish to mess with your setup, you should skip this step. Just use the conda command instead whenever you see mamba.

Installing Snakemake

1. Install the package manager mamba

https://github.com/conda-forge/miniforge

1. Scroll to the Install section and copy and paste these commands into your shell
2. Follow the onscreen prompts to accept the license agreement and choose an install location ($HOME, by default)
3. When prompted to initialize mamba, say yes. You will have to reconnect.



Installing Snakemake

1. Install the package manager mamba

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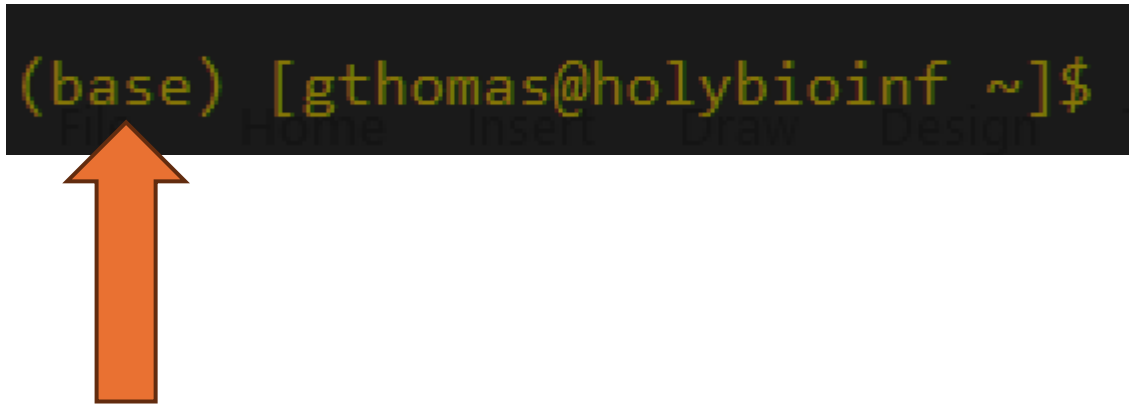
If the install was successful, you should now see `(base)` appended to your command prompt.

`(base)` indicates you are in the base conda environment from which you create other environments.



Installing Snakemake

2. Setup your channels for bioconda

https://bioconda.github.io/

```
conda config --add channels bioconda
conda config --add channels conda-forge
conda config --set channel_priority strict
```

Installing Snakemake

3. Create and activate an environment for Snakemake

Create:

```
mamba create -n snakemake-env
```

Activate:

```
mamba activate snakemake-env
```

Installing Snakemake

4. Install the snakemake-minimal and snakemake slurm packages

https://anaconda.org/bioconda/snakemake-minimal

https://anaconda.org/bioconda/snakemake-executor-plugin-slurm

snakemake-minimal:

```
mamba install bioconda::snakemake-minimal
```

SLURM snakemake plugin:

```
mamba install bioconda::snakemake-executor-plugin-slurm
```

Installing snpArcher

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- snpArcher is installed directly from github:

  https://github.com/harvardinformatics/snpArcher/

1. Make a project folder

   mkdir my-project/

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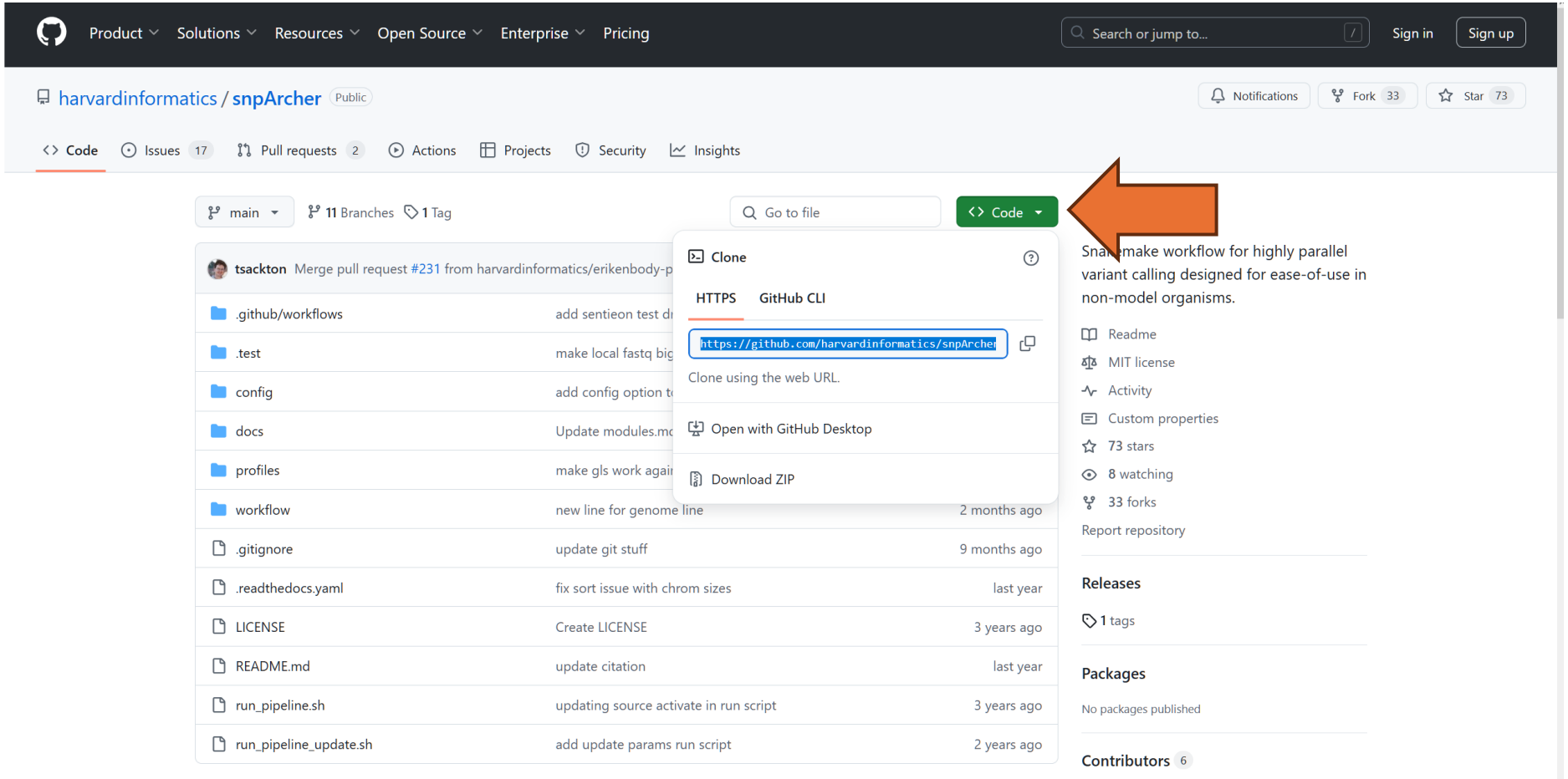
1. Make a project folder

   mkdir my-project/

2. Copy the link from github

3. In your project folder type:

   `git clone <link>`



Preparing your data for snpArcher

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You will need:

1. A sample sheet (.csv file)
2. A Snakemake config file (template provided in github repo)
3. OPTIONAL: To adjust the resources in the Snakemake profile

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Preparing your data for snpArcher: sample sheet

Data can be used locally or by automatically downloading from NCBI.

You will need:

	NCBI	**Local**
Reference genome	Assembly accession	Path to FASTA file
For each sample	The SRR run accession for the raw reads	Paths to FASTQ files

Preparing your data for snpArcher: sample sheet

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You will need:

	NCBI	Local
Reference genome	Assembly accession	Path to FASTA file
For each sample	The SRR run accession for the raw reads	Paths to FASTQ files

Other optional information for each sample includes sample type, and map coordinates (lat and lon).

Preparing your data for snpArcher: sample sheet

Compile your input data into a sample sheet, a CSV file with one sample per row:

Save your samples.csv file in your project folder

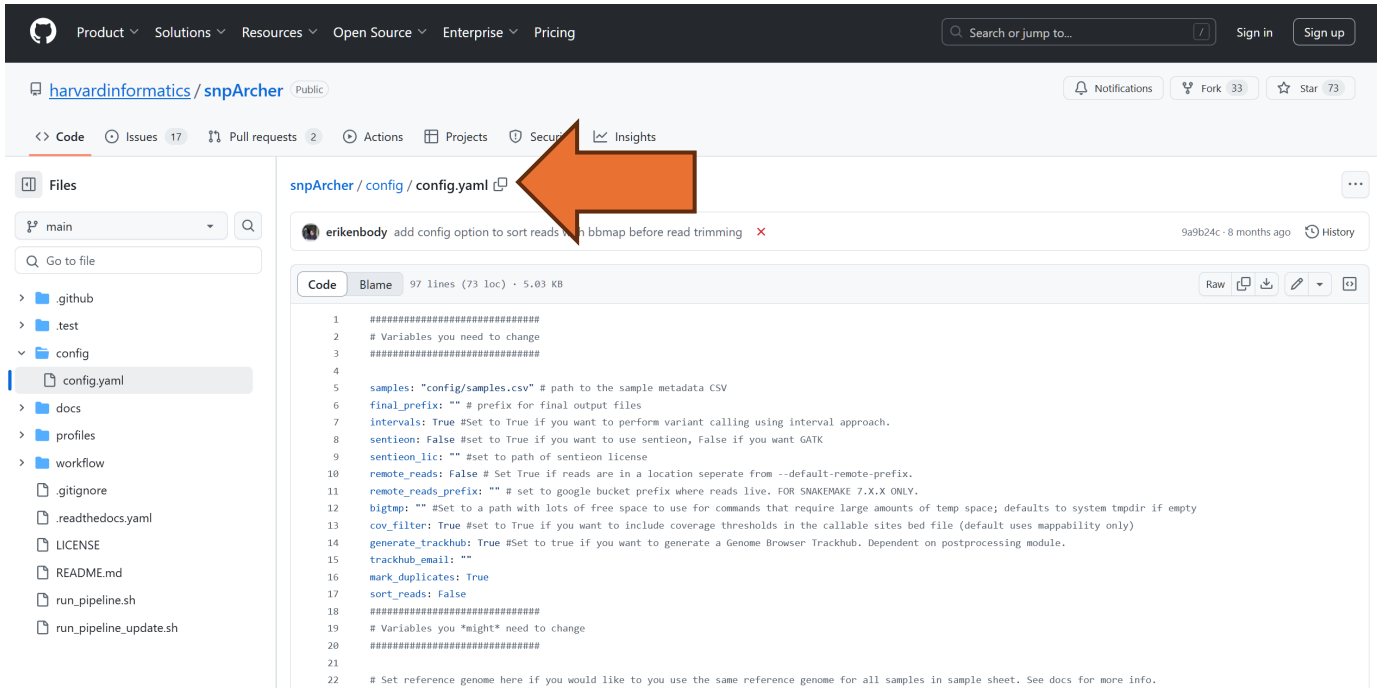
samples.csv

agam-test > config > samples.csv

```
1  BioSample,LibraryName,refGenome,Run
2  AA0040-C,AA0040-C,GCF_943734735.2,ERR387821
3  AA0041-C,AA0041-C,GCF_943734735.2,ERR387920
4  AA0042-C,AA0042-C,GCF_943734735.2,ERR387921
5  AB0087-C,AB0087-C,GCF_943734735.2,ERR501782
6  AB0088-C,AB0088-C,GCF_943734735.2,ERR332013
7  AB0089-C,AB0089-C,GCF_943734735.2,ERR502048
```

Preparing your data for snpArcher: snakemake config file

You will also need to set-up the Snakemake config file. A template is provided in the repository you downloaded:



Preparing your data for snpArcher: snakemake config file

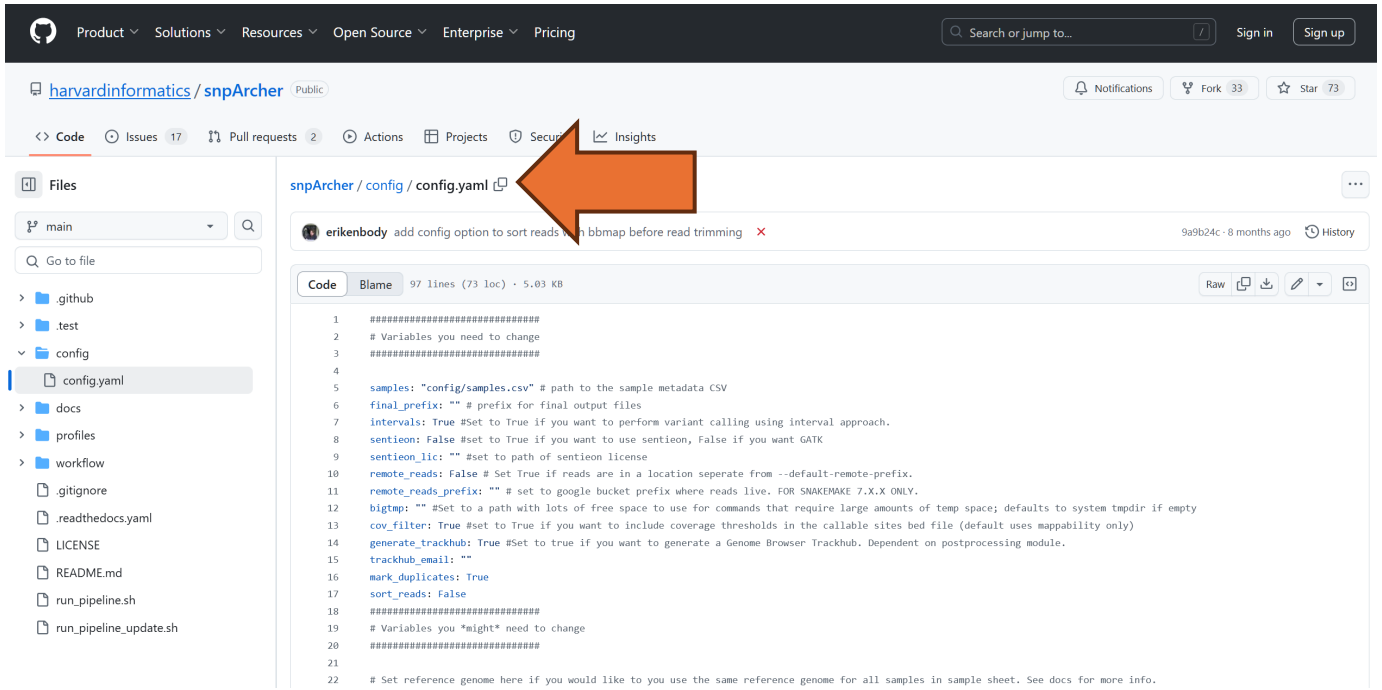
You will also need to set-up the Snakemake config file. A template is provided in the repository you downloaded:

1. In your project folder, create a sub-folder called configs:

```
mkdir configs/
```

2. Copy the template config file:

```
cp snpArcher/config/config.yaml configs/.
```



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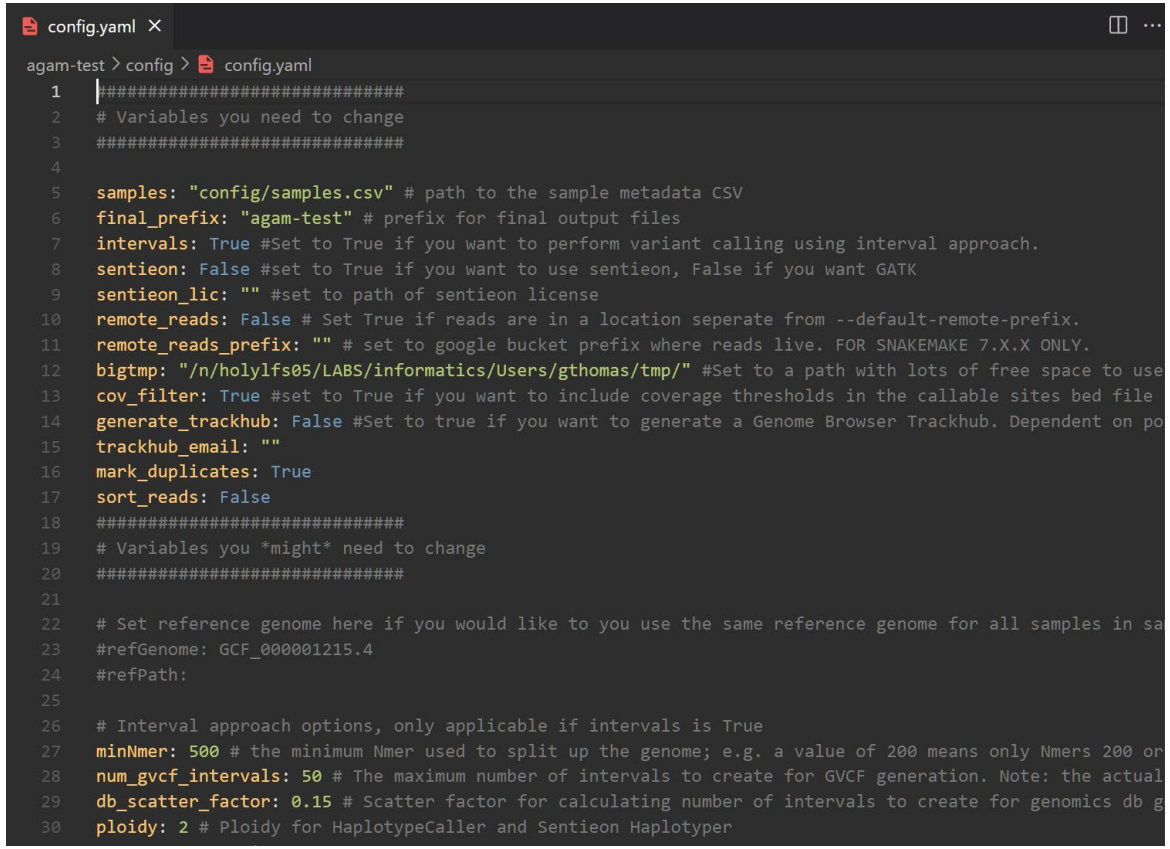
cp snpArcher/config/config.yaml configs/.
```

3. Edit the relevant parts of the copied config file



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config.yaml

agam-test > config > config.yaml

```
1  ##############################
2  # Variables you need to change
3  ##############################
9  sentieon_lic: "" #set to path of sentieon license
10 remote_reads: False # Set True if reads are in a location seperate from --default-remote-prefix.
11 remote_reads_prefix: "" # set to google bucket prefix where reads live. FOR SNAKEMAKE 7.X.X ONLY.
12 bigtmp: "/n/holylfs05/LABS/informatics/Users/gthomas/tmp/" #Set to a path with lots of free space to use
13 cov_filter: True #set to True if you want to include coverage thresholds in the callable sites bed file
14 generate_trackhub: False #Set to true if you want to generate a Genome Browser Trackhub. Dependent on po
15 trackhub_email: ""
16 mark_duplicates: True
17 sort_reads: False
18 ##############################
19 # Variables you *might* need to change
20 ##############################
21
22 # Set reference genome here if you would like to you use the same reference genome for all samples in sa
23 #refGenome: GCF_000001215.4
24 #refPath:
25
26 # Interval approach options, only applicable if intervals is True
27 minNmer: 500 # the minimum Nmer used to split up the genome; e.g. a value of 200 means only Nmers 200 or
28 num_gvcf_intervals: 50 # The maximum number of intervals to create for GVCF generation. Note: the actual
29 db_scatter_factor: 0.15 # Scatter factor for calculating number of intervals to create for genomics db g
30 ploidy: 2 # Ploidy for HaplotypeCaller and Sentieon Haplotyper
```

You are now ready to run snpArcher!

Running snpArcher

Running snpArcher

From your project folder and with your Snakemake environment activated, snpArcher can be run with a single command:

```
snakemake -p -s snpArcher/workflow/Snakefile --jobs 8 --use-conda --workflow-profile \
                        snpArcher/profiles/default/ --dryrun
```

Running snpArcher – local execution

From your project folder and with your Snakemake environment activated, snpArcher can be run with a single command:

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snakemake -p -s snpArcher/workflow/Snakefile --jobs 8 --use-conda --workflow-profile \
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```

Running snpArcher – on cluster

From your project folder and with your Snakemake environment activated, snpArcher can be run with a single command:

```
snakemake –p –e slurm -s snpArcher/workflow/Snakefile --jobs 8 --use-conda \
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Automatically finds your config file in `configs/config.yaml`

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```

Automatically finds your config file in `configs/config.yaml`

Path can also be provided with `--config`

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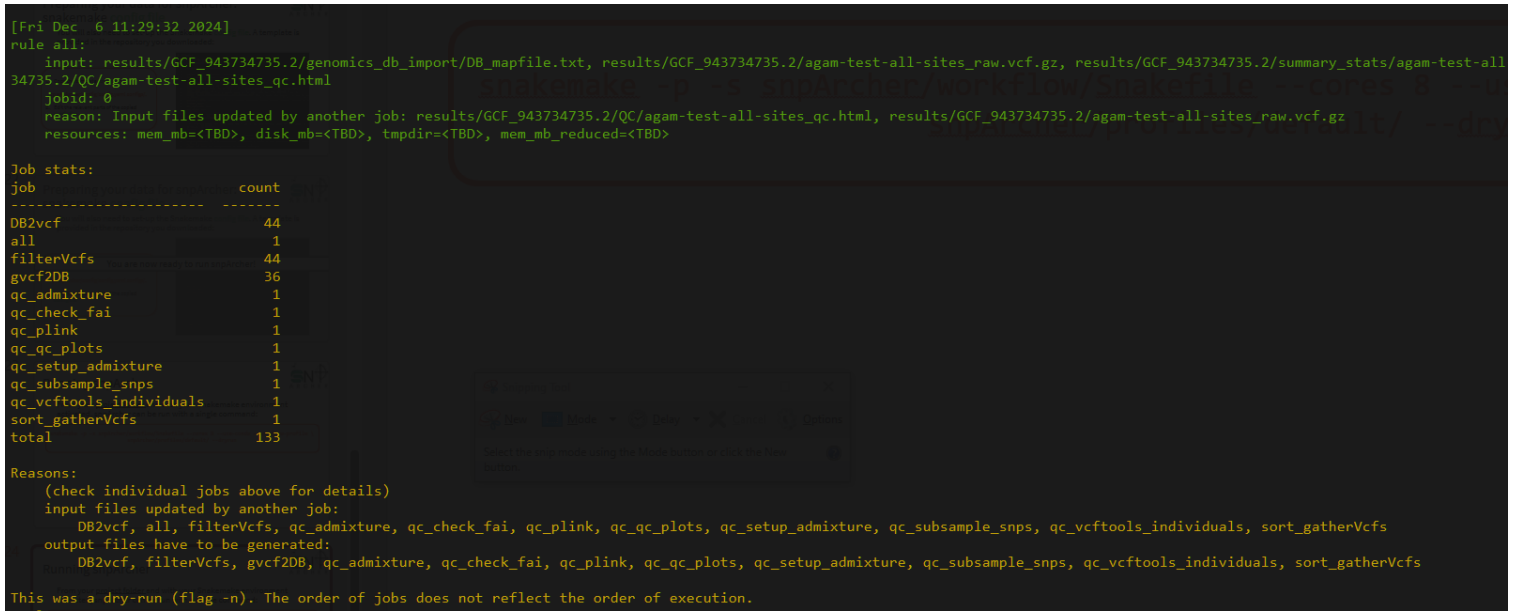

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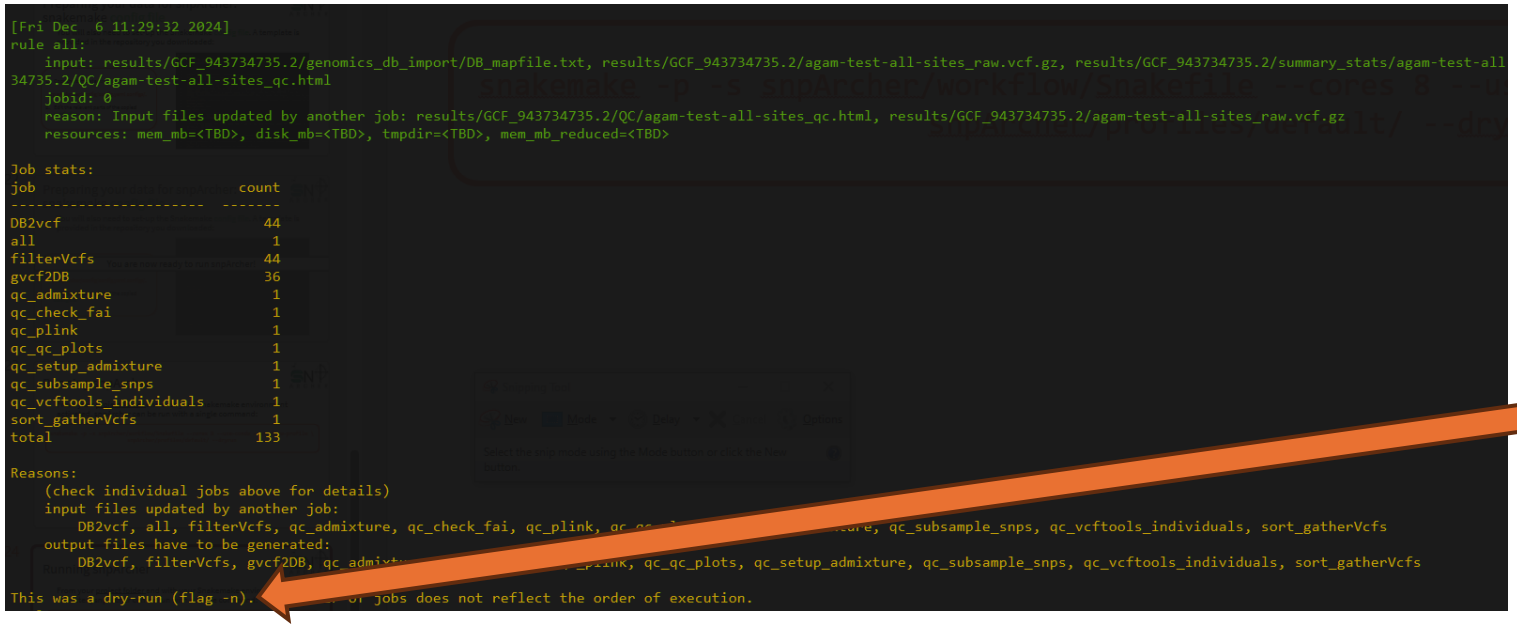

This didn't actually run anything!

Always do a `--dryrun` first!

Running snpArcher

When actually running jobs, you will need to ensure that the main snakemake process is persistent even if you disconnect from the server.

1. Submit the snakemake command itself as a SLURM job

2. Use nohup

3. Use a terminal multiplexer (e.g. screen or tmux)

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Running snpArcher

When your dryrun completes without errors, you have a persistent connection, and you are ready to start submitting jobs:

```
snakemake -p -e slurm -s snpArcher/workflow/Snakefile --jobs 8 --use-conda \
    --workflow-profile snpArcher/profiles/default/
```

Running snpArcher

Test data is provided if you'd like to quickly ensure everything works before you run your own data:

```
Snakemake –e slurm -d .test/ecoli --jobs 1 --use-conda --workflow-profile /
                    workflow-profiles/default/ --dryrun
```

Running snpArcher

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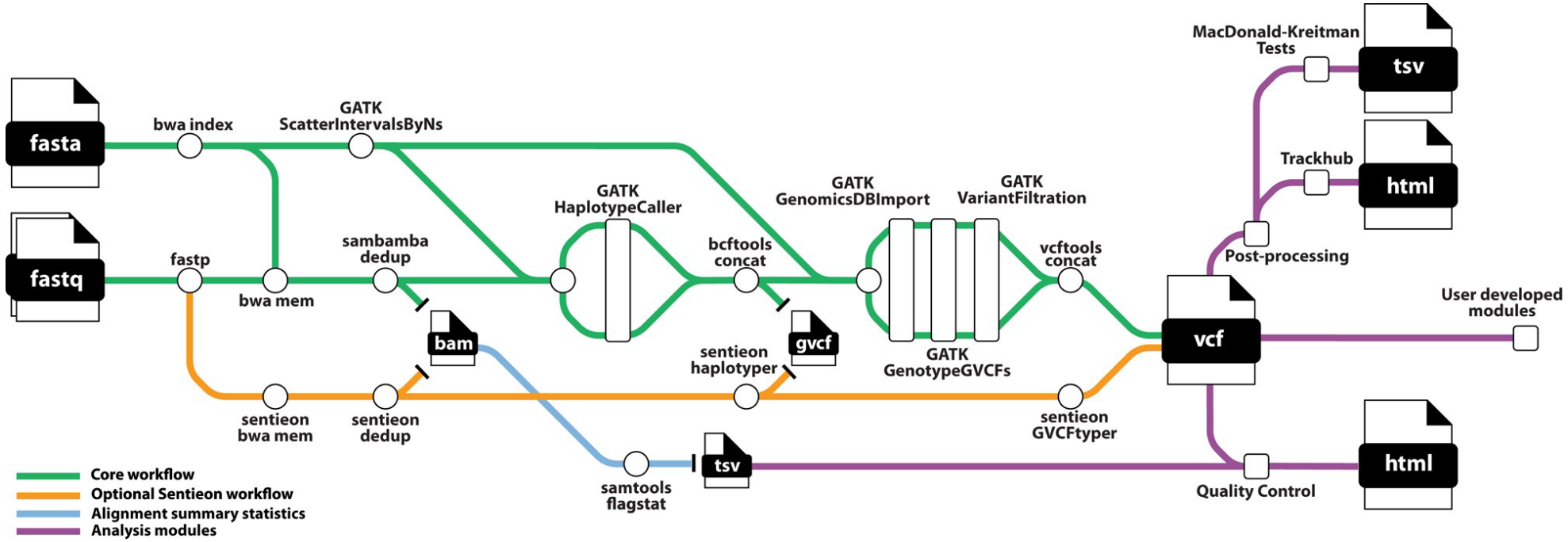
```
Snakemake –e slurm -d .test/ecoli --jobs 1 --use-conda --workflow-profile /
workflow-profiles/default/ --dryrun
```

Remember the --dryrun option! Remove it if you want to actually run the pipeline on the test data

snpArcher output and modules

snpArcher has a range of other modules



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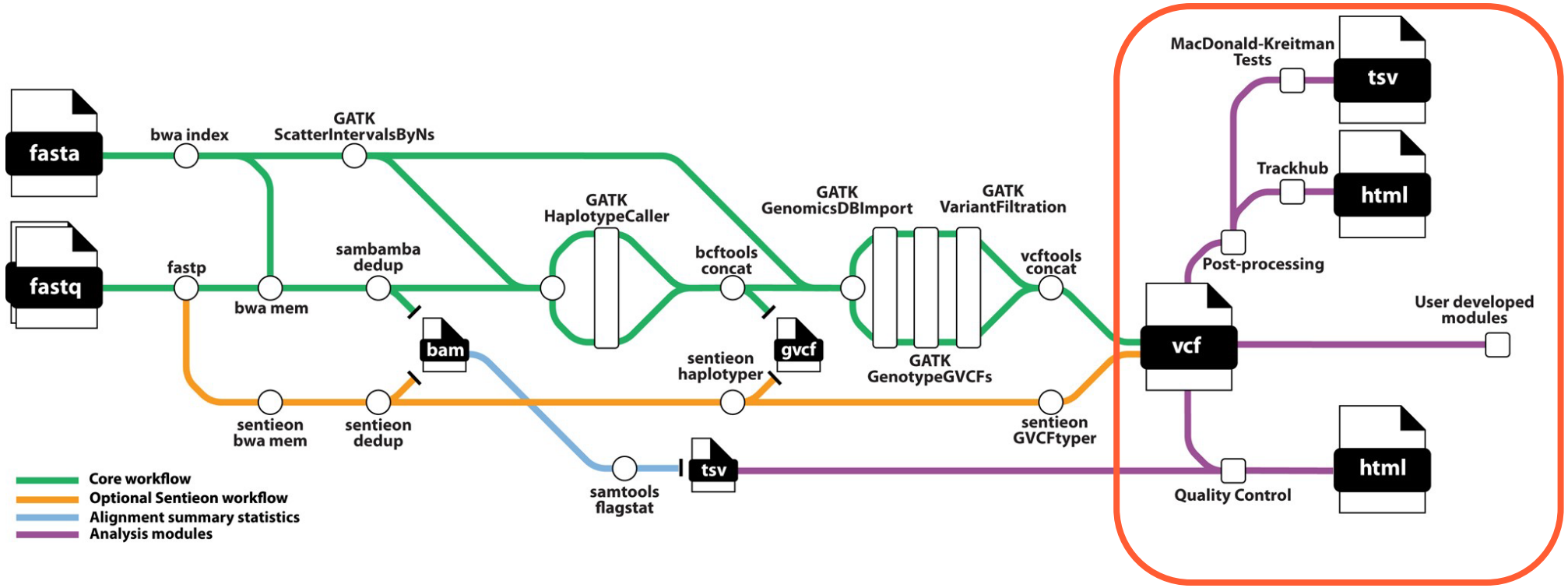
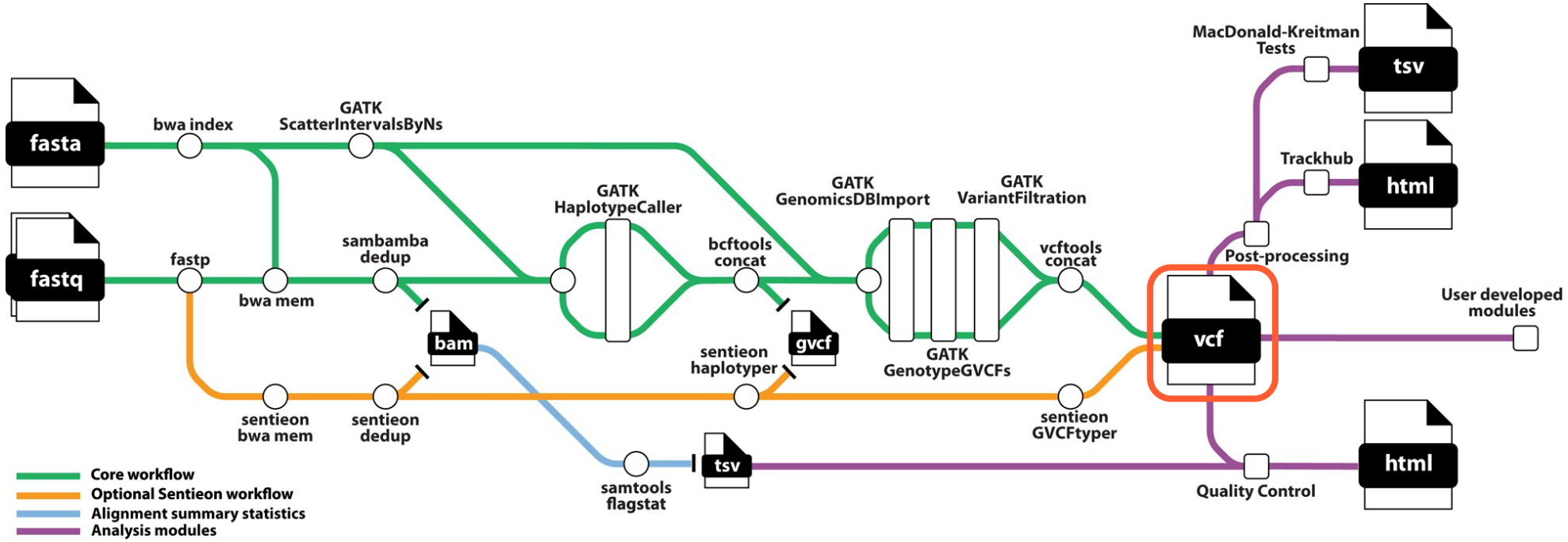


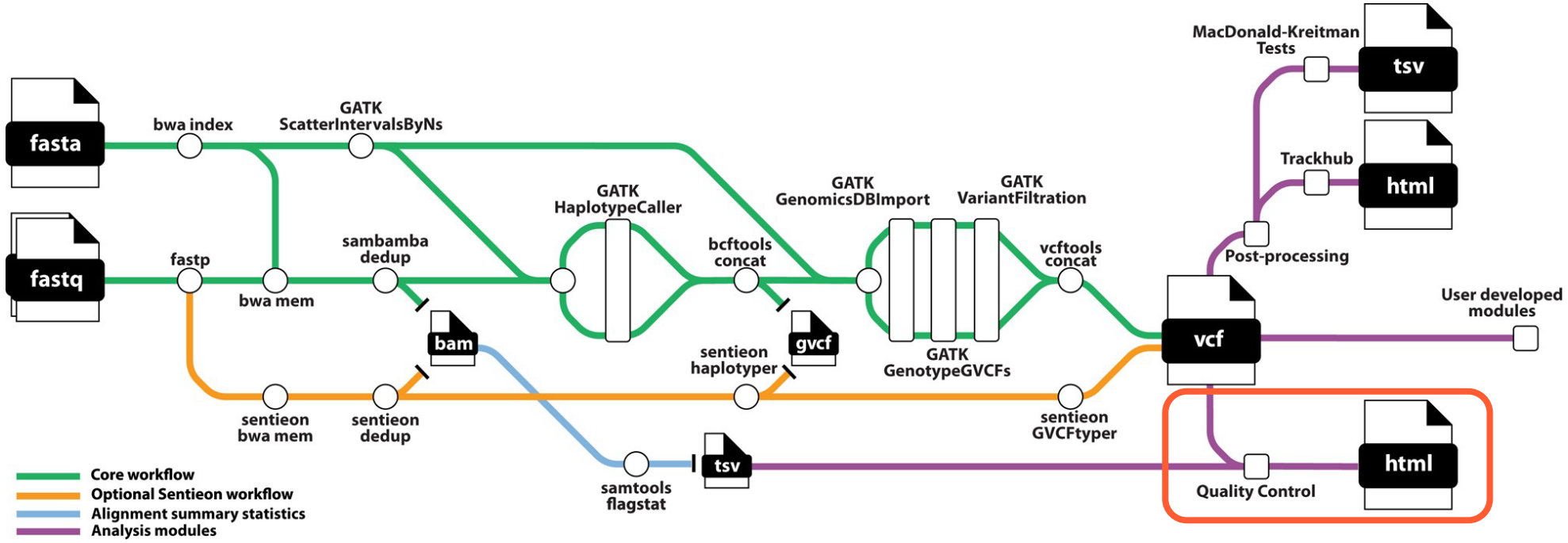
snpArcher's main output is a VCF file



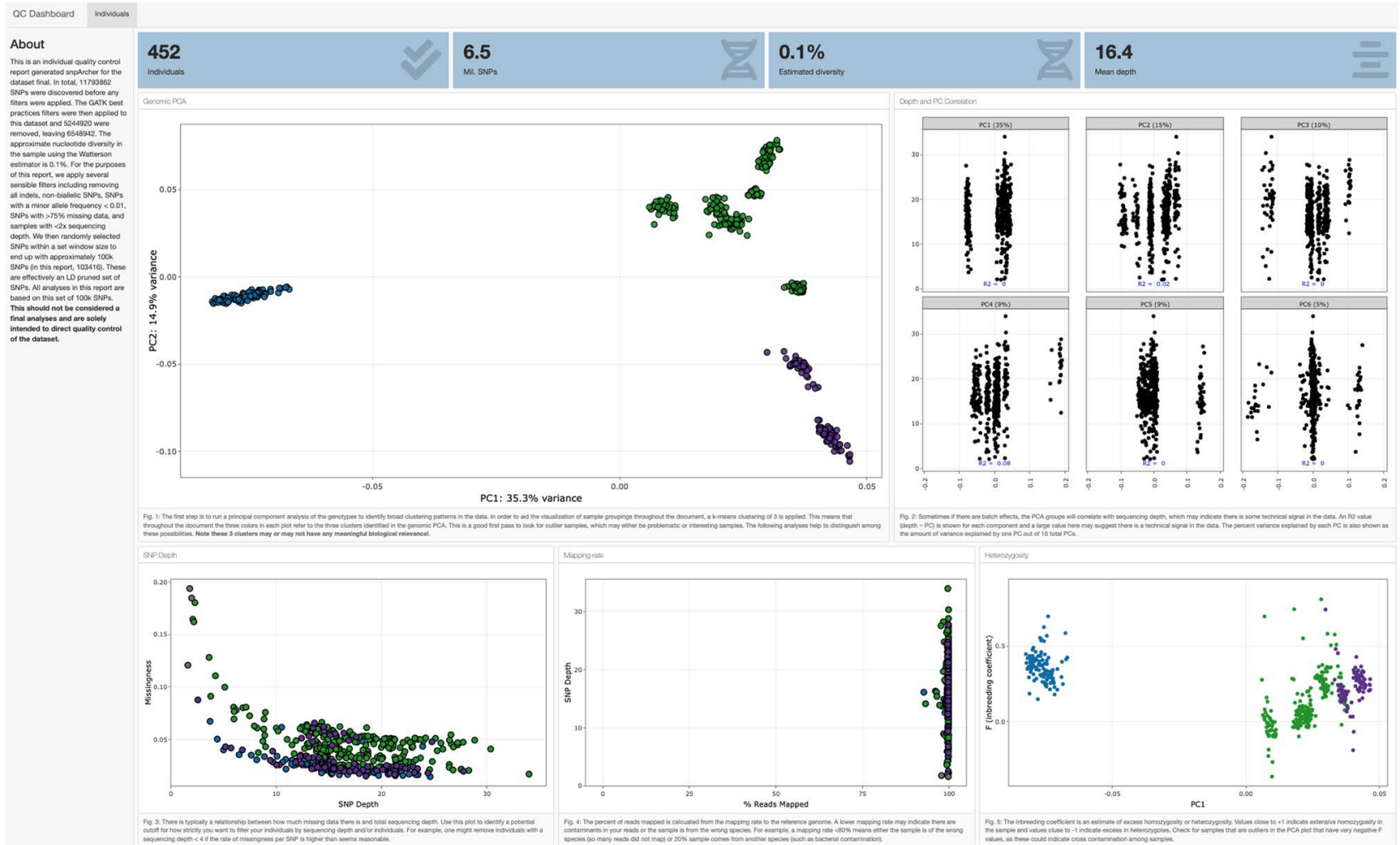
snpArcher's main output is a VCF file

```
##fileformat=VCFv4.2
##fileDate=20151002
##source=callMomV0.2
##reference=gi|251831106|ref|NC_012920.1| Homo sapiens mitochondrion, complete genome
##contig=<ID=MT,length=16569,assembly=b37>
##INFO=<ID=VT,Number=.,Type=String,Description="Alternate allele type. S=SNP, M=MNP, I=Indel">
##INFO=<ID=AC,Number=.,Type=Integer,Description="Alternate allele counts, comma delimited when multiple">
##FILTER=<ID=fa,Description="Genotypes called from fasta file">
##FORMAT=<ID=GT,Number=1,Type=String,Description="Genotype">
#CHROM  POS ID  REF ALT QUAL    FILTER  INFO    FORMAT  HG00096 HG00097 HG00099 HG00100 HG00101 HG00102 HG00103 HG00105 HG00106 HG00107
MT  10  .   T   C   100 fa  VT=S;AC=3   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  16  .   A   T   100 fa  VT=S;AC=3   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  26  .   C   T   100 fa  VT=S;AC=3   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  35  .   G   A   100 fa  VT=S;AC=2   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  40  .   TC  CT  100 fa  VT=M;AC=1   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  41  .   C   T   100 fa  VT=S;AC=4   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  42  .   TCC CCC,T   100 fa  VT=S,I;AC=1,1   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  46  .   T   C   100 fa  VT=S;AC=1   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  47  .   G   A   100 fa  VT=S;AC=1   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  52  .   TGG CAA 100 fa  VT=M;AC=1   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  55  .   TATTTT  T,CATTTT,AATTTT,TTT,TTTTT   100 fa  VT=I,S,S,I,I;AC=5,3,2,1,1   GT  0   0   0   0   0   0   0   0   0   0   0   0
MT  57  .   T   C   100 fa  VT=S;AC=3   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  58  .   TTT T   100 fa  VT=I;AC=4   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
MT  59  .   T   A   100 fa  VT=S;AC=1   GT  0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0   0
```

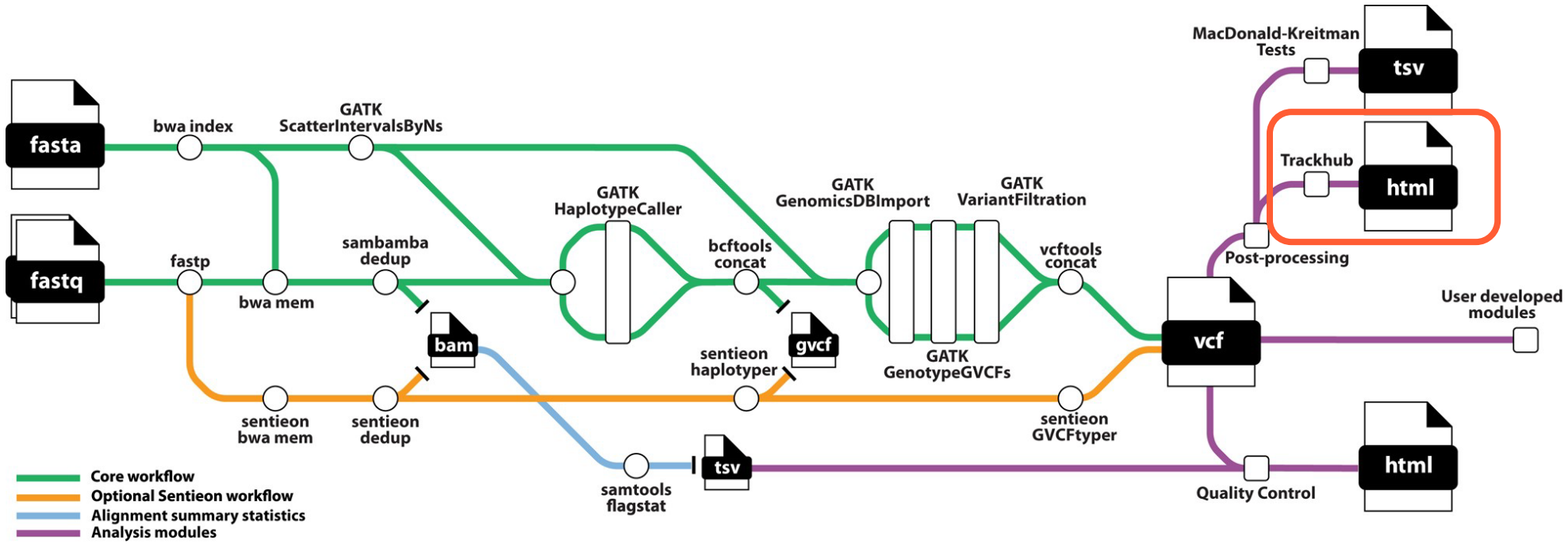
Summary statistics are provided as an HTML page



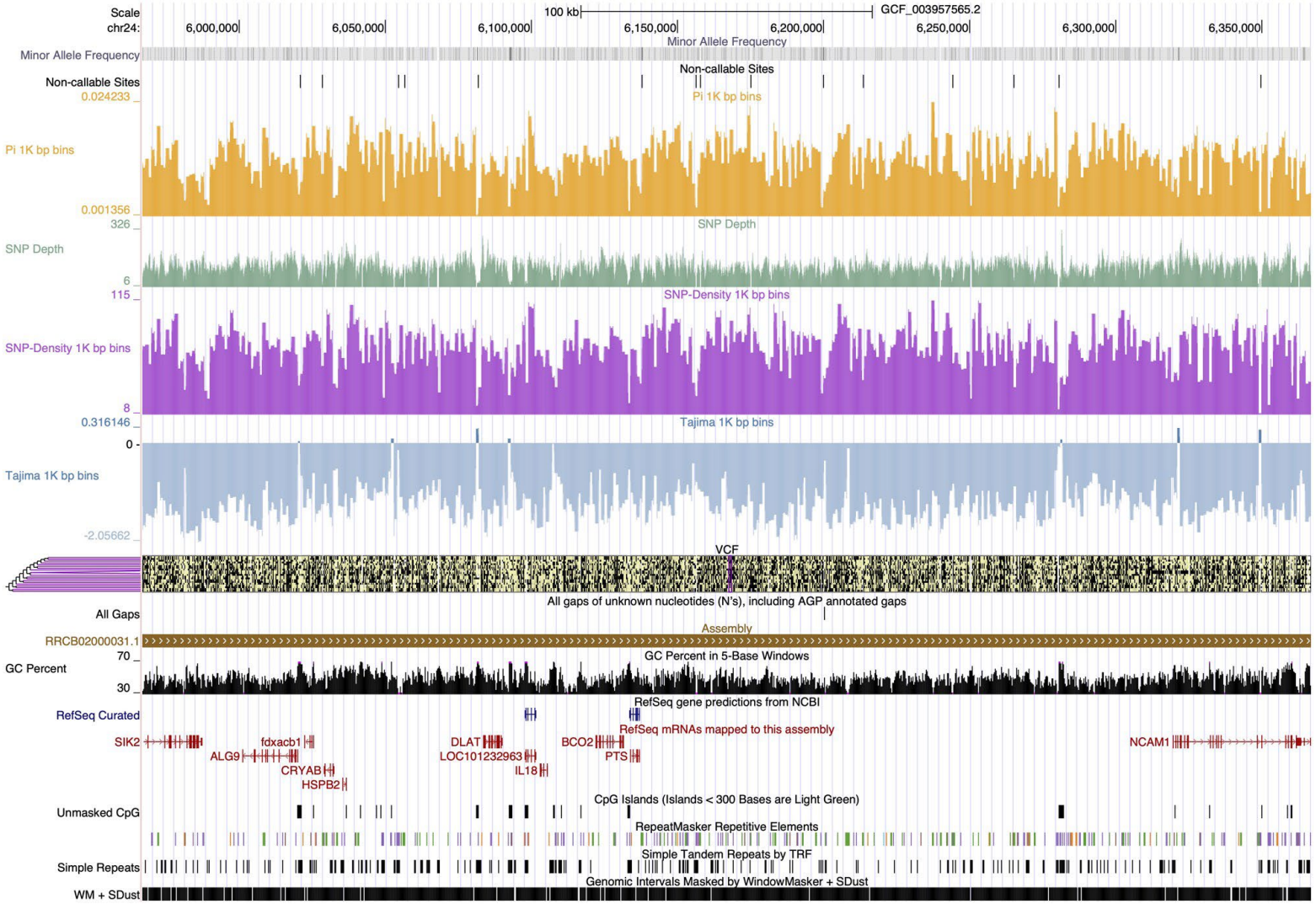
Summary statistics are provided as an HTML page



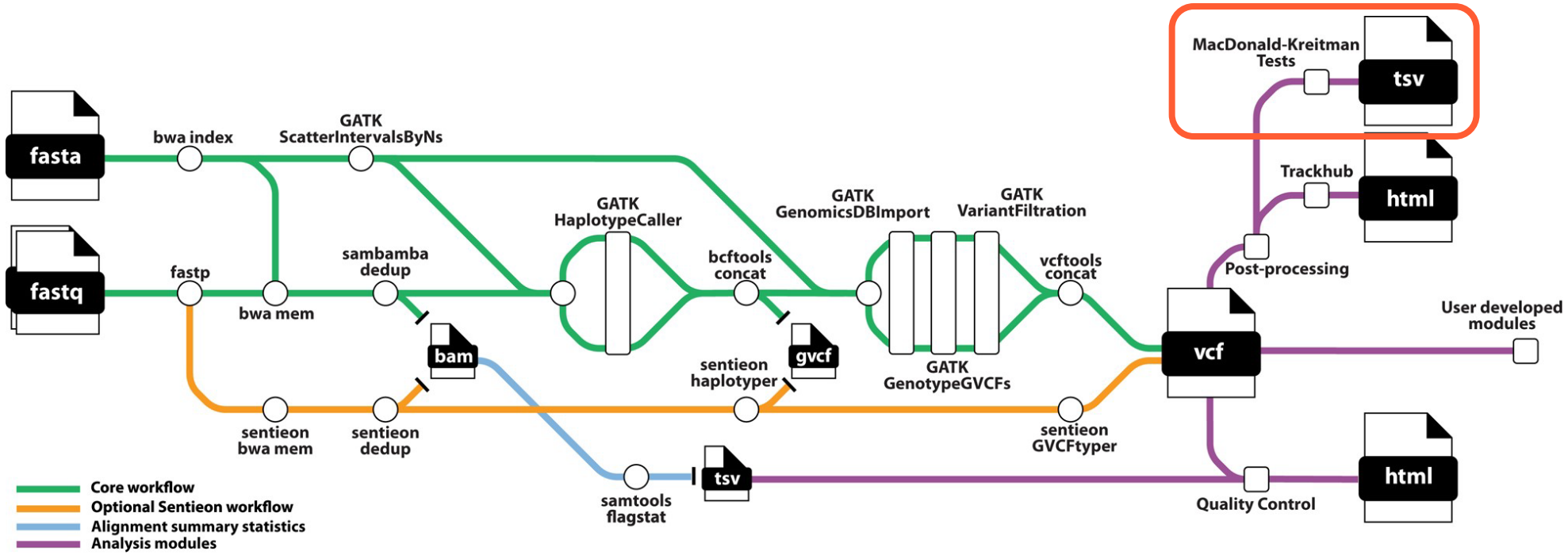
Trackhubs can be generated to visualize where SNPs occur



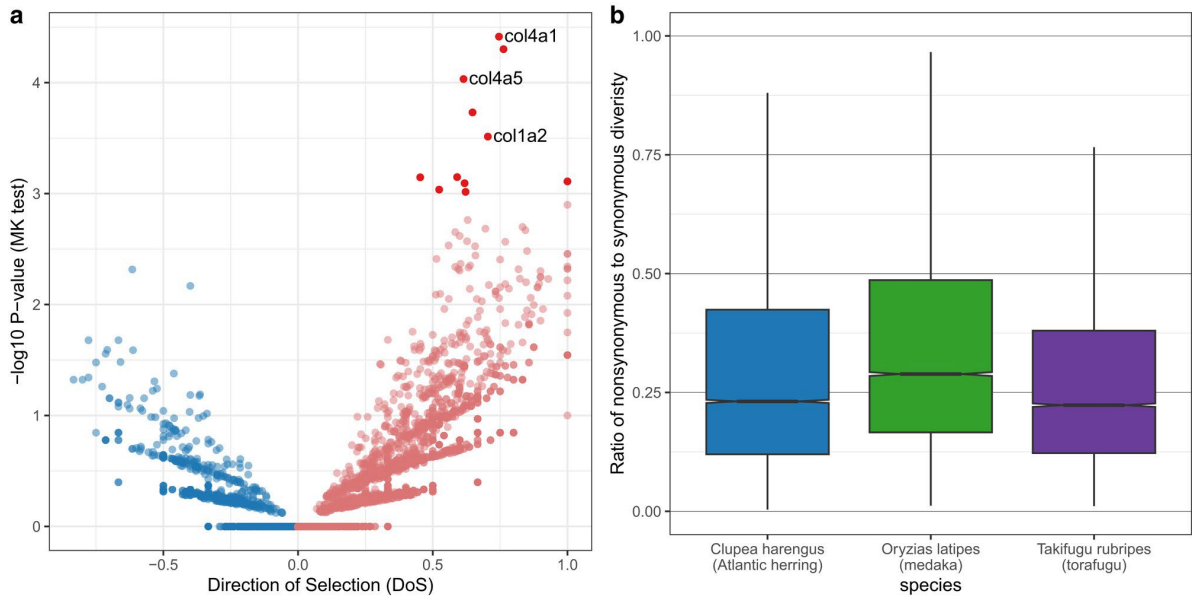
Trackhubs can be generated to visualize where SNPs occur



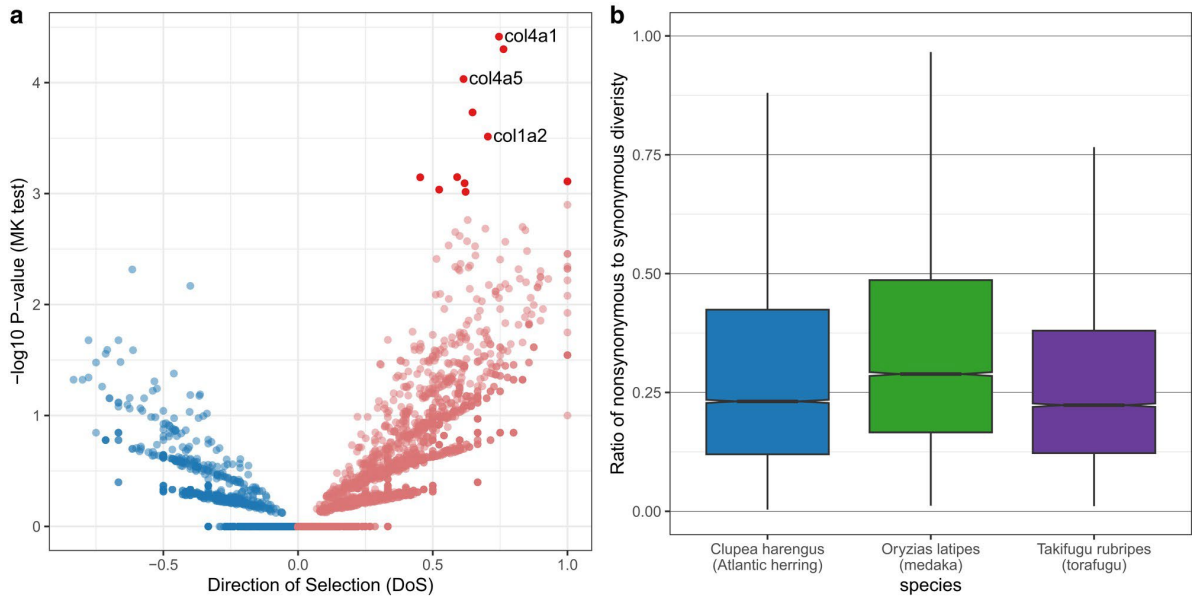
MK tests can be performed to test for selection



MK tests can be performed to test for selection



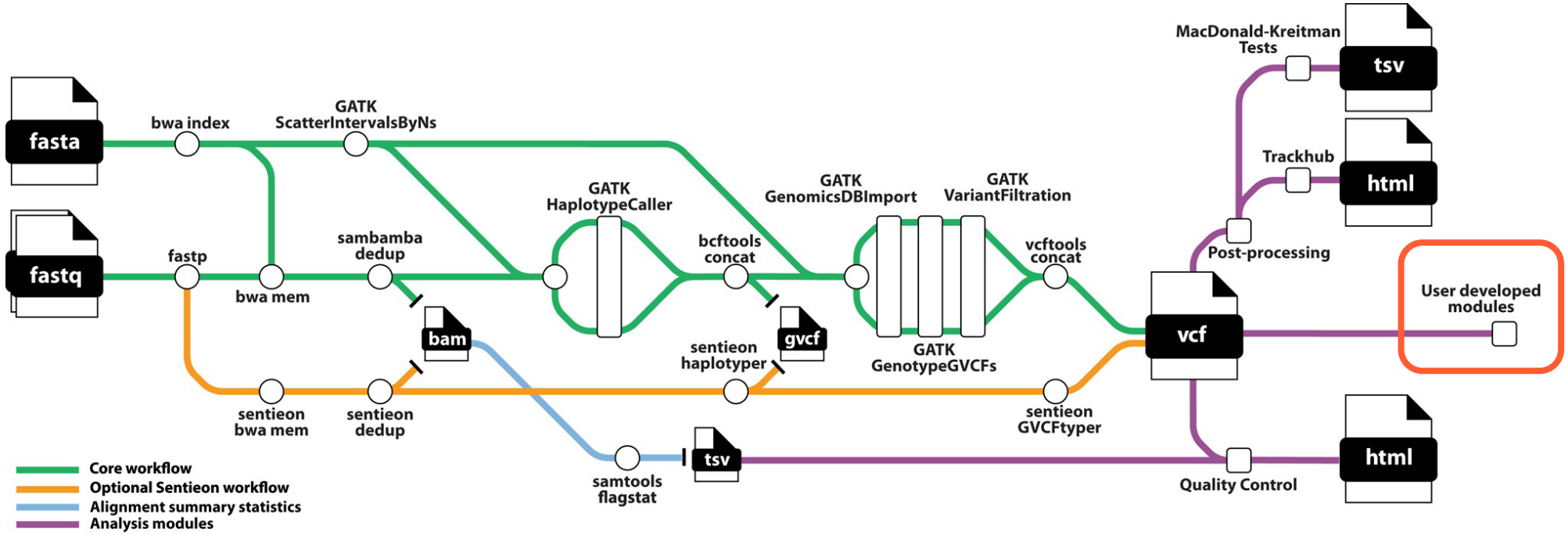
MK tests can be performed to test for selection



https://github.com/harvardinformatics/degenotate

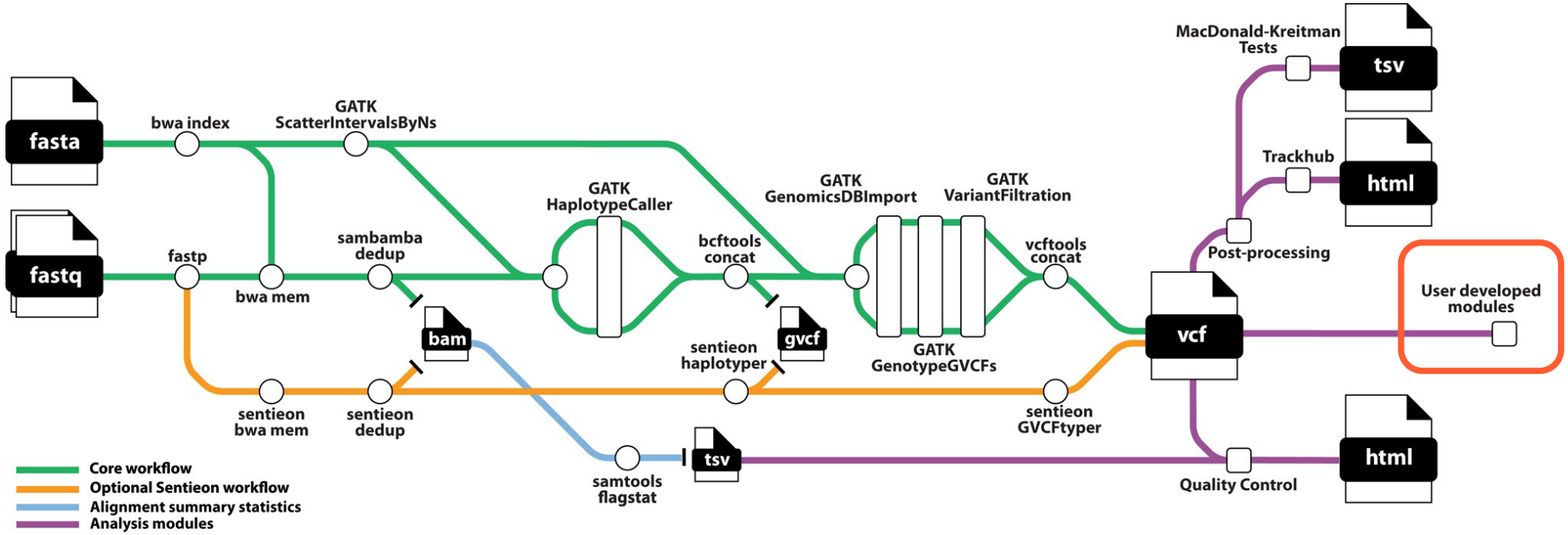
A (user-developed) module!

Users can develop their own modules and integrate them into snpArcher



Users can develop their own modules and integrate them into snpArcher

Module to infer population size: https://github.com/tforest/popsize



Thanks for your time!

Links:

snpArcher repository.....https://github.com/harvardinformatics/snpArcher
snpArcher documentation...https://snparcher.readthedocs.io/
snpArcher paper.....https://doi.org/10.1093/molbev/msad270

Informatics contact.....https://informatics.fas.harvard.edu/contact/