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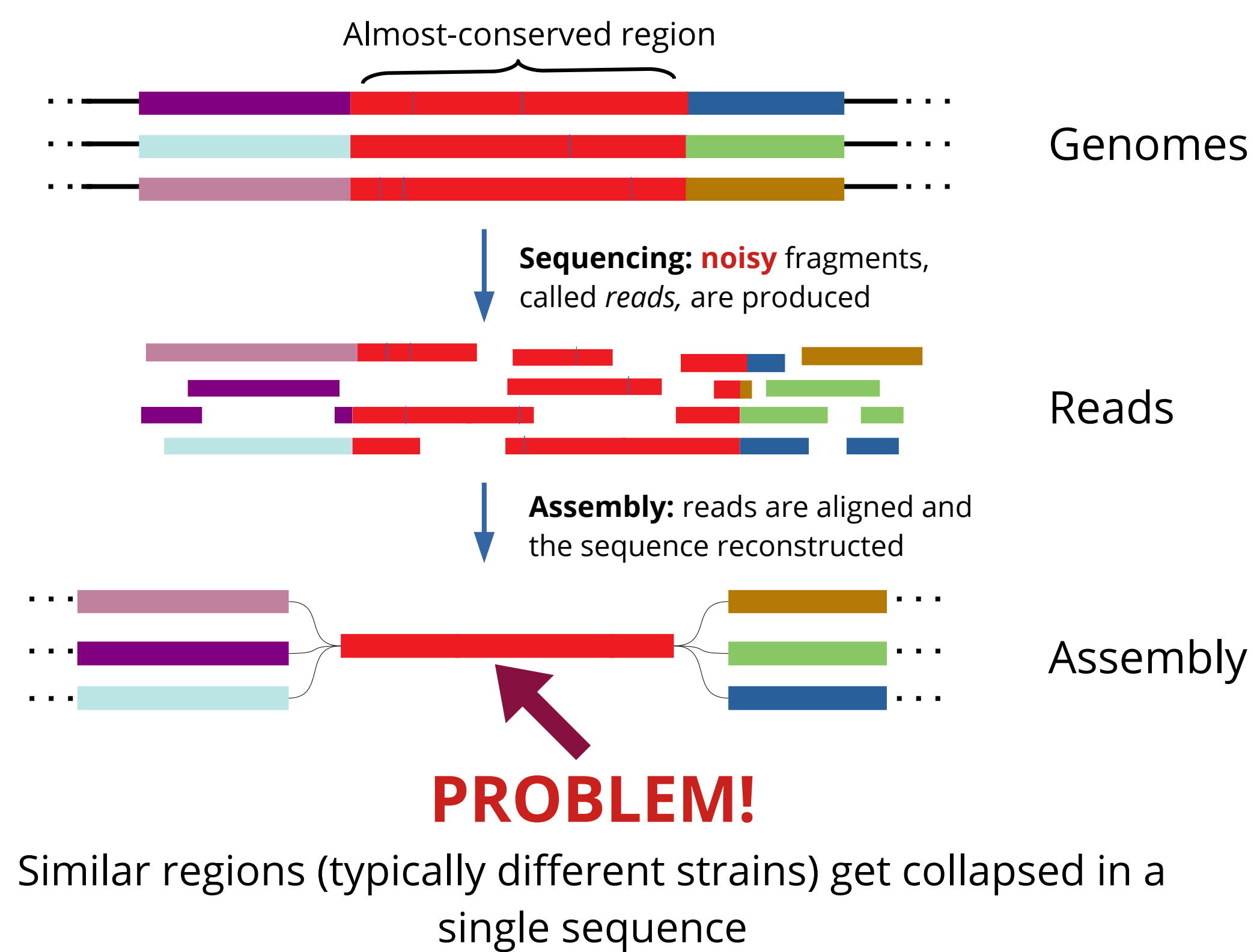
HairSplitter: separating similar strains in metagenome assembly

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

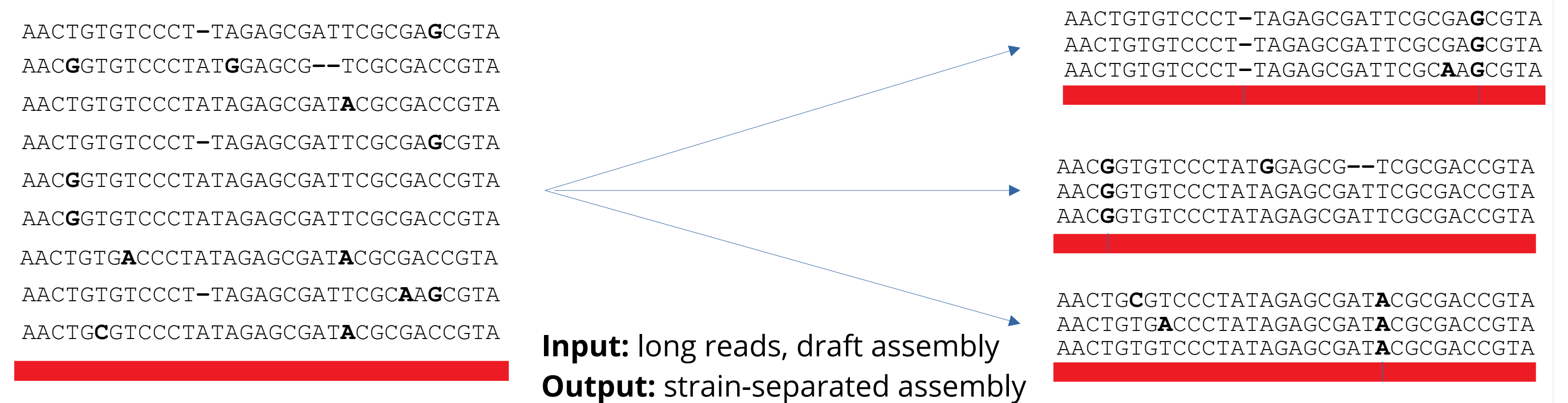
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github.com/RolandFaure/Hairsplitter

Problem: assembling similar sequences



State of the art



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

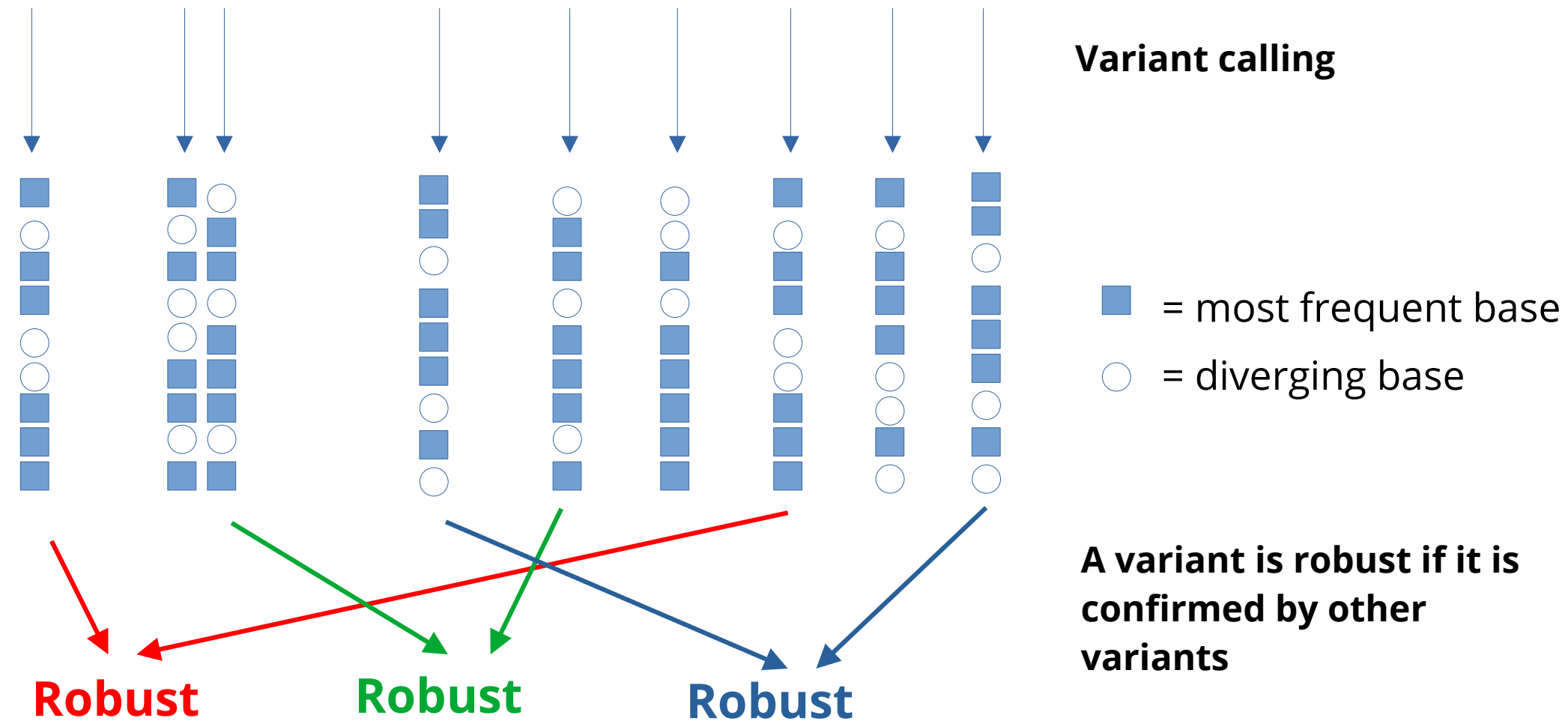
Existing software: Strainberry [1], stRainy (under development) [2], hifiasm [3]

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

Algorithm

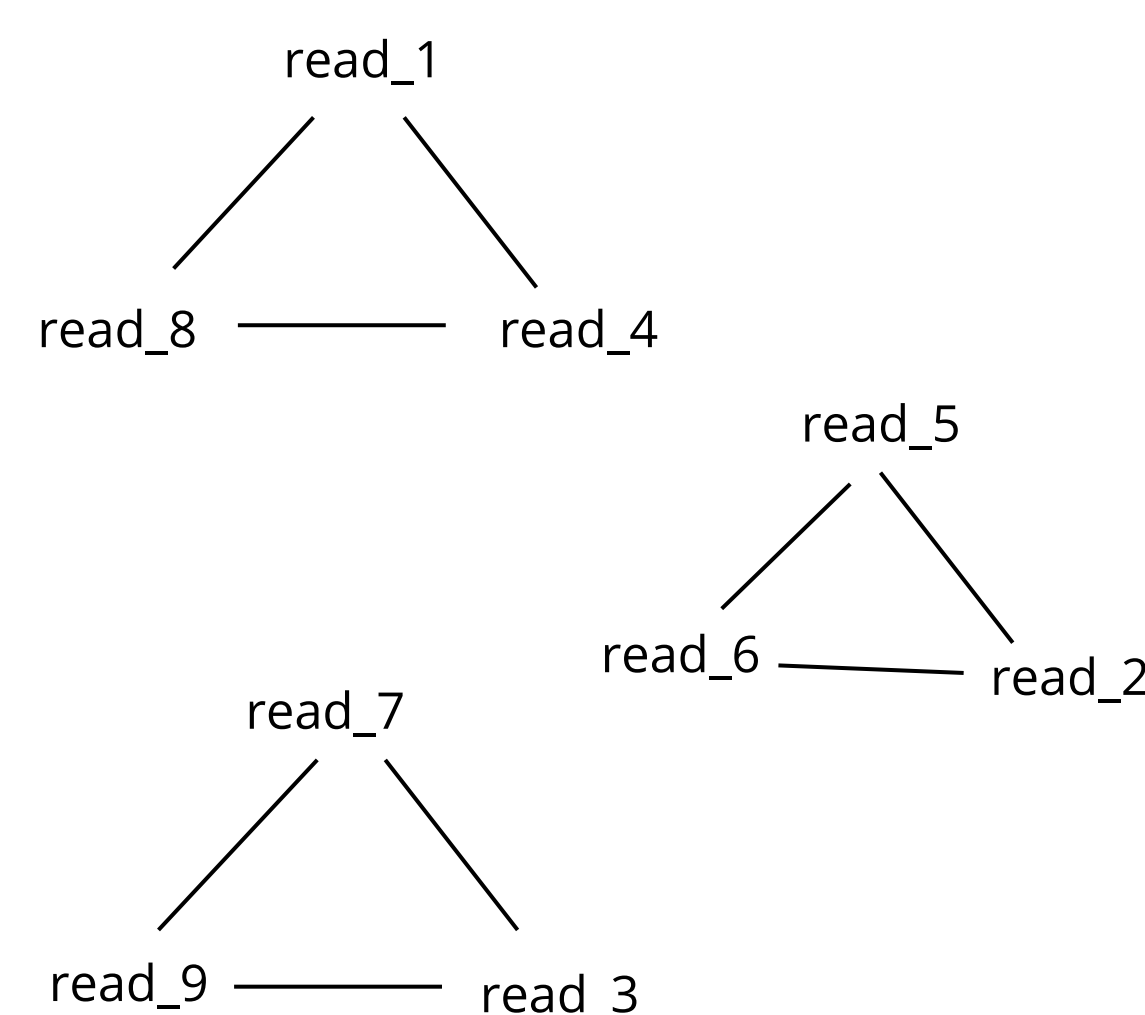
1. Robust variant calling

draft asm	A	A	C	T	G	T	G	T	G	T	G
read_1	T	C	-	T	G	T	G	T	G	-	-
read_2	G	A	A	T	C	T	A	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



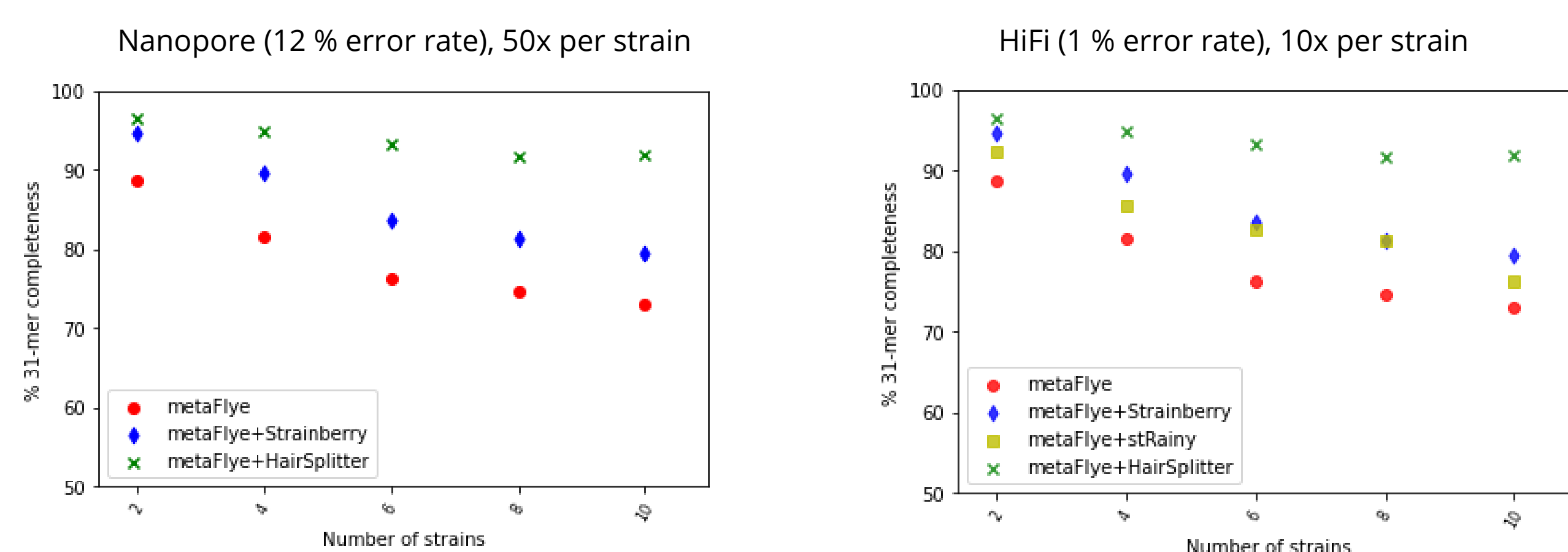
Graph is clustered by the Chinese Whispers algorithm

3. Reassembly

read_1	AACTGTGCCCT-TAGAGCGATTTCGGAGCGTATCTCGGAA
read_4	AACTGTGCCAT-TAGAGCGATTTCGGAGCGTATCTCGGAA
read_8	AACTGTGCCAT-TAGAGCGATTTCGCAAGCGTACCTCGGAA
read_2	AACGGTGTCCATATGGAGCG--TCGCGACCGTATCTCGAAA
read_5	AACGGTGTCCATATAGAGCGATTTCGGAGCGTACCTCGAAA
read_6	AACGGTGTCCCTATAGAGCGATTTCGGAGCGTACCTCGAAA
read_3	AACTGTGCCCTATAGAGCGATACGGAGCCGTACCTCGGAA
read_7	AACTGTGACCCCTATAGAGCGATACGGAGCCGTACCTCGGAA
read_9	AACTGCGTCCCTATAGAGCGATACGGAGCCGTACCTCGGAA

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

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