nf-core/pangenome
Pangenome growth

#MEMPANG24

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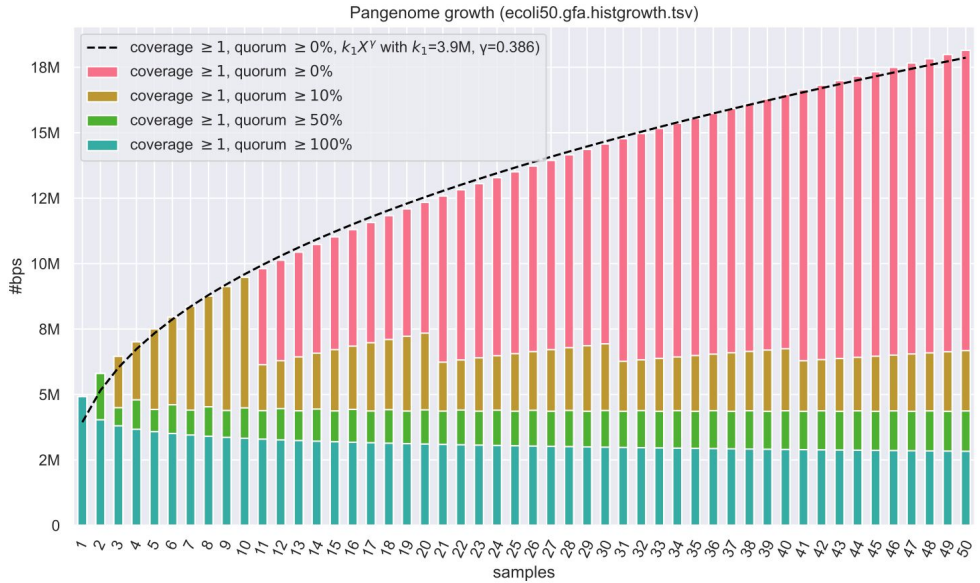
Day 2b - 2024/05/19

nf-core/pangenome




nf-core/
pangenome

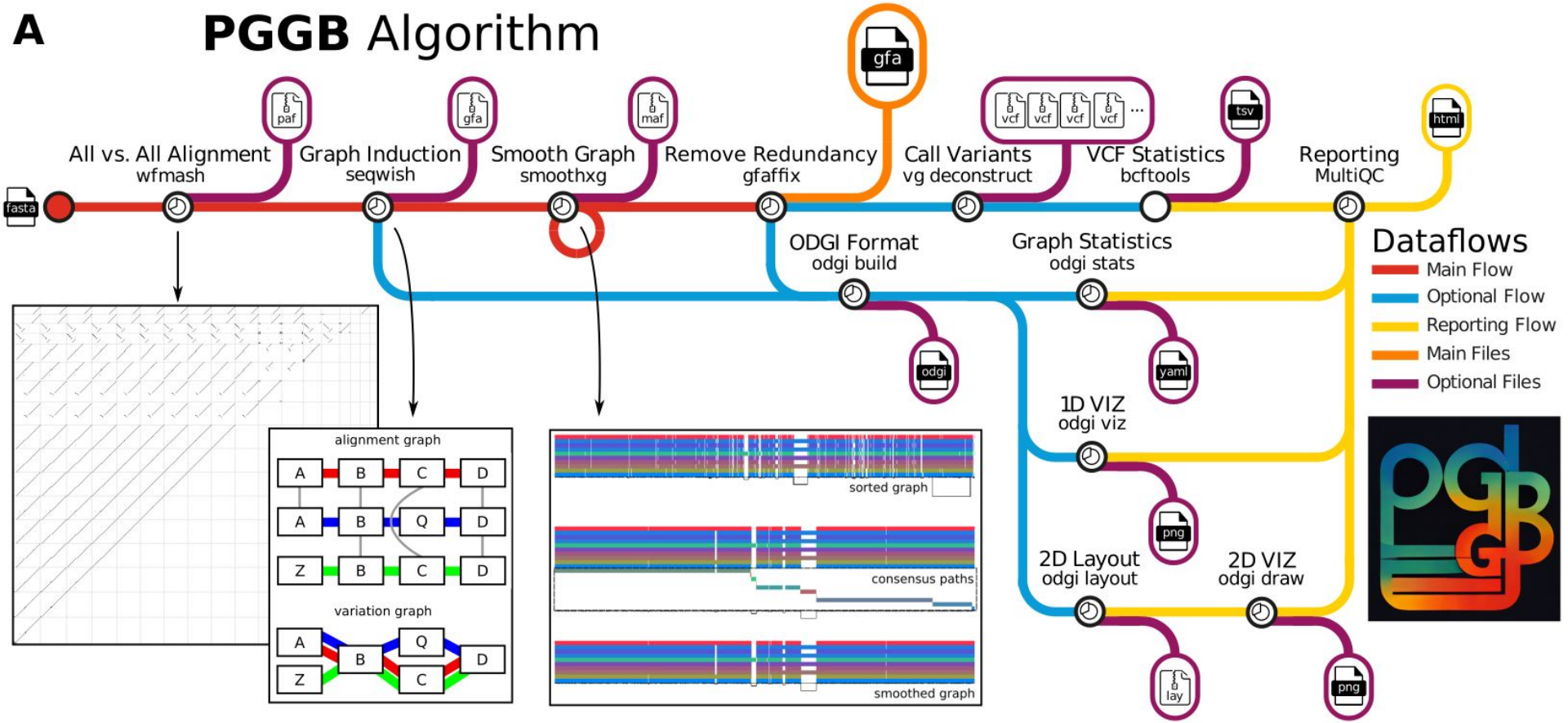
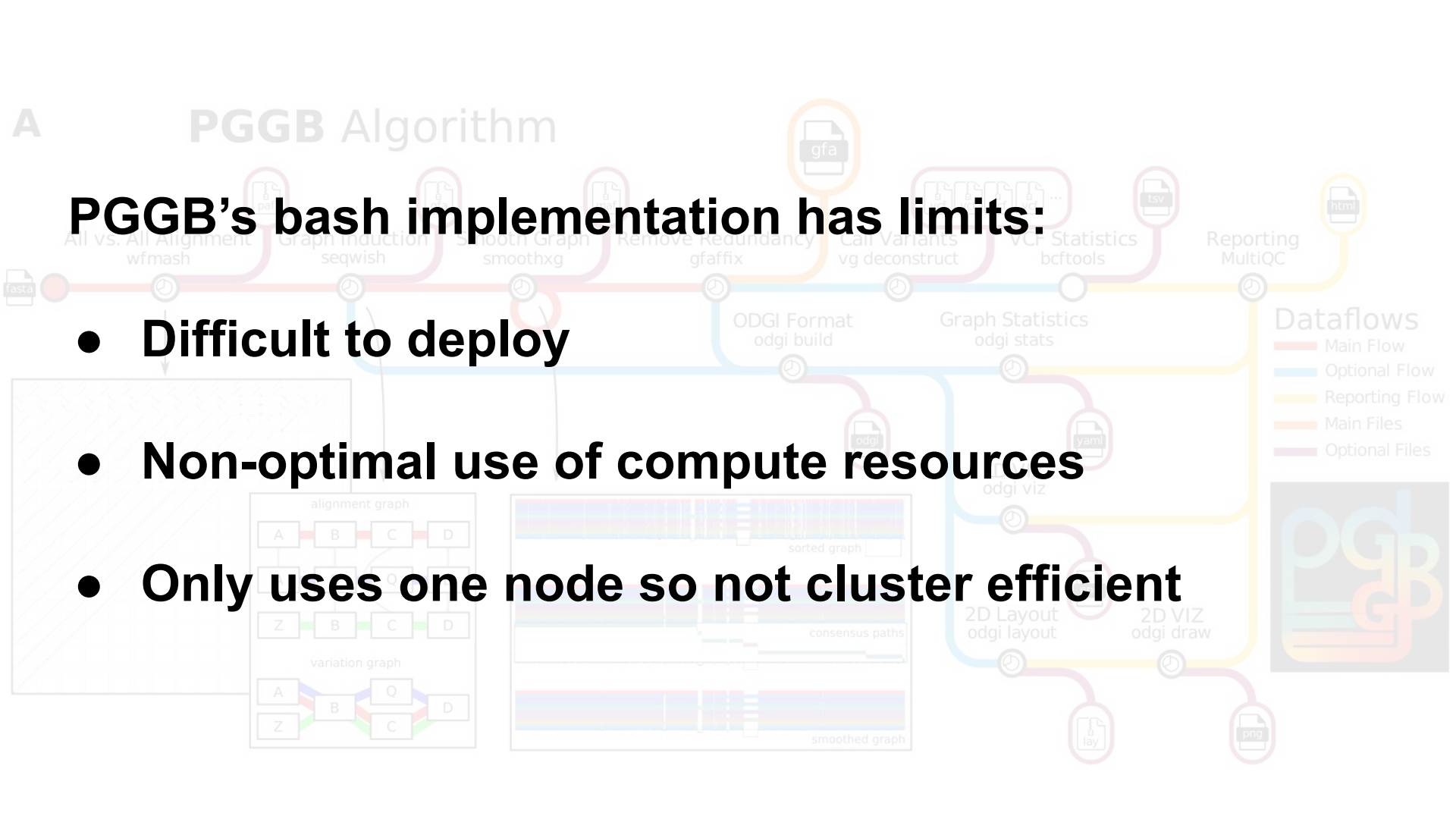


Figure from: [Garrison, Guarracino et al., 2023]



PGGB's bash implementation has limits:

- Difficult to deploy
- Non-optimal use of compute resources
- Only uses one node so not cluster efficient

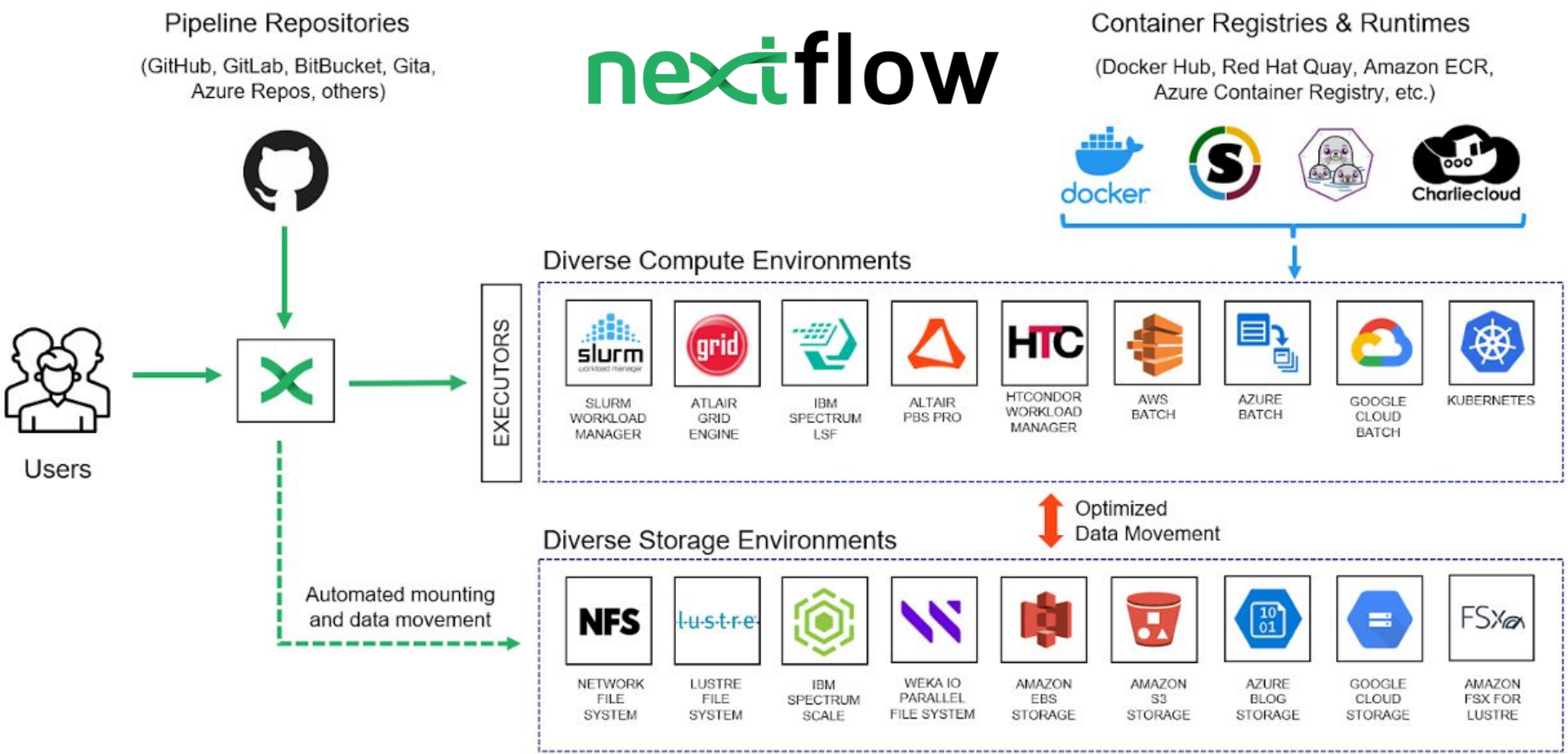


Figure from Di Tomasso P. et al., 2017.

nf-core

A community effort to collect a curated set of Nextflow pipelines

Stable releases

Packaged software

Documentation

Portable

Continuous integration

Cloud ready

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Figure from Ewels et al., 2020.

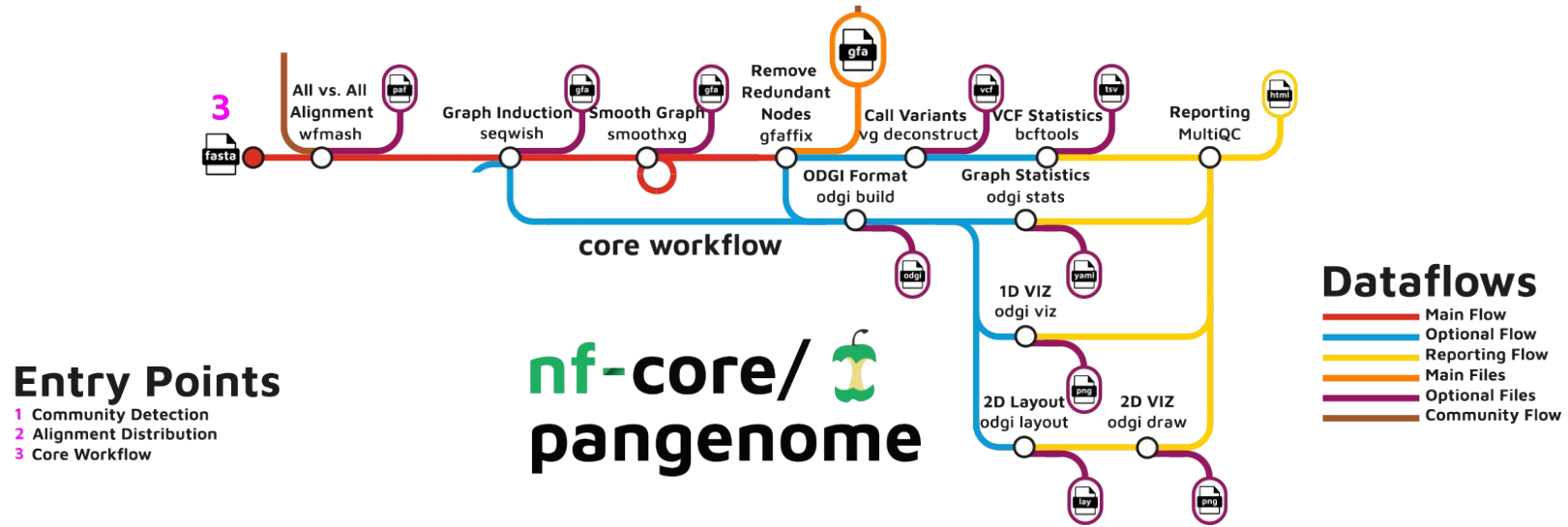


Figure from: [Heumos et al., 2024](#).

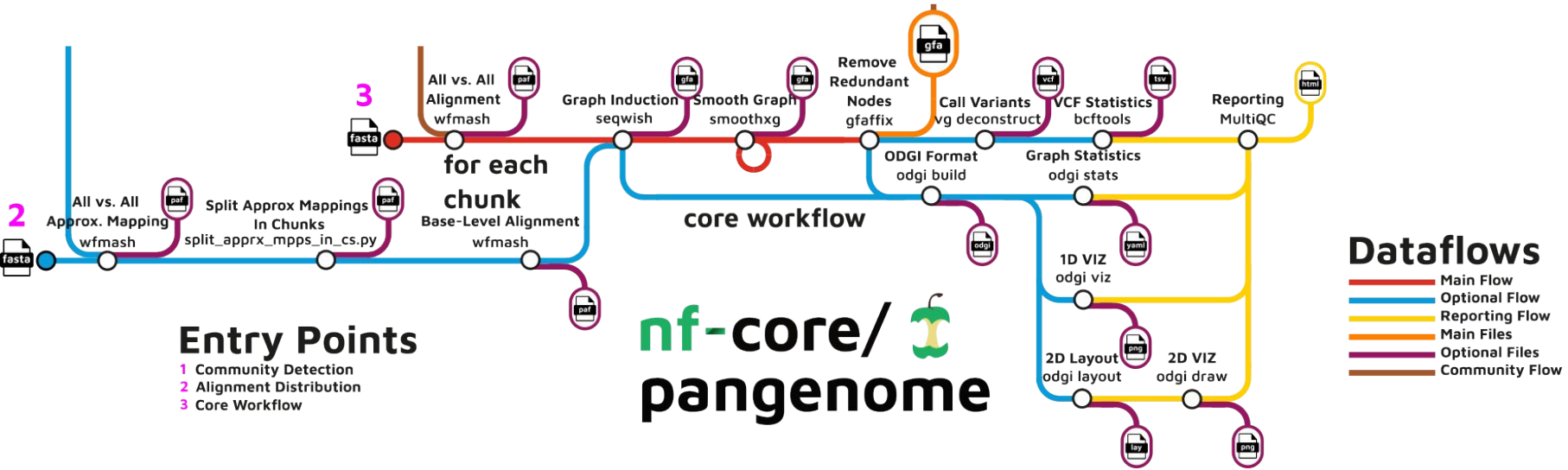
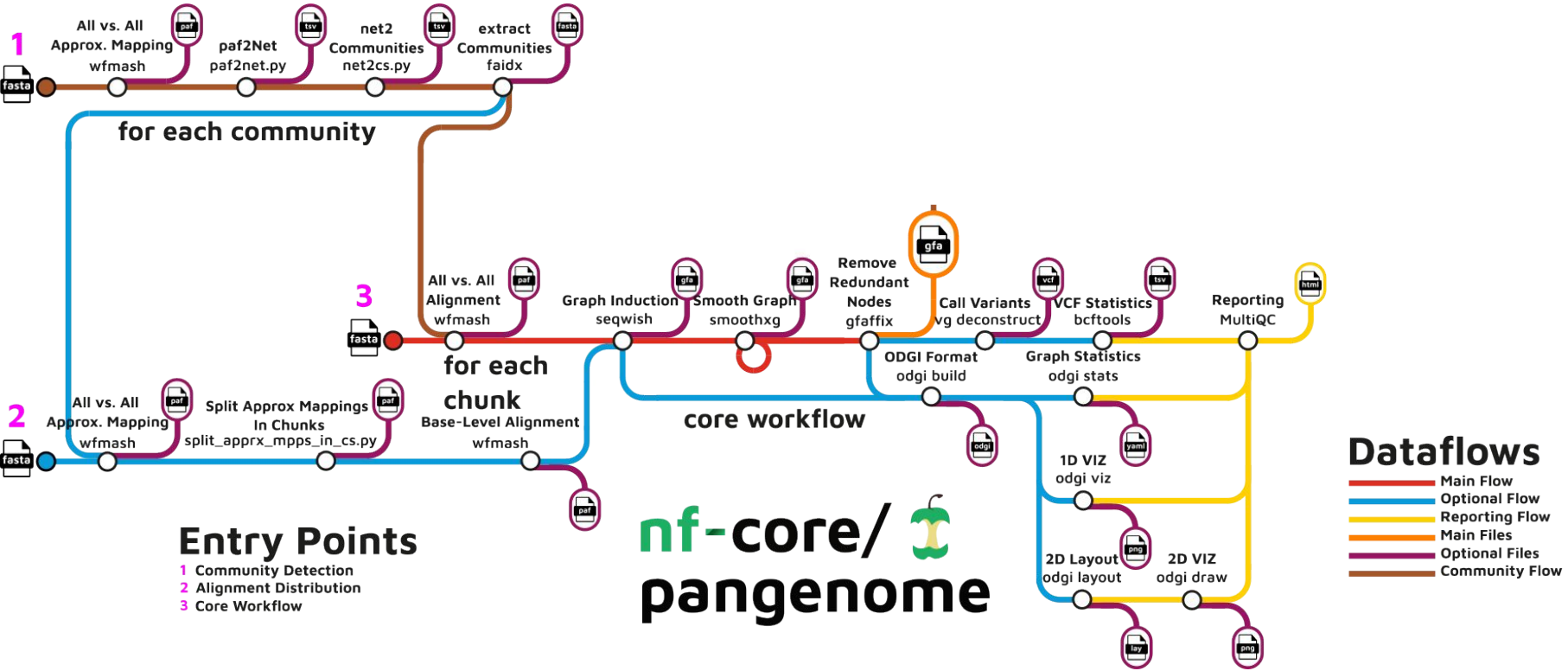


Figure from: [Heumos et al., 2024](#).



Clustering with the Leiden algorithm: Edge weight is `mapped_length * mapped_identity`

Leiden was applied in Guarracino et al., 2023.

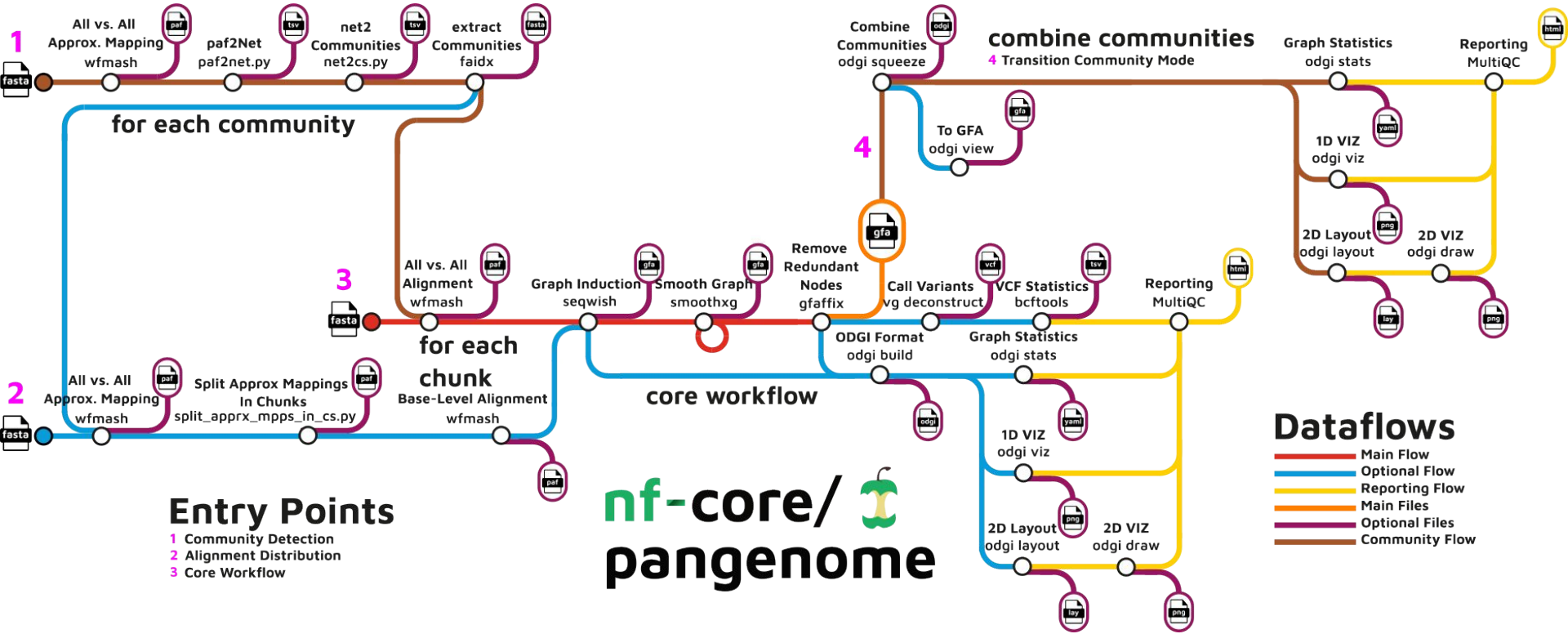


Figure from: [Heumos et al., 2024](#).

Building a cluster scalable version of PGGB

- Approximate mappings are split into chunks
- Processing of chunks is parallelized

⇒ Alignment can be distributed to cluster nodes

⇒ Time spent on base-pair level alignments is reduced linearly with increase in chunks

Time scales linearly with number of chunks

Base-pair level alignment of 1024 E.coli genomes

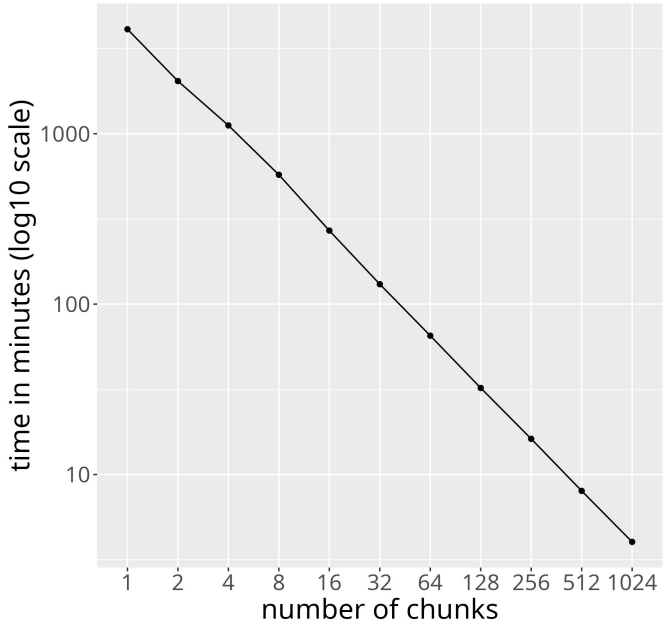


Figure from: Heumos et al., 2024.

Building a cluster scalable version of PGGB

- Approximate mappings are split into chunks
- Processing of chunks is parallelized

⇒ CO2 equivalent (CO2e) emissions do not rise with increasing number of chunks

CO2e exhaust is stable with number of chunks

Base-pair level alignment of 1024 E.coli genomes

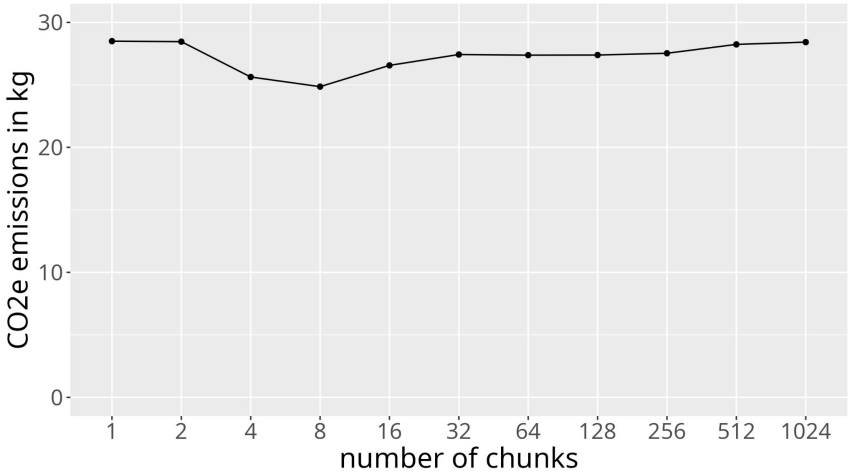


Figure from: Heumos et al., 2024.

Building a 1000 haplotypes 1KGP chr19 graph

nf-core/pangenome: 3 days

PGGB: 7 days

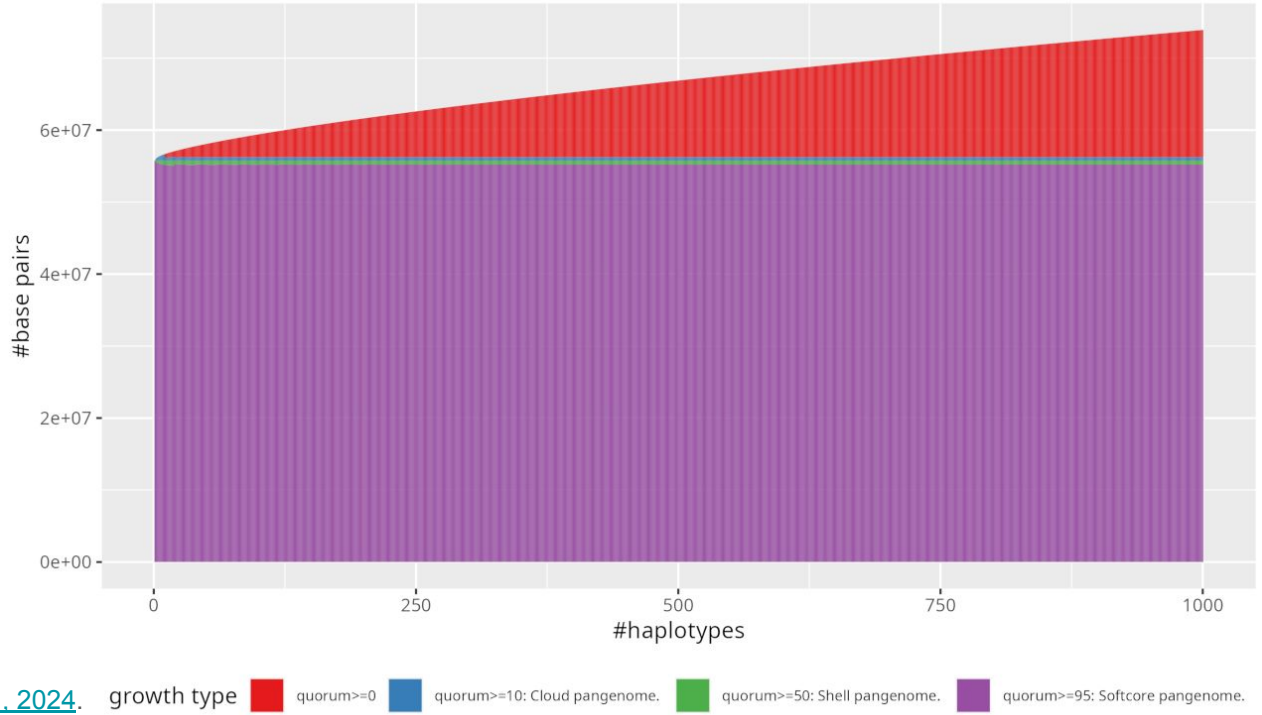


Figure from: [Heumos et al., 2024](#).

Building a 2146 sequences E. coli graph

nf-core/pangenome: 10 days

PGGB: didn't finish after 30 days

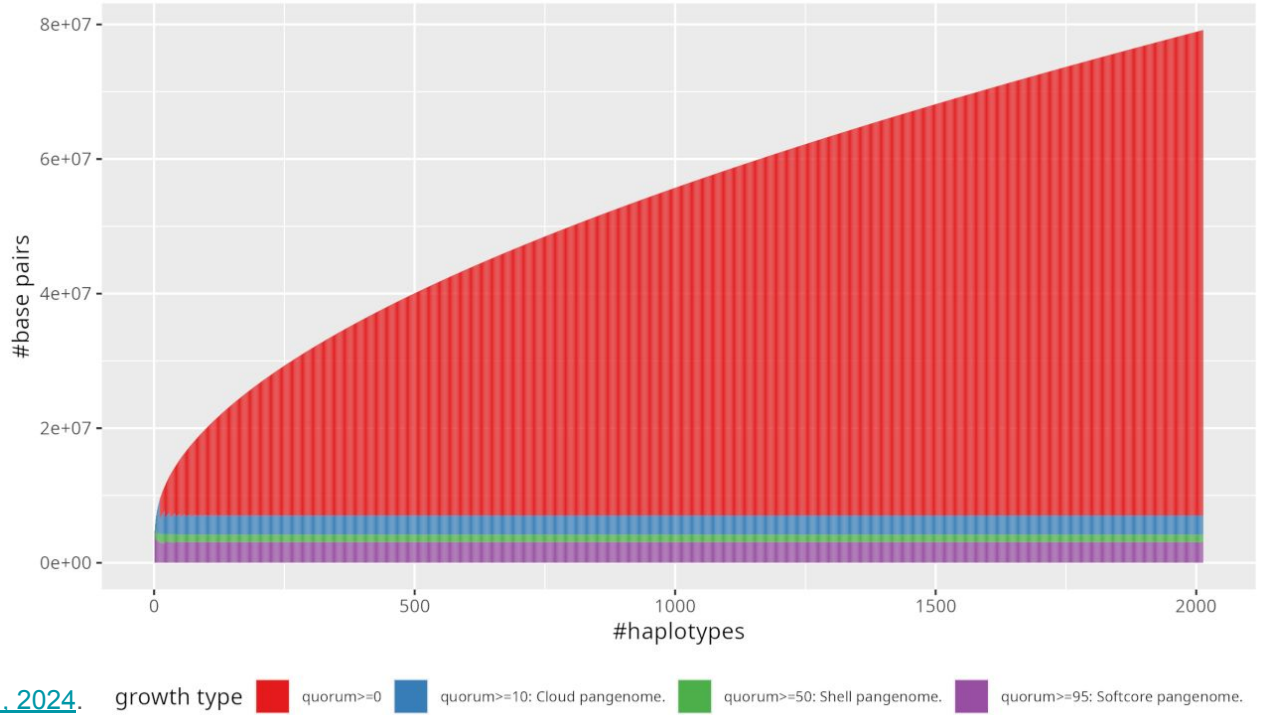


Figure from: Heumos et al., 2024.

nf-core/pangenome example run

```
nextflow run nf-core/pangenome -r a_brave_new_world -profile docker -config git/pangenome/conf/hla.config --input git/pggb/data/HLA/
DRB1-3123.fa.gz --wfmash_map_pct_id 70 --wfmash_segment_length 2000 --outdir DRB1-3123_pan --n_haplotypes 12
[ba/4d19e2] process > NFCORE_PANGENOME:PANGENOME:PGGB:WFMASH_MAP_ALIGN (DRB1-3123.fa.gz)                                [100%] 1 of 1 ✔
[f9/98e332] process > NFCORE_PANGENOME:PANGENOME:PGGB:SEQWISH (DRB1-3123.fa.gz)                                         [100%] 1 of 1 ✔
[34/01dc90] process > NFCORE_PANGENOME:PANGENOME:PGGB:SMOOTHXG (DRB1-3123.fa.gz)                                        [100%] 1 of 1 ✔
[81/ba4e25] process > NFCORE_PANGENOME:PANGENOME:PGGB:GFAFFIX (DRB1-3123.fa.gz)                                         [100%] 1 of 1 ✔
[88/081d82] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_BUILD (DRB1-3123.fa.gz.gfaffix)                              [100%] 2 of 2 ✔
[bd/b4a715] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_UNCHOP (DRB1-3123.fa.gz.gfaffix)                             [100%] 1 of 1 ✔
[6d/358413] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_SORT (DRB1-3123.fa.gz.gfaffix)                               [100%] 1 of 1 ✔
[ae/e3b97a] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_VIEW (DRB1-3123.fa.gz.gfaffix)                               [100%] 1 of 1 ✔
[9f/c04a92] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_QC:ODGI_STATS (DRB1-3123.fa.gz.gfaffix)                      [100%] 2 of 2 ✔
[3f/55484a] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_QC:ODGI_VIZ_COLOR (DRB1-3123.fa.gz.gfaffix.viz)              [100%] 1 of 1 ✔
[90/1aded7] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_QC:ODGI_VIZ_POS (DRB1-3123.fa.gz.gfaffix.viz_pos)           [100%] 1 of 1 ✔
[bf/1e22c8] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_QC:ODGI_VIZ_DEPTH (DRB1-3123.fa.gz.gfaffix.viz_depth)       [100%] 1 of 1 ✔
[2e/387271] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_QC:ODGI_VIZ_INV (DRB1-3123.fa.gz.gfaffix.viz_inv)          [100%] 1 of 1 ✔
[98/f89280] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_QC:ODGI_VIZ_COMPR (DRB1-3123.fa.gz.gfaffix.viz_O)          [100%] 1 of 1 ✔
[4e/9f113c] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_QC:ODGI_VIZ_UNCALLED (DRB1-3123.fa.gz.gfaffix.viz_uncalled) [100%] 1 of 1 ✔
[72/d583b1] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_QC:ODGI_LAYOUT (DRB1-3123.fa.gz.gfaffix)                    [100%] 1 of 1 ✔
[4b/ff48d1] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_QC:ODGI_DRAW_MULTIQC (DRB1-3123.fa.gz.gfaffix)               [100%] 1 of 1 ✔
[c2/469298] process > NFCORE_PANGENOME:PANGENOME:PGGB:ODGI_QC:ODGI_DRAW_HEIGHT (DRB1-3123.fa.gz.gfaffix)               [100%] 1 of 1 ✔
[06/0c9f72] process > NFCORE_PANGENOME:PANGENOME:CUSTOM_DUMPSOFTWAREVERSIONS (1)                                        [100%] 1 of 1 ✔
[50/a8350a] process > NFCORE_PANGENOME:PANGENOME:MULTIQC                                                                [100%] 1 of 1 ✔
-[nf-core/pangenome] Pipeline completed successfully-
```

Set pipeline resources

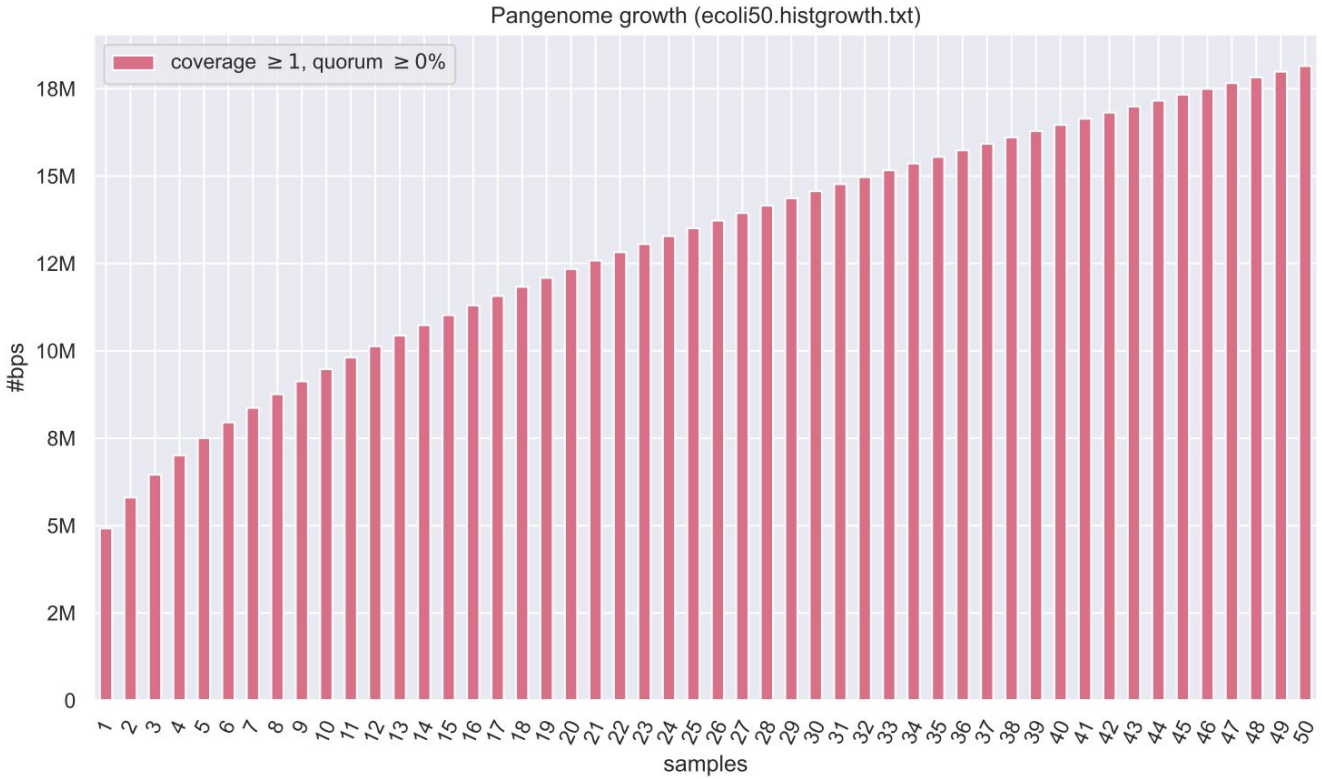
```
process {
    withName:'MULTIQC|MULTIQC_COMMUNITY|SAMTOOLS_FAIDX|CUSTOM_DUMPSOFTWAREVERSIONS' {
        cpus = 1
        memory = 1.GB
    }

    withName:'TABIX_BGZIP|ODGI_STATS|WFMASH_ALIGN|VG_DECONSTRUCT' {
        cpus = 4
        memory = 1.GB
    }

    withName:'WFMASH_MAP_ALIGN|WFMASH_MAP|SEQWISH|ODGI_BUILD|ODGI_UNCHOP|ODGI_SORT|ODGI_LAYOUT|WFMASH_MAP_COMMUNITY|ODGI_SQUEEZE' {
        cpus = 4
        memory = 4.GB
    }

    withName:'SMOOTHXG' {
        cpus = 4
        memory = 8.GB
    }

    withName:'GFAFFIX|ODGI_VIEW|ODGI_VIZ*|ODGI_DRAW|SPLIT_APPROX_MAPPINGS_IN_CHUNKS|PAF2NET|NET2COMMUNITIES|EXTRACT_COMMUNITIES' {
        cpus = 1
        memory = 4.GB
    }
}
```

What do we get?

- No new biological results or algorithms compared to PGGB
- Same CPU hours than PGGB
- Highly reduced wall clock time when running on a cluster
- The load of a cluster is more balanced
- Easily run the pipeline in all major clouds saving resources and money

Computing pangenome growth

Slide modified from
Daniel Doerr et al.



- Genomic variation within a species

Computing pangenome growth

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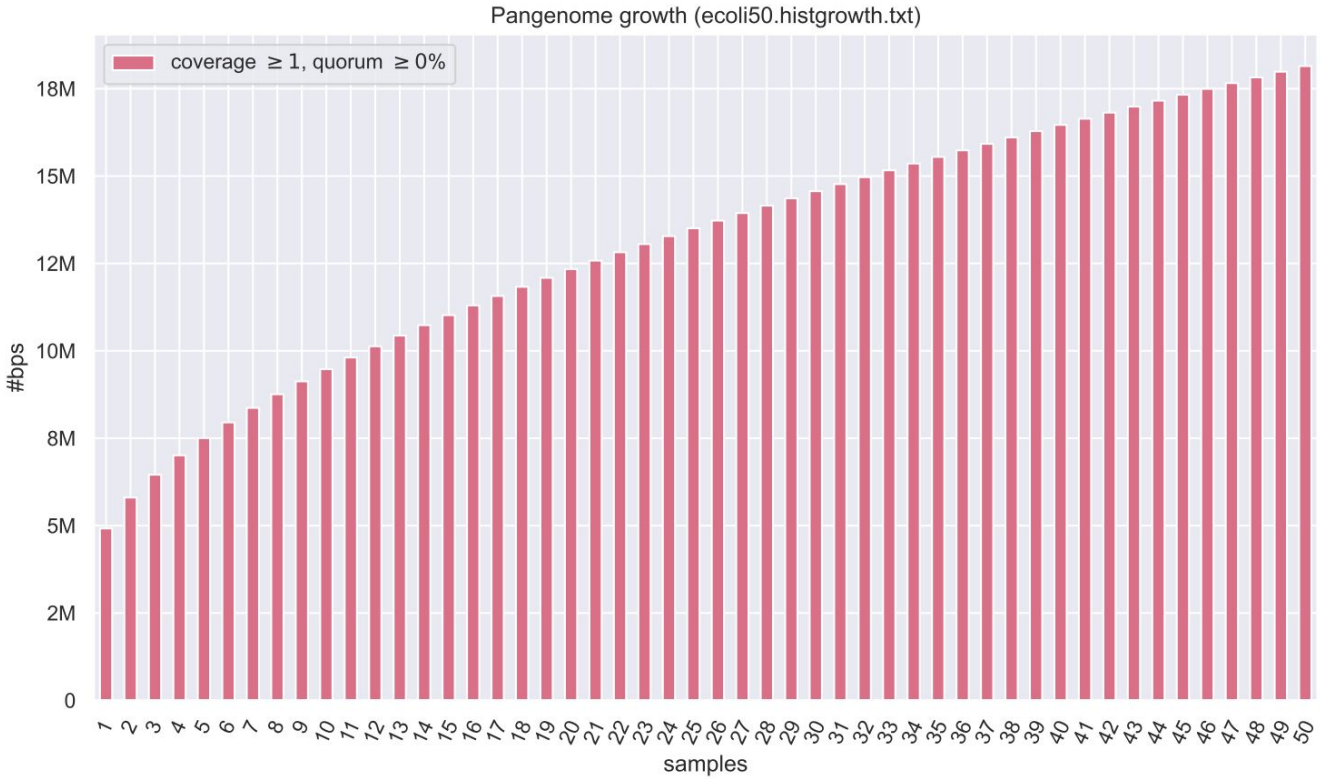

- Genomic variation within a species
- Population structure

Computing pangenome growth

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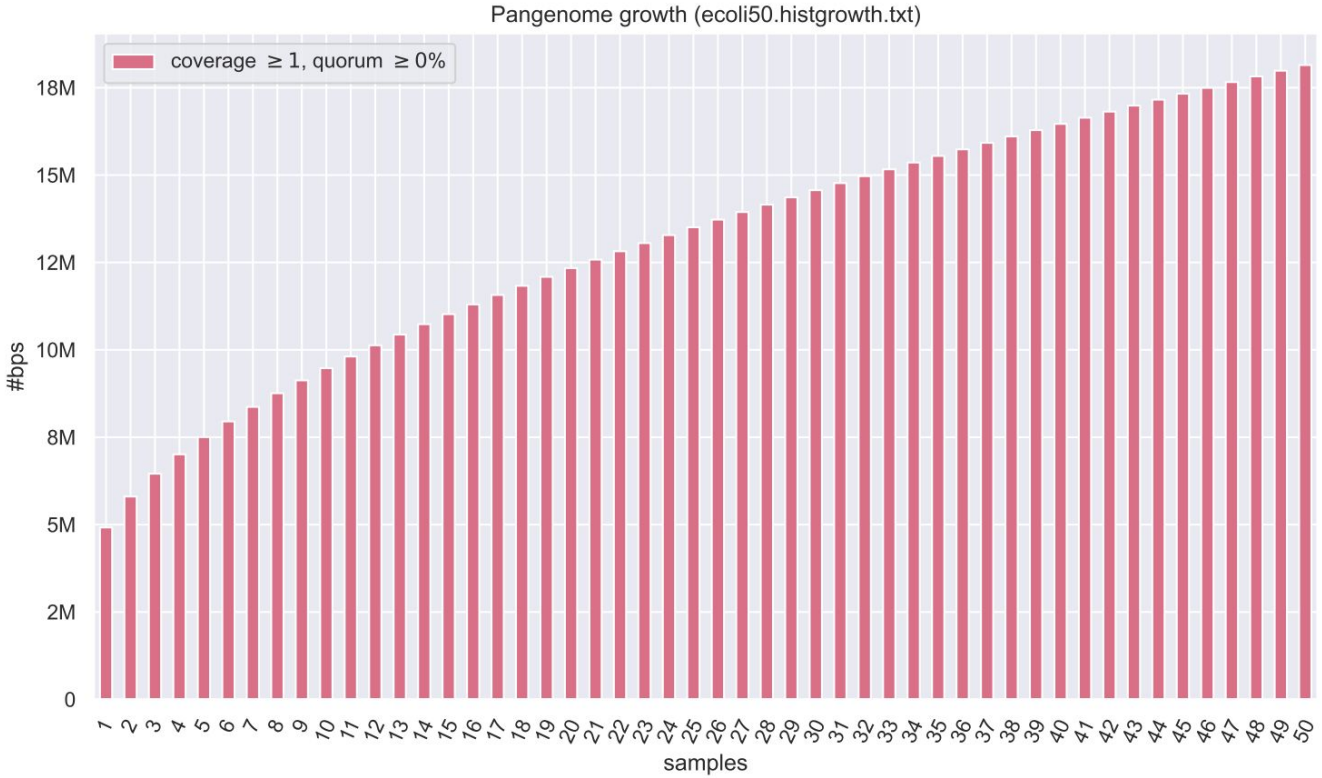

- Genomic variation within a species
- Population structure
- Genetic evolution: Pathogen research

Computing pangenome growth

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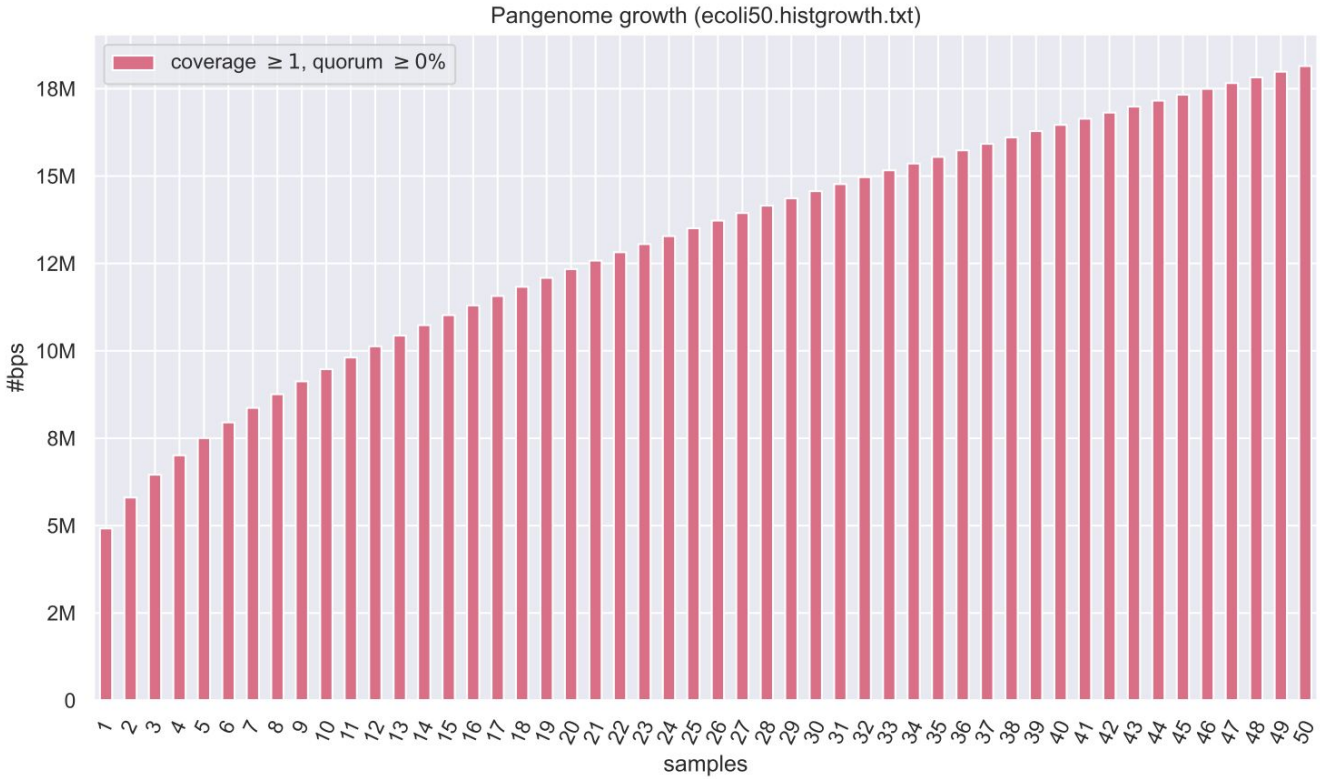
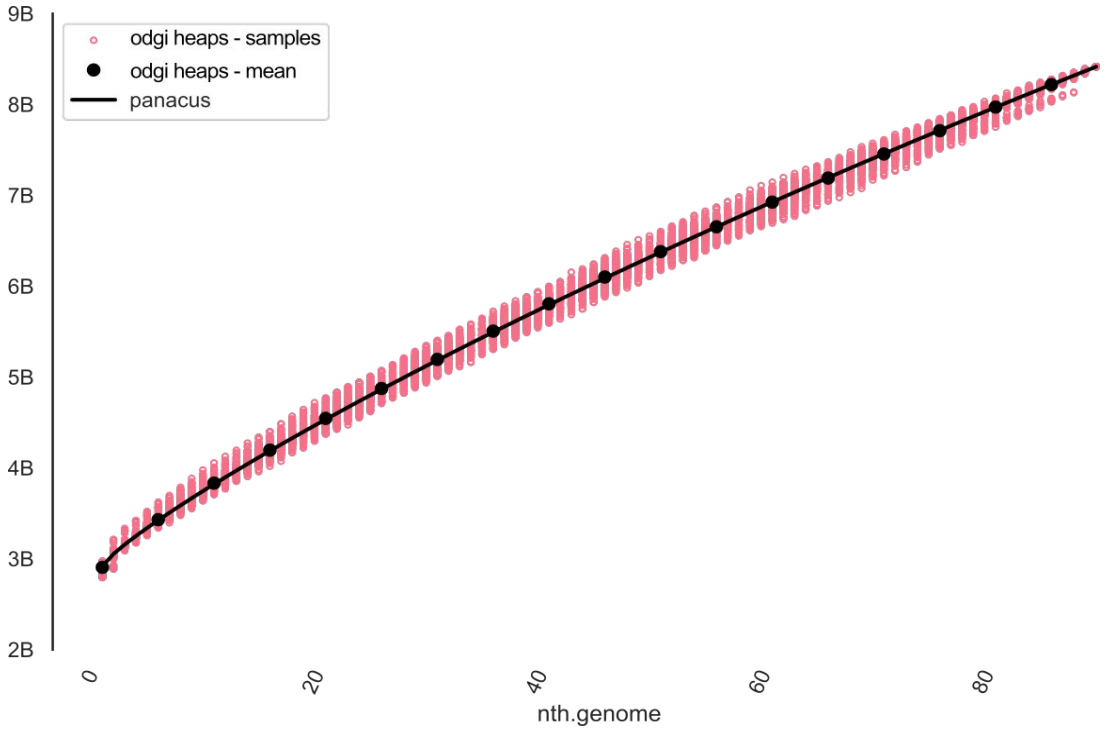


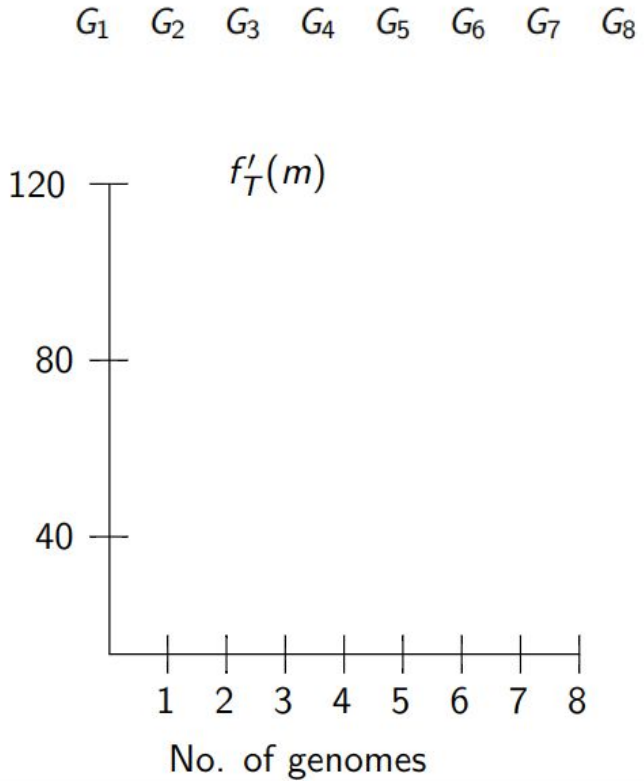
- Genomic variation within a species
- Population structure
- Genetic evolution: Pathogen research
- Biodiversity conservation

Computing pangenome growth statistics



Slide taken from
[Daniel Doerr et al.]

Pangenome growth computation



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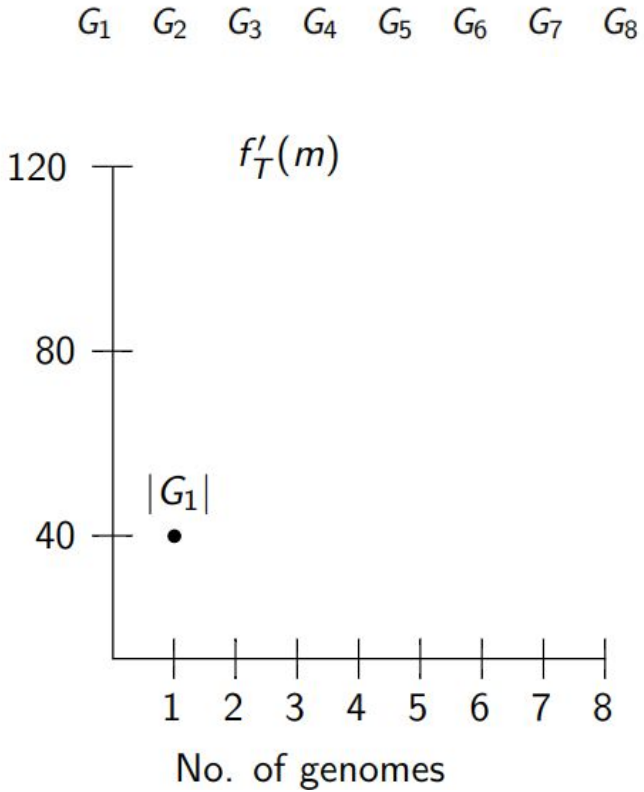

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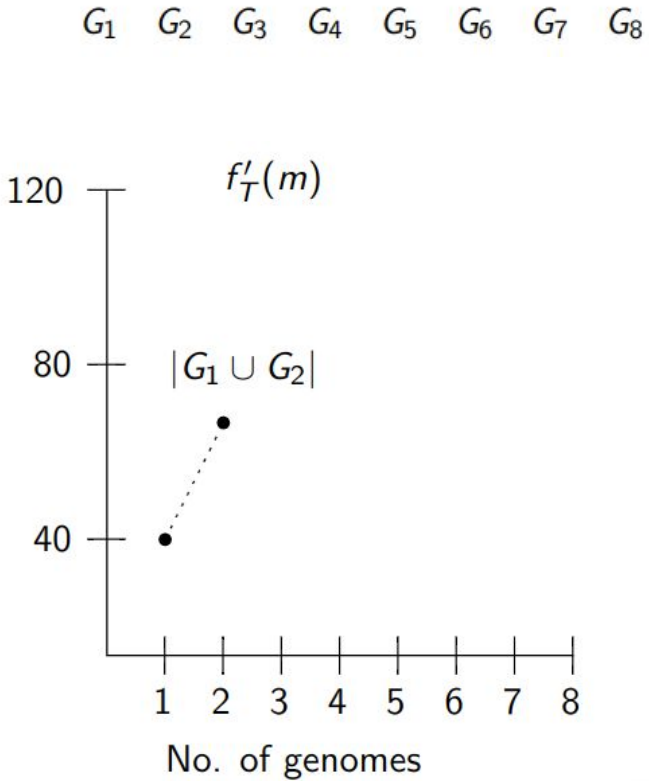

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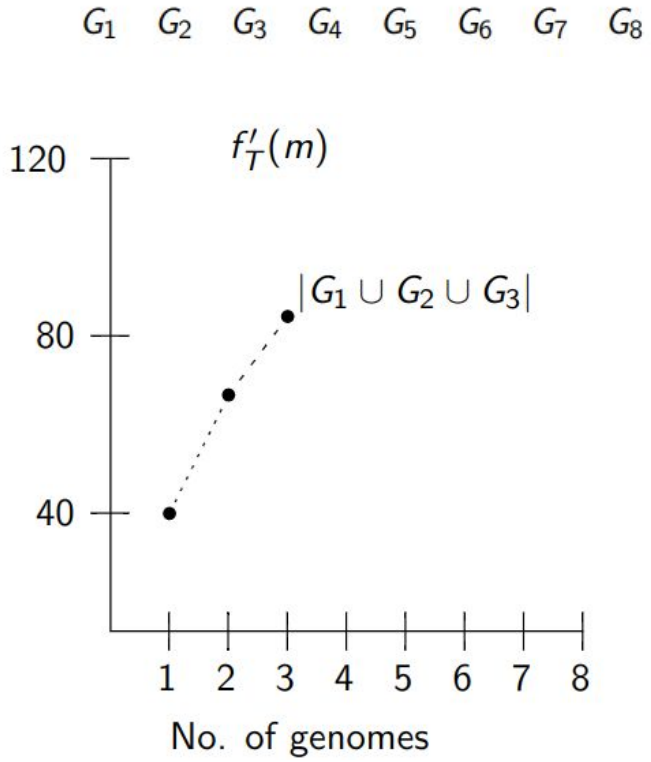

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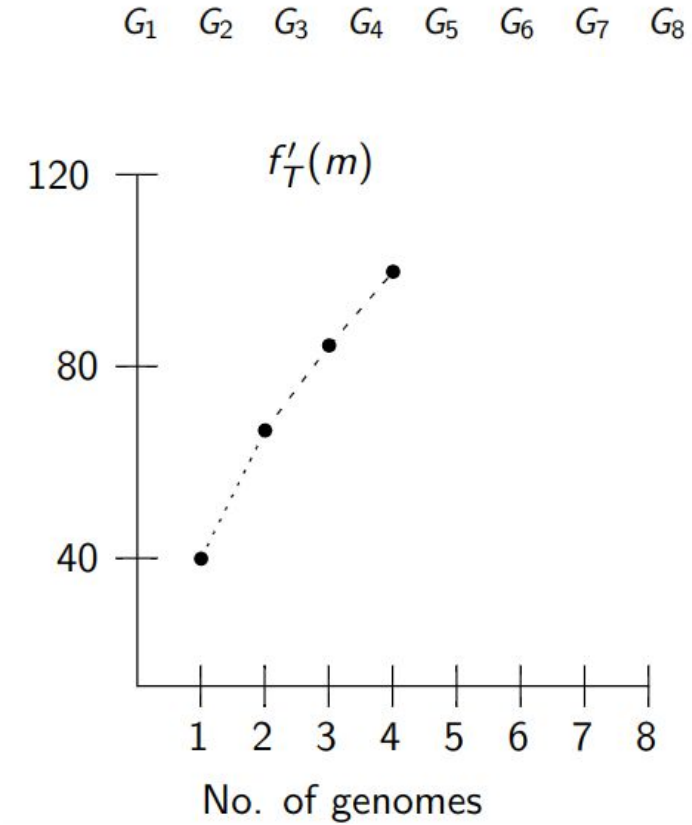

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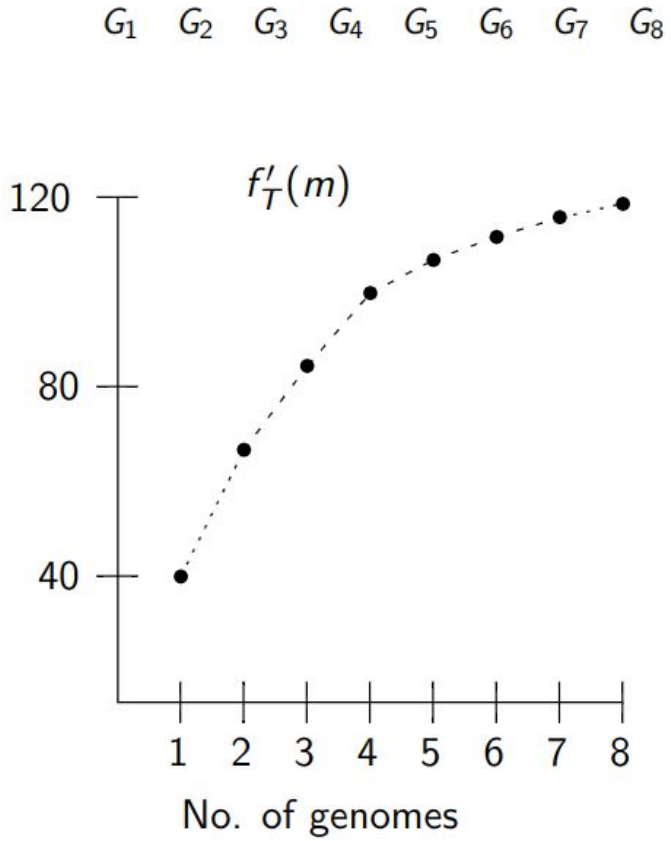

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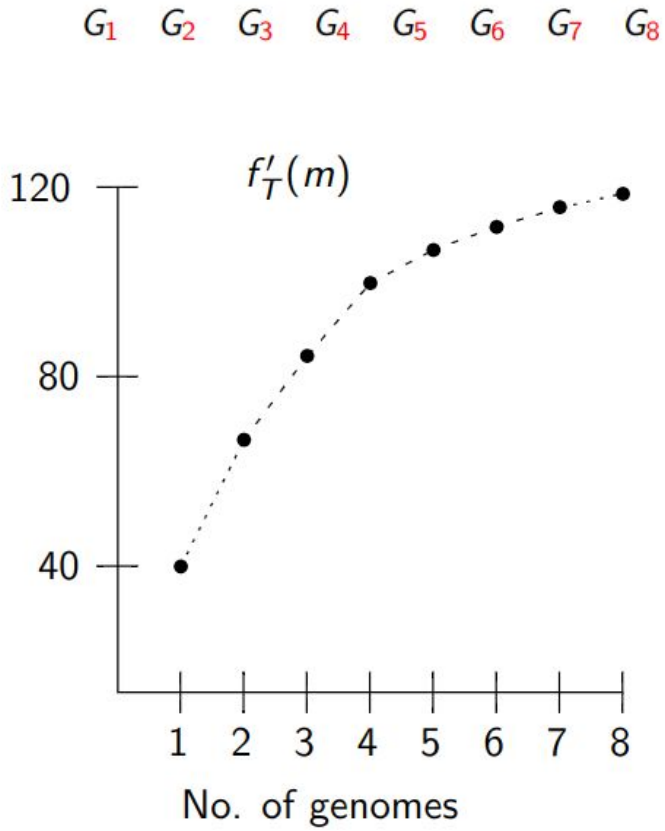

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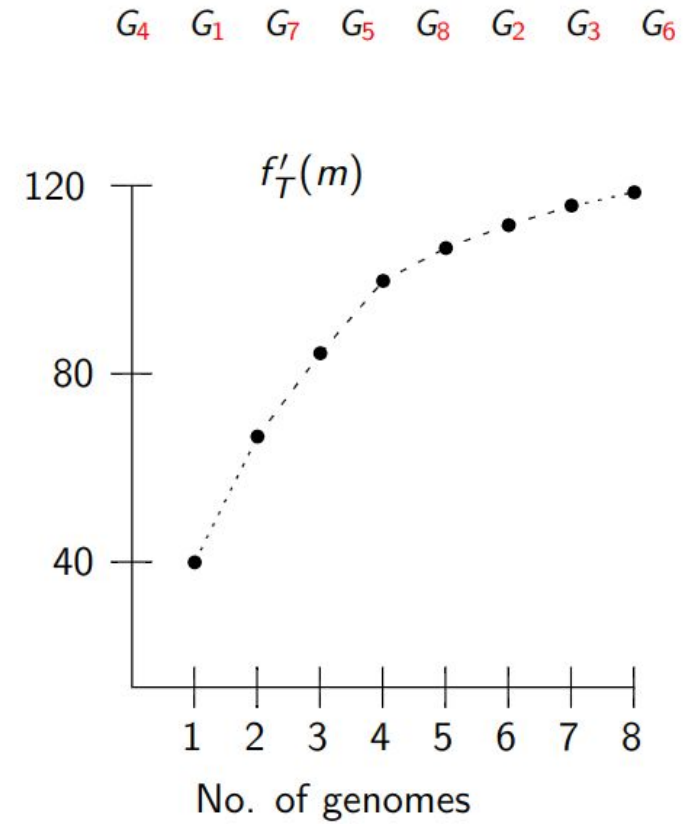

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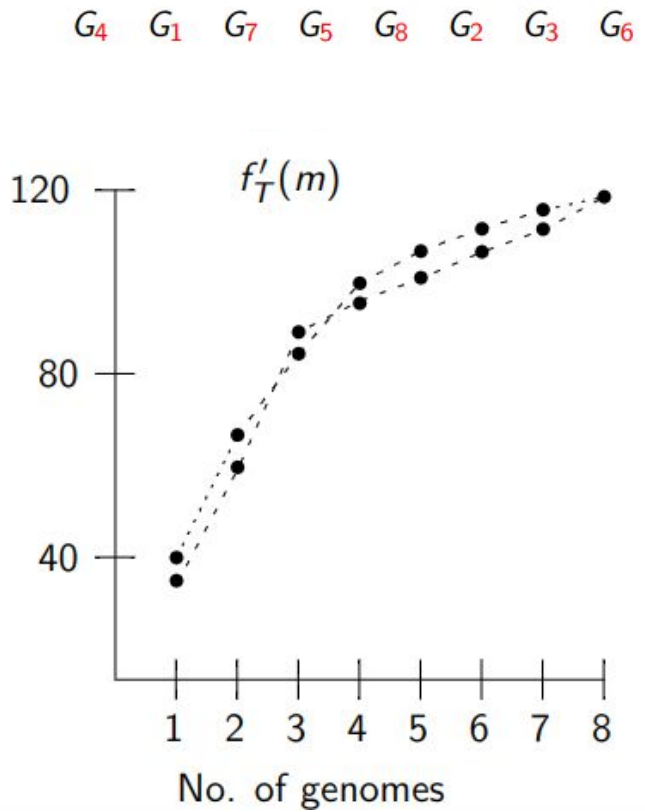

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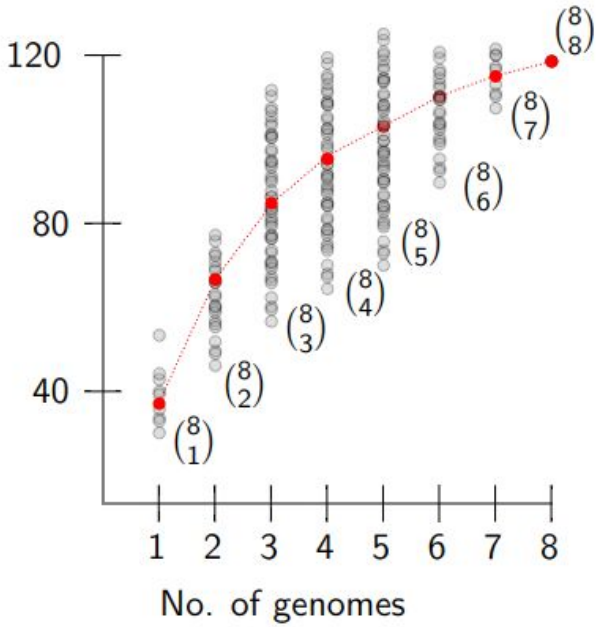

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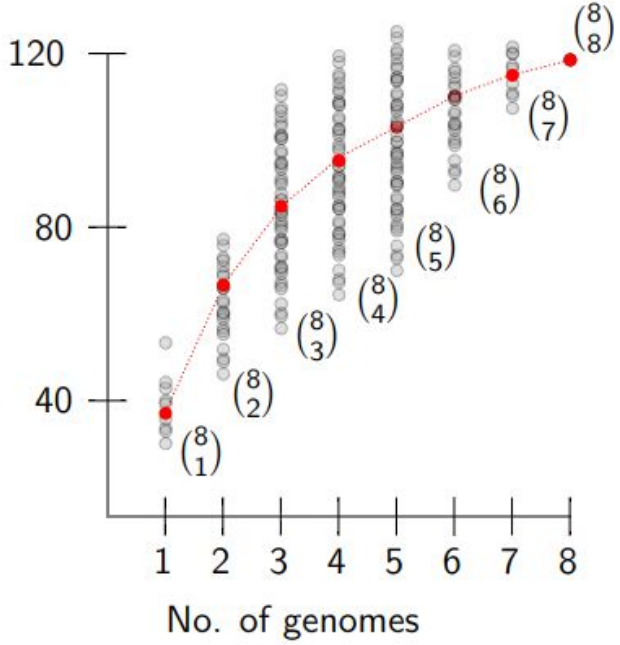
Daniel Doerr et al.

Pangenome growth computation - *odgi heaps*



$$f_{\text{tot}}(m) = \frac{1}{\binom{n}{m}} \sum_{\mathcal{G}' \in \mathcal{G}_m} \left| \bigcup_{G \in \mathcal{G}'} G \right|$$

m: total number of genomes

n: number of genomes in current growth computation

Slide modified from
Daniel Doerr et al.

Pangenome growth computation - *Panacus*

Slide modified from
Daniel Doerr et al.

$$f_{\text{tot}}(m) = \frac{1}{\binom{n}{m}} \sum_{\mathcal{G}' \in \mathcal{G}_m} \left| \bigcup_{G \in \mathcal{G}'} G \right| =$$

$h(i) =$ number of items occuring in **exactly** i genomes

- Time complexity $O(n^2)$ << Number of countables (nodes, edges, bps)
- 1971, Stuart H. Hurlbert[a]

[a]Hurlbert, S. H. (1971). The Nonconcept of Species Diversity: A Critique and Alternative Parameters. Ecology, 52(4), 577–586
[b]A. Chacoma and D. H. Zanette. Heaps' law and Heaps functions in tagged texts:evidences of their linguistic relevance. Royal Society Open Science, 7(3),2020

Pangenome growth computation - *Panacus*

Slide modified from
Daniel Doerr et al.

$$f_{\text{tot}}(m) = \frac{1}{\binom{n}{m}} \sum_{\mathcal{G}' \in \mathcal{G}_m} \left| \bigcup_{G \in \mathcal{G}'} G \right| = \sum_{i=1}^{n} h(i) \left(1 - \frac{(n-i)^{\underline{m}}}{n^{\underline{m}}}\right)$$

$h(i)$ = number of items occuring in **exactly** i genomes

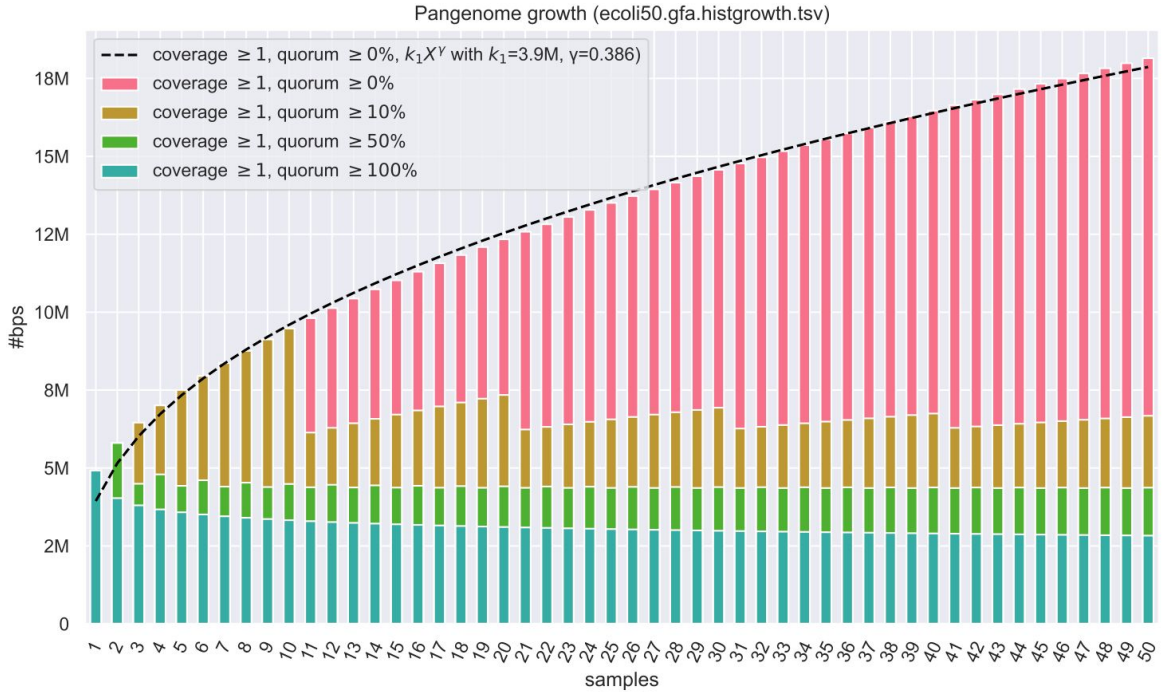
- Time complexity $O(n^2)$ << Number of countables (nodes, edges, bps)
- 1971, Stuart H. Hurlbert[a]
- 2020, A. Chacoma and D. H. Zanette[b]

> [...] “it seems to have passed unnoticed that its exact analytical expression has been available in the literature since at least four decades ago.”

[a]Hurlbert, S. H. (1971). The Nonconcept of Species Diversity: A Critique and Alternative Parameters. Ecology, 52(4), 577–586
[b]A. Chacoma and D. H. Zanette. Heaps’ law and Heaps functions in tagged texts:evidences of their linguistic relevance. Royal Society Open Science, 7(3),2020

$$n^{\underline{m}} = \overbrace{n(n-1)\dots(n-m+1)}^{m \text{ factors}}$$

Pangenome growth curve with Panacus



quorum >= 0%: all seqs of all haps

quorum >= 10%: seqs traversed by at least 10% of haps - ***cloud pangenome***

quorum >= 50%: seqs traversed by at least 50% of haps - ***shell pangenome***

quorum >= 100%: seqs traversed by 100% of haps - ***core pangenome***

Pangenome growth curve HPRC

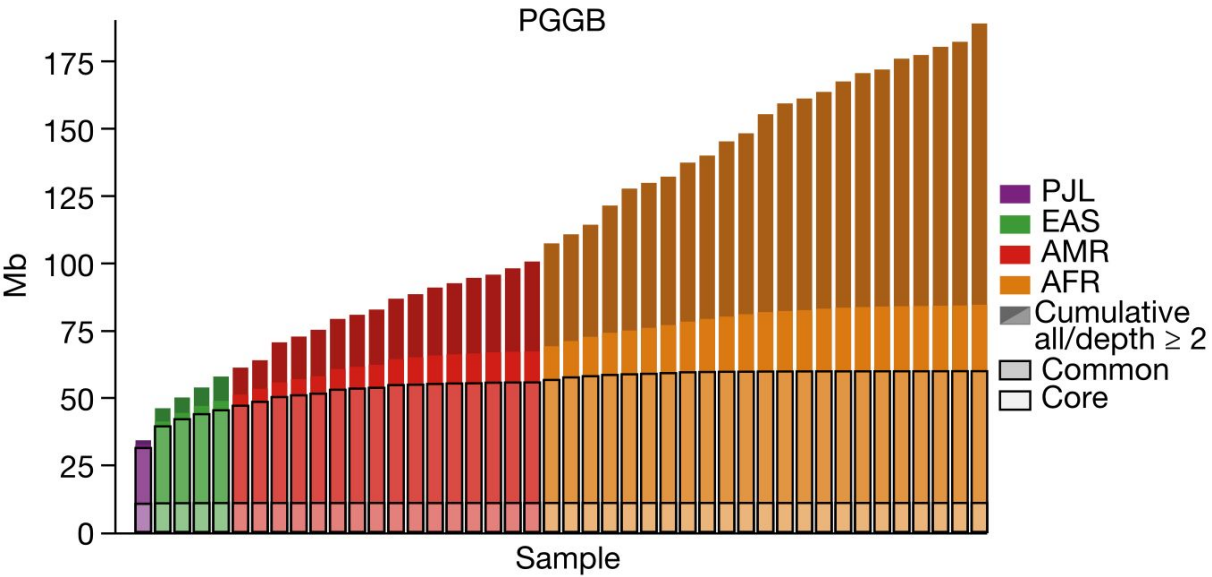


Figure from: Liao et al., 2023.

PJL: Punjabi in Lahore

EAS: East Asia

AMR: American

AFR: African

Common: Sequences traversed by at least 5% of haplotypes

Core: Sequences traversed by at least 95% of haplotypes

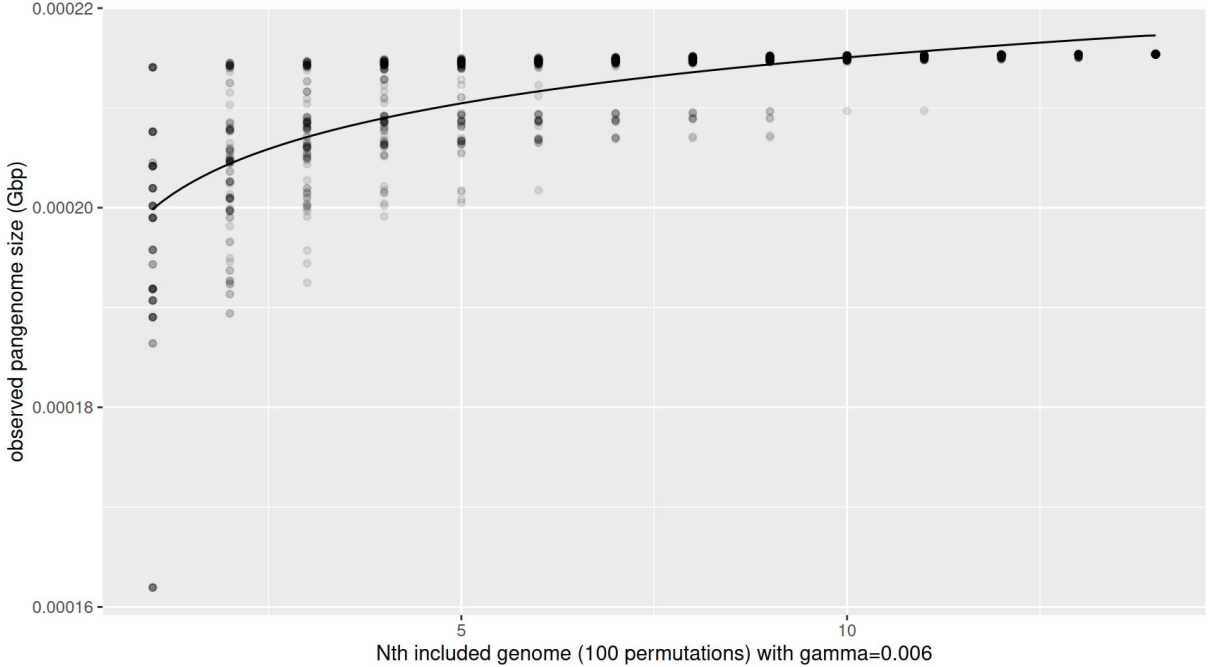
Activities

https://hackmd.io/snceiMesSECepJGzBdDIkw?view=

In this tutorial you will learn to

- run a nf-core Nextflow pipeline,
- configure the resources according to what is available,
- deal with alternative parameter names,
- understand the nf-core/pangenome pipeline output,
- and evaluate and interpret the growth of a pangenome.

Heap’s law for measuring pangenome openness



Pangenome growth curve of the LPA pangenome graph

$$n = \kappa N^{\gamma}$$

n is pangenome size

N is the number of genomes

κ and **γ** are fitting parameters

γ<0: closed pangenome

γ>0: open pangenome

Tettelin H. et al. (2008). Current Opinion in Microbiology, 11(5), 472-477.

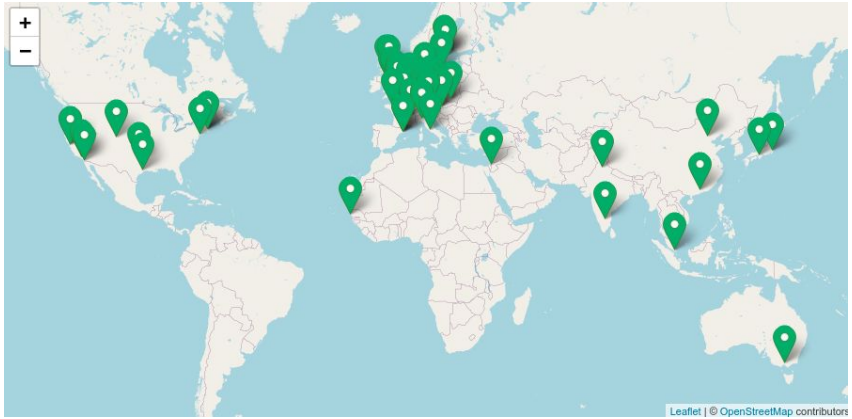
nf-core

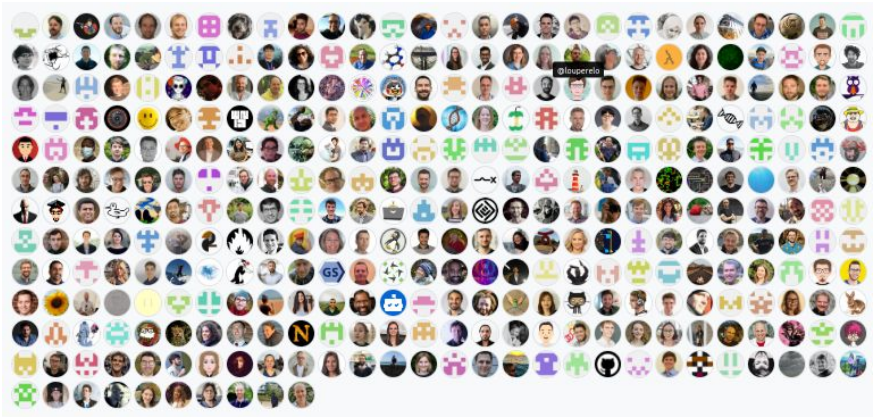
>6000

Slack Members

>700

GitHub Organisation Members





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nf-core

49

✅ Released pipelines

19

🔧 Under development

Genomics	Metagenomics
Proteomics	Metabolomics
Epigenetics	(Bio)imaging
Transcriptomics	Analysis/Utility
Immunology	Economics*

* and astronomy and earth sciences coming soon ™

& many more…

https://nf-co.re

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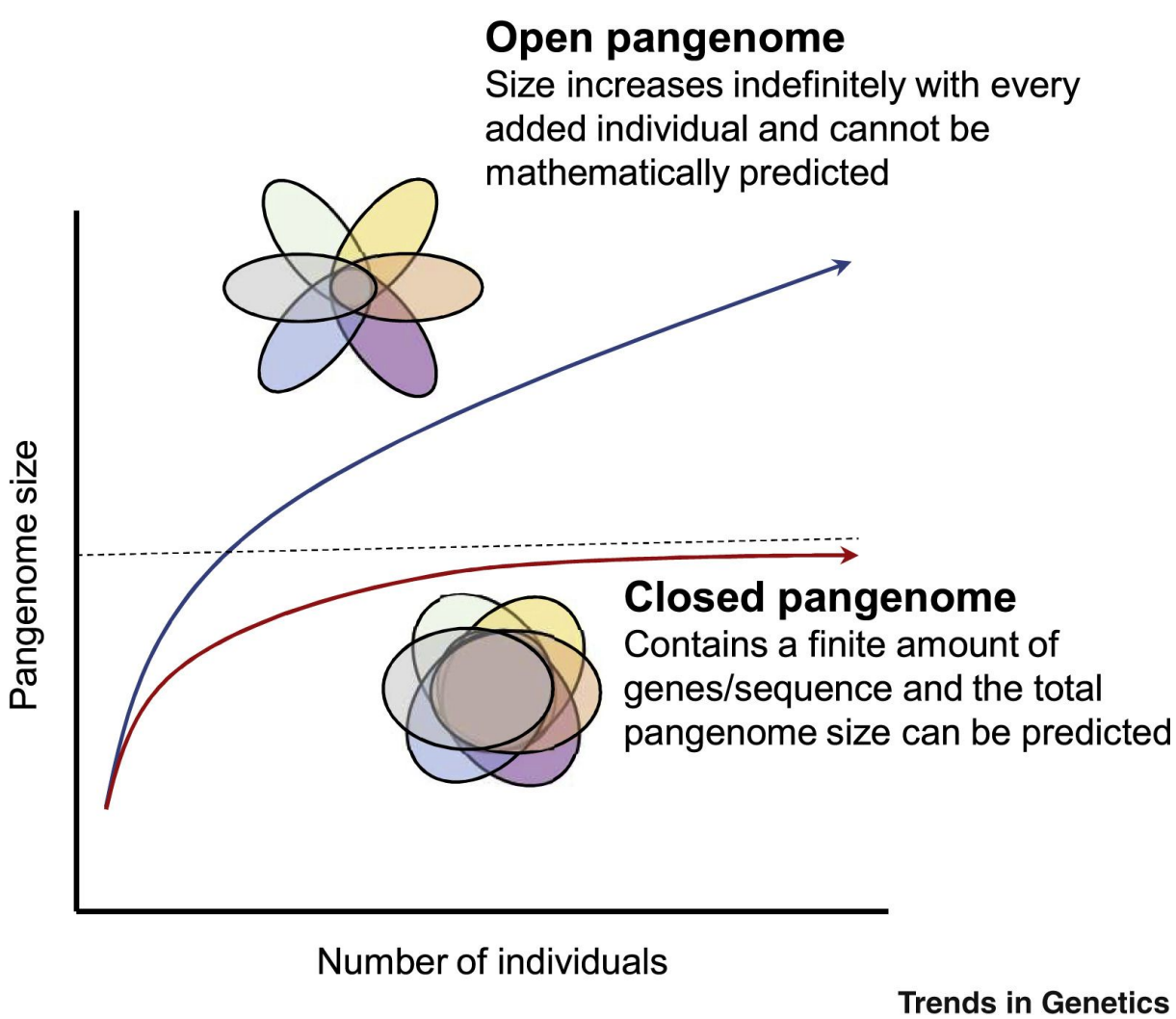
Perspective | Published: 23 September 2021

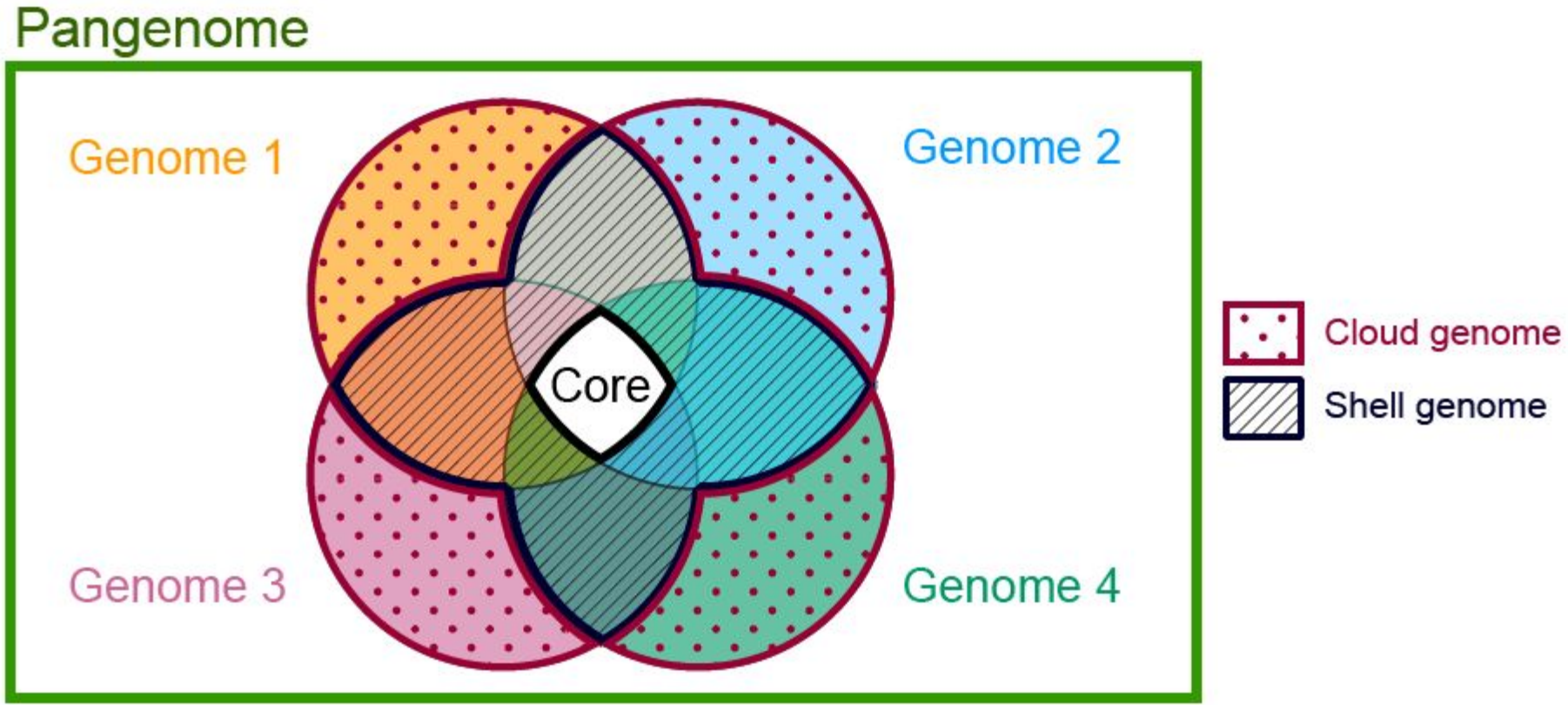
Reproducible, scalable, and shareable analysis pipelines with bioinformatics workflow managers

Laura Wratten, Andreas Wilm & Jonathan Göke ✉

Nature Methods **18**, 1161–1168 (2021) | Cite this article

Tool	Class	Ease of use[a]	Expressiveness[b]	Portability[c]	Scalability[d]	Learning resources[e]	Pipeline initiatives[f]
Galaxy	Graphical	●●●	●○○	●●●	●●●	●●●	●●○
KNIME	Graphical	●●●	●○○	○○○	●●◐	●●●	●●○
Nextflow	DSL	●●○	●●●	●●●	●●●	●●●	●●●
Snakemake	DSL	●●○	●●●	●●◐	●●●	●●○	●●●
GenPipes	DSL	●●○	●●●	●●○	●●○	●●○	●●○
bPipe	DSL	●●○	●●●	●●○	●●◐	●●○	●○○
Pachyderm	DSL	●●○	●●●	●○○	●●○	●●●	○○○
SciPipe	Library	●●○	●●●	○○○	○○○	●●○	○○○
Luigi	Library	●●○	●●●	●○○	●●◐	●●○	○○○
Cromwell + WDL	Execution + workflow specification	●○○	●●○	●●●	●●◐	●●○	●●○
cwltool + CWL	Execution + workflow specification	●○○	●●○	●●◐	○○○	●●●	●●○
Toil + CWL/WDL/Python	Execution + workflow specification	●○○	●●●	●◐○	●●●	●●○	●●○


Open pangenome
Size increases indefinitely with every added individual and cannot be mathematically predicted
Pangenome size
Closed pangenome
Contains a finite amount of genes/sequence and the total pangenome size can be predicted
Number of individuals
Trends in Genetics



https://upload.wikimedia.org/wikipedia/commons/9/9b/Parts_of_the_pangenome.png

Core: 100% of genomes, minimum fraction → quorum: 1.0
Shell: 50% of genomes, minimum fraction → quorum: 0.5
Cloud: 10% of genomes, minimum fraction → quorum: 0.1