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► To cite this version:

Roland Faure, Jean-François Flot, Dominique Lavenier. HairSplitter: separating similar strains in metagenome assembly. ISMB/ECCB 2023 - 31st Annual Intelligent Systems For Molecular Biology and the 22nd Annual European Conference on Computational Biology, Jul 2023, Lyon, France. pp.1-1, 2023. hal-04272480

HAL Id: hal-04272480

<https://hal.science/hal-04272480v1>

Submitted on 6 Nov 2023

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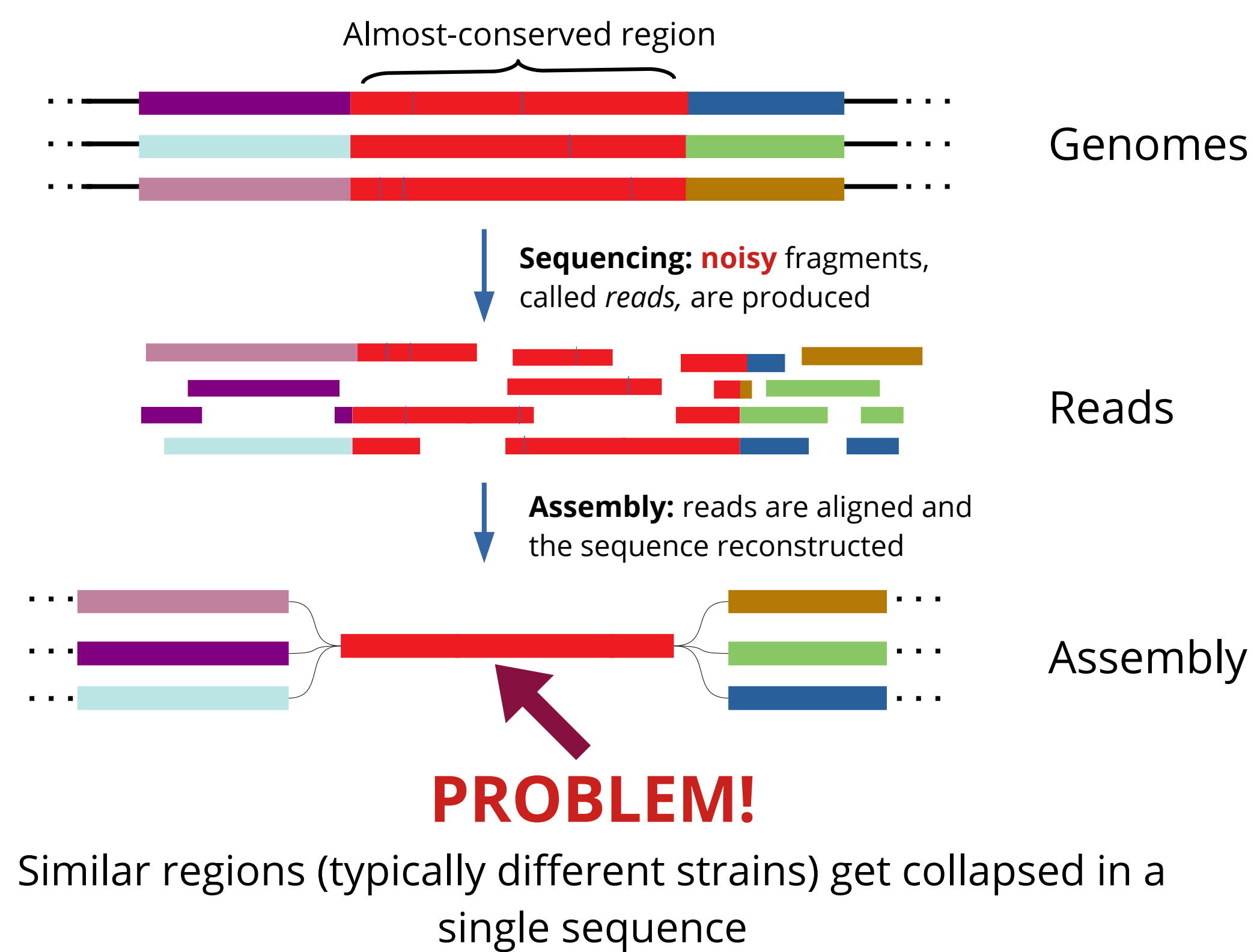
HairSplitter: separating similar strains in metagenome assembly

Roland Faure^{1,2}, Jean-François Flot¹, Dominique Lavenier²

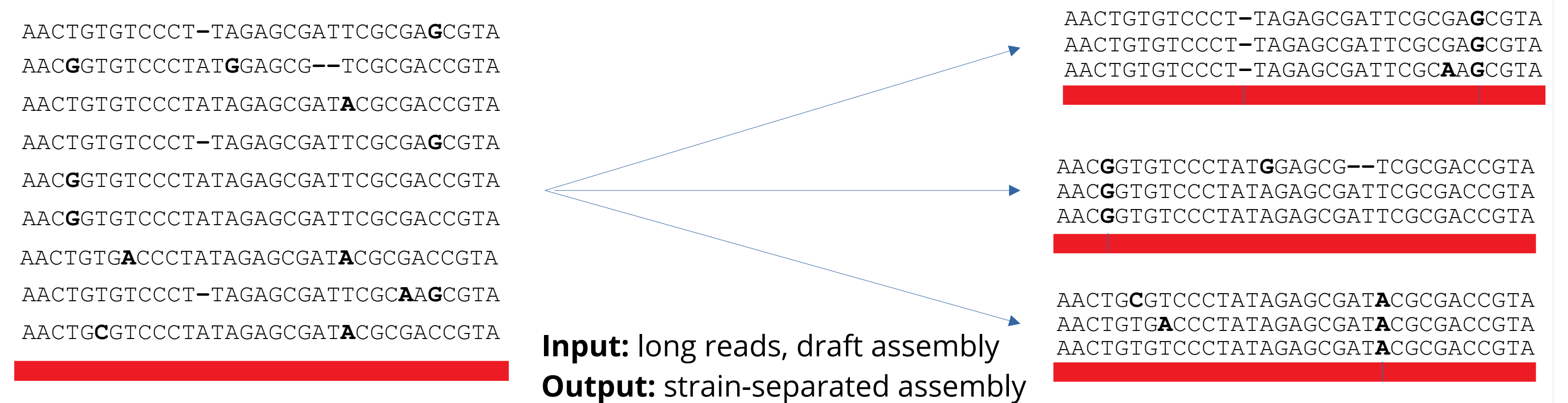
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github.com/RolandFaure/Hairsplitter

Problem: assembling similar sequences



State of the art



Difficulties: Unknown number of strains (potentially high), uneven coverage

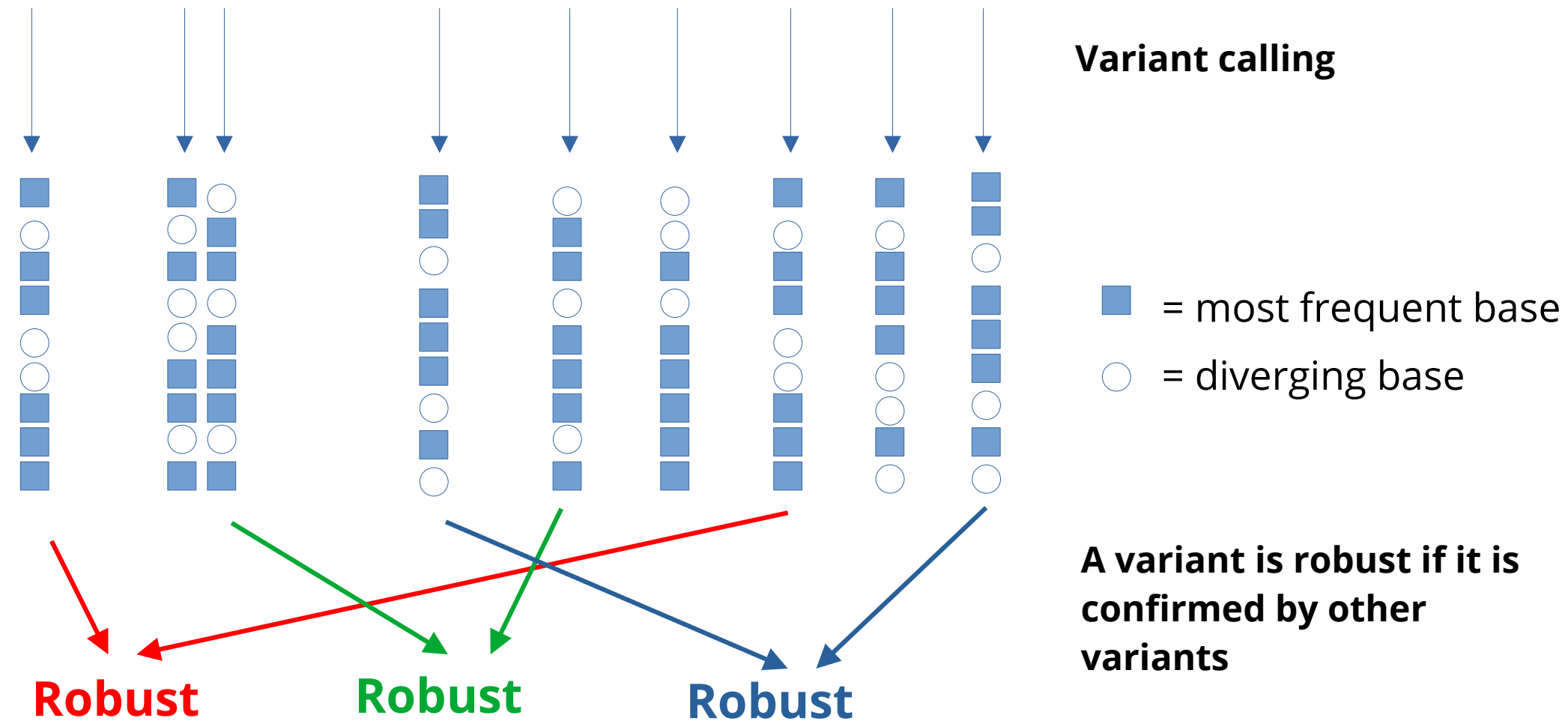
Existing software: Strainberry [1], stRainy (under development) [2], hifiasm [3]

But: To be improved for noisy reads and high number of strains

Algorithm

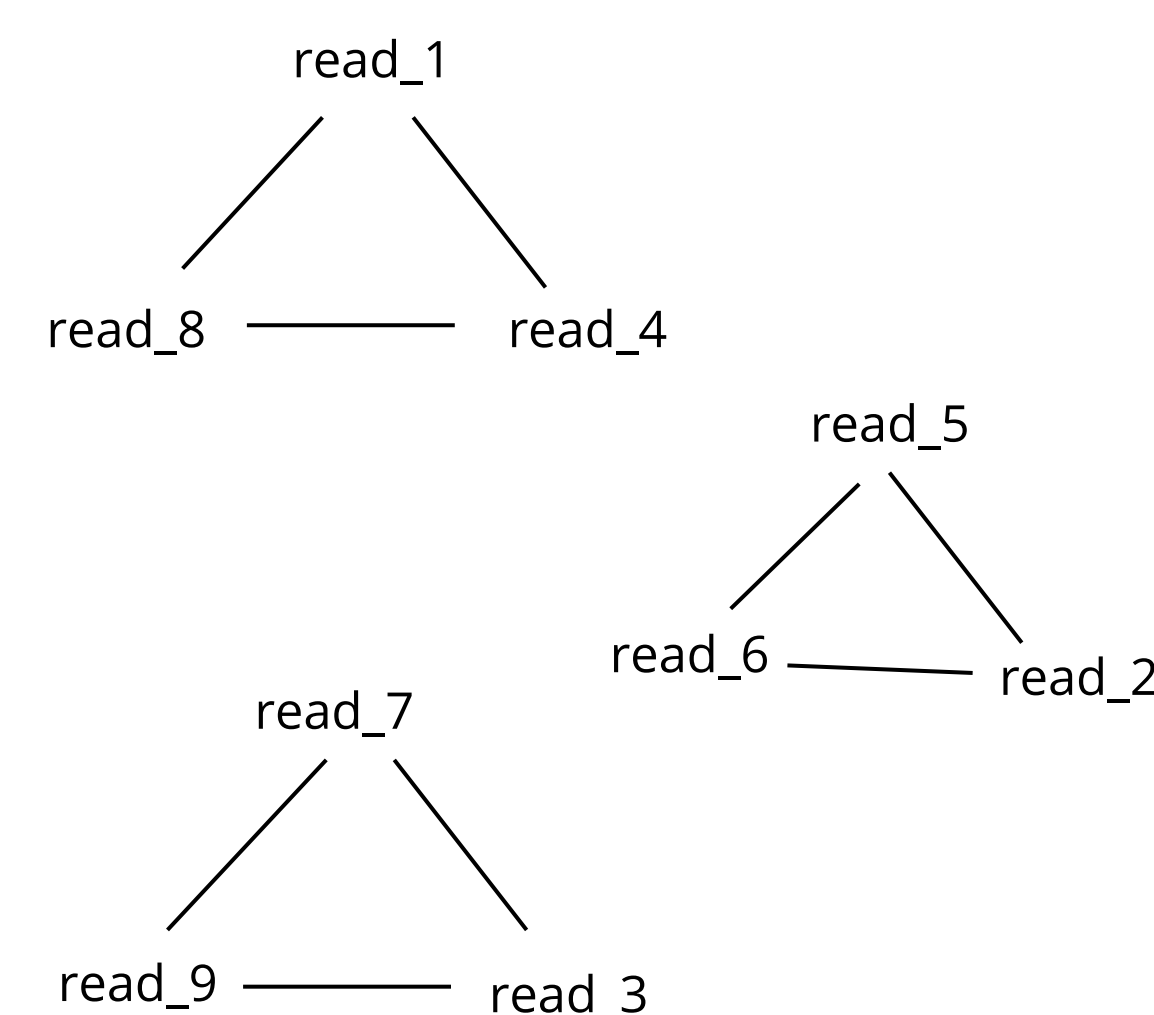
1. Robust variant calling

draft asm	A	A	C	T	G	T	G	T	G
read_1	T	C	-	T	G	T	G	T	G
read_2	G	A	A	T	C	T	A	A	G
read_3	T	C	A	A	C	C	G	T	-
read_4	T	A	-	T	G	T	G	T	G
read_5	G	A	A	T	C	C	A	T	G
read_6	G	C	A	T	C	C	A	A	G
read_7	T	C	A	A	C	C	G	A	-
read_8	T	A	-	T	G	C	G	T	G
read_9	T	C	A	A	C	C	G	A	-



2. Read clustering

Each read is linked to the k nearest reads ($k=2$ here), computed using robust variants



Graph is clustered by the Chinese Whispers algorithm

3. Reassembly

```

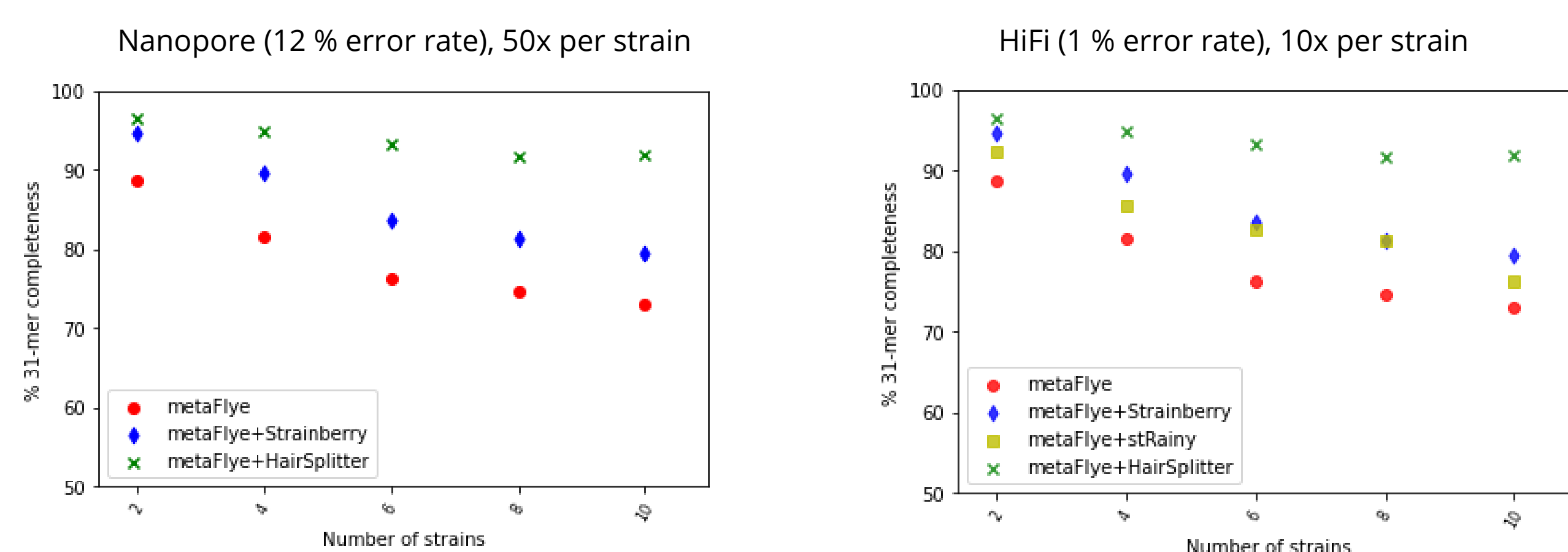
read_1 AACTGTGTCCT-TAGAGCGATTTCGGAGCGTATCTCGGAA
read_4 AACTGTGTCCT-TAGAGCGATTTCGGAGCGTATCTCGGAA
read_8 AACTGTGTCCT-TAGAGCGATTTCGGAGCGTATCTCGGAA

read_2 AACGGTGTCCATATGGAGCG--TCGCGACCGTATCTCGAAA
read_5 AACGGTGTCCATATAGAGCGATTTCGGAGCGTATCTCGAAA
read_6 AACGGTGTCCATATAGAGCGATTTCGGAGCGTATCTCGAAA

read_3 AACTGTGTCCTATAGAGCGATTTCGGAGCGTATCTCGGAA
read_7 AACTGTGTCCTATAGAGCGATTTCGGAGCGTATCTCGGAA
read_9 AACTGTGTCCTATAGAGCGATTTCGGAGCGTATCTCGGAA
    
```

Results

> Mix of 2 to 10 *E. coli* strains, simulated sequencing from RefSeq genomes



> Mix of 5 *E. coli* strains, Zymbiomics gut microbiome standard

	metaFlye	metaFlye+Strainberry	metaFlye+HairSplitter
Nanopore Q9	0.586	0.749	0.957
Nanopore Q20	0.7524	0.9527	0.961
PacBio HiFi	0.9589	0.9793	0.9895

Table: 31-mer completeness of assemblies w.r.t. the reference

Conclusion & Perspectives

- > *Hairsplitter* reconstructs a **strain-separated assembly** from a draft assembly, improving on the state-of-the-art
- > *Hairsplitter* uses **any type of long reads** (incl. high-error reads) on any type of assembly (incl. polyploid genome assemblies)
- > Perspective: improve the understanding of true microbiomes

References

- [1] Vicedomini, R., Quince, C., Darling, A.E. et al. Strainberry: automated strain separation in low-complexity metagenomes using long reads. *Nat Commun* 12, 4485 (2021). <https://doi.org/10.1038/s41467-021-24515-9>
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- [3] Cheng, H., Concepcion, G.T., Feng, X. et al. Haplotype-resolved de novo assembly using phased assembly graphs with hifiasm. *Nat Methods* 18, 170–175 (2021). doi.org/10.1038/s41592-020-01056-5
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