Correction and assembly of long reads

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Plan

Idea

- Like NaS, produce synthetic long reads from an assembly of short reads
- Get rid of the alignment of short reads against each other
- Deduce information only from the mapping of short reads on long reads

Workflow

We present the method for the correction of one long read

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Principle

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- Have an aligned suffix of length at least *lmin*

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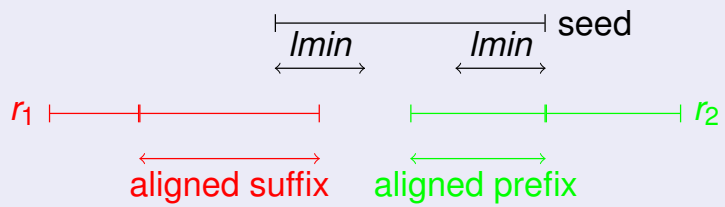
1. Recruitment of partially aligned reads, similar to the seeds



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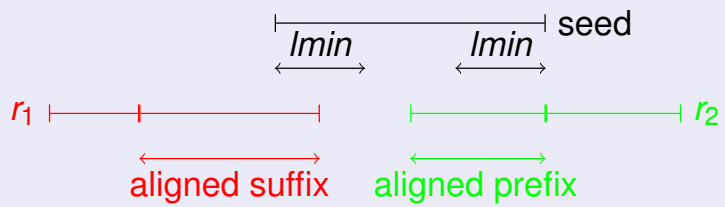
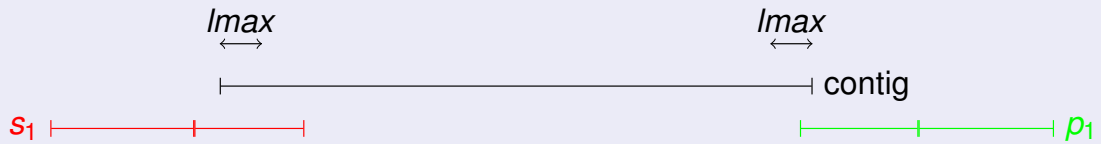


2. Recruiting of new partially aligned reads, without similarity relation, by fixing a new threshold *lmax*



Example

template

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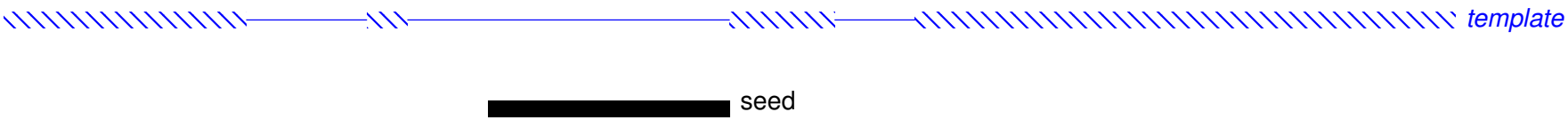

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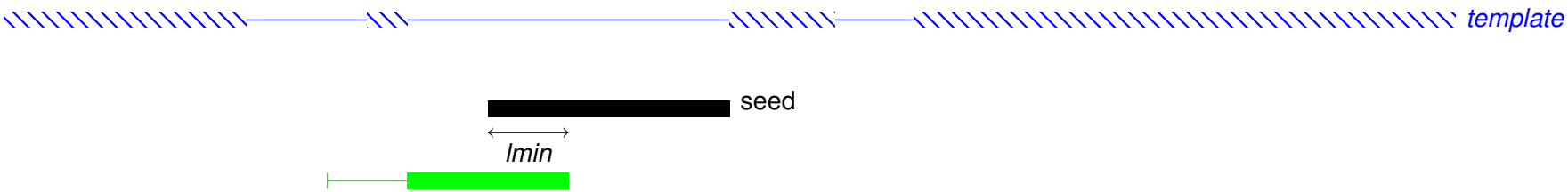

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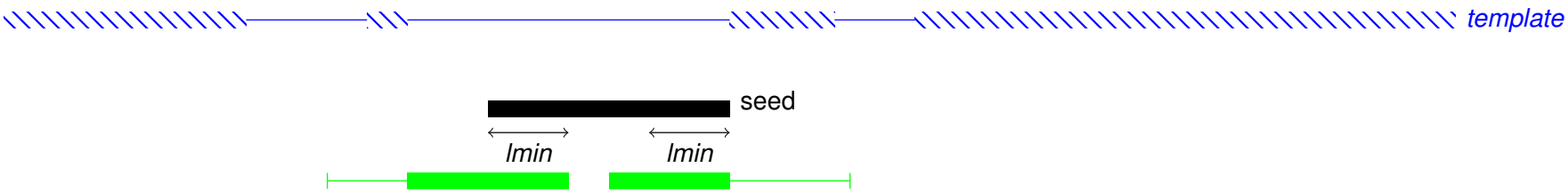

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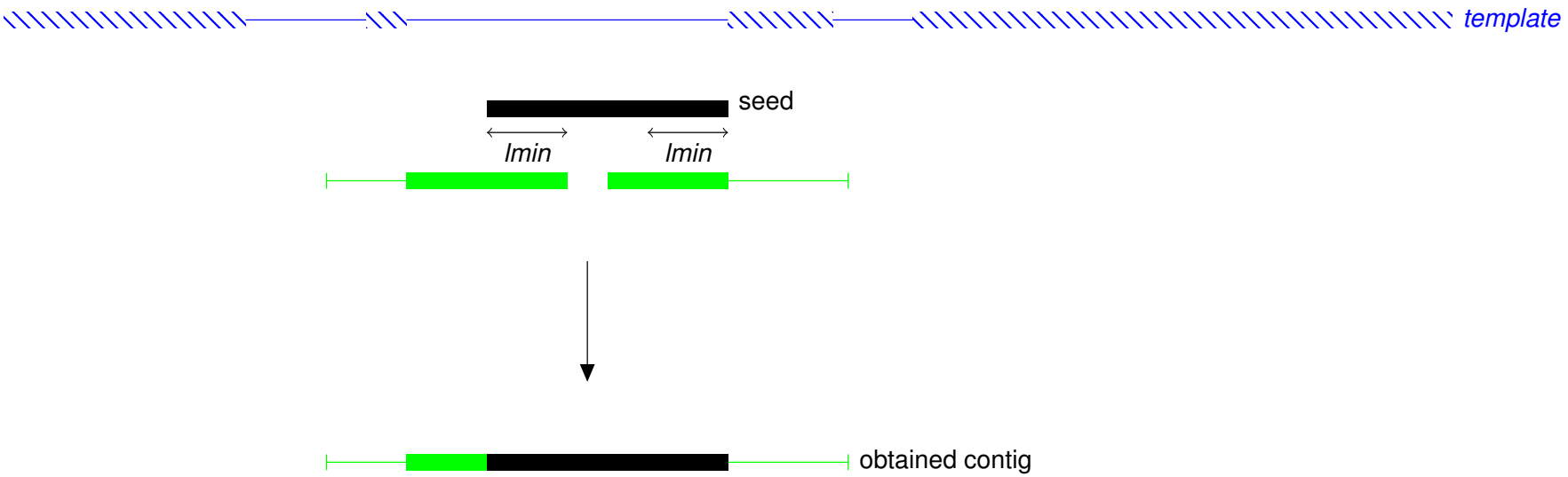

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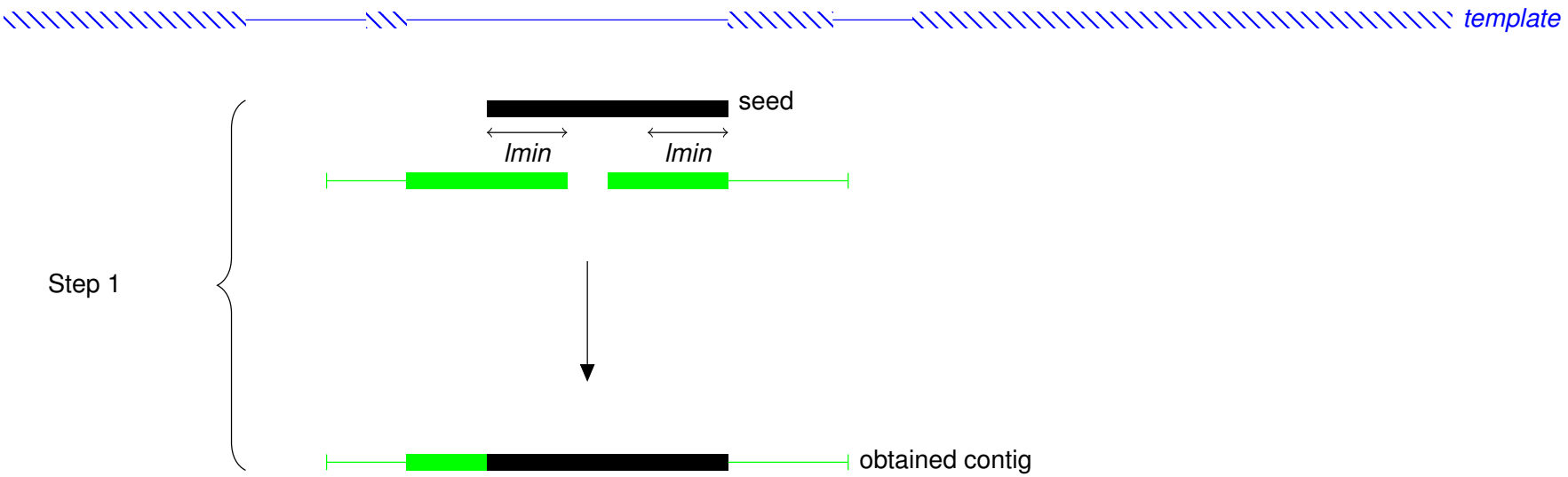

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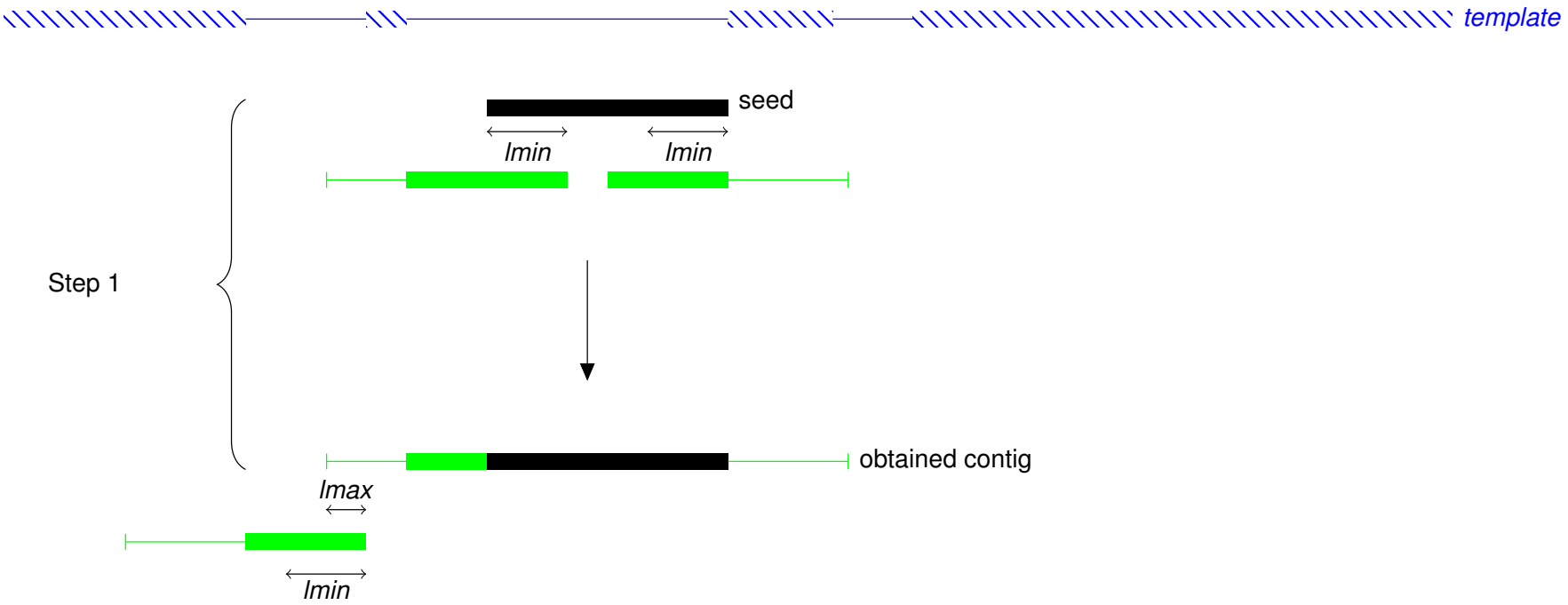

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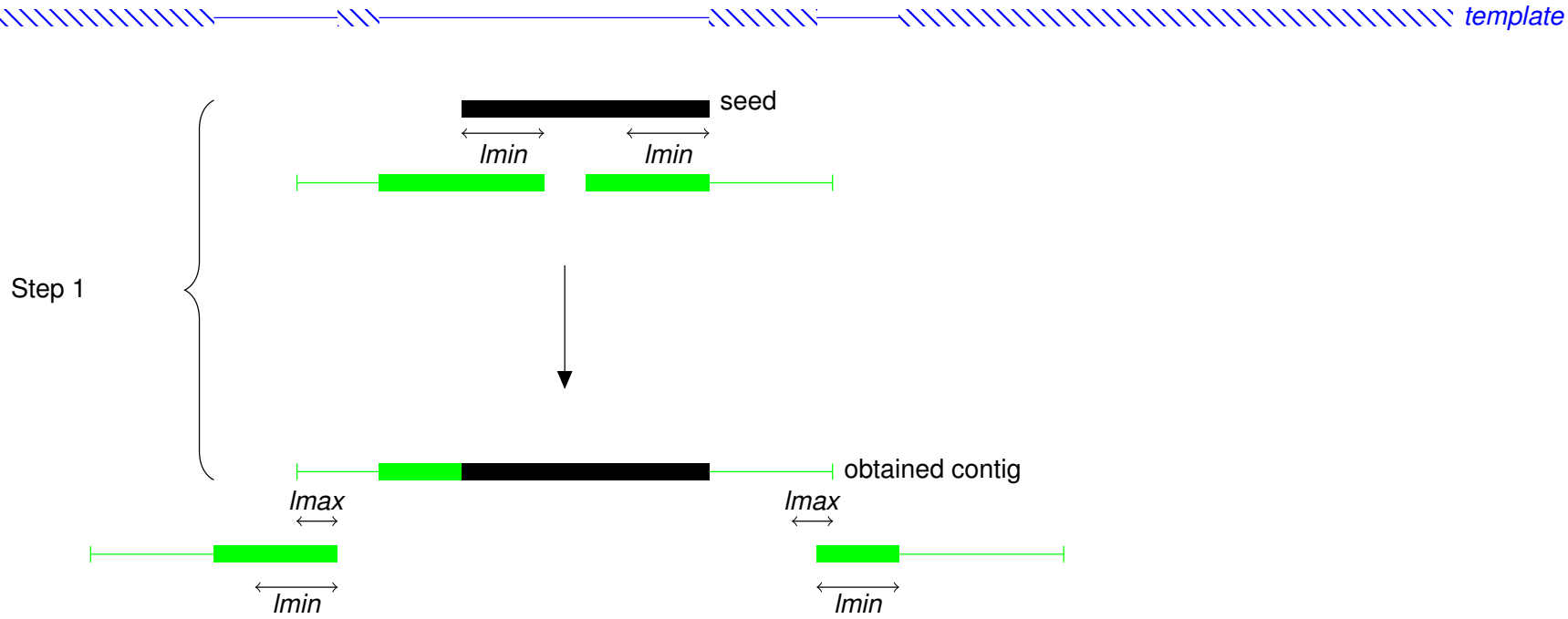
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lmin
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Step 1
obtained contig
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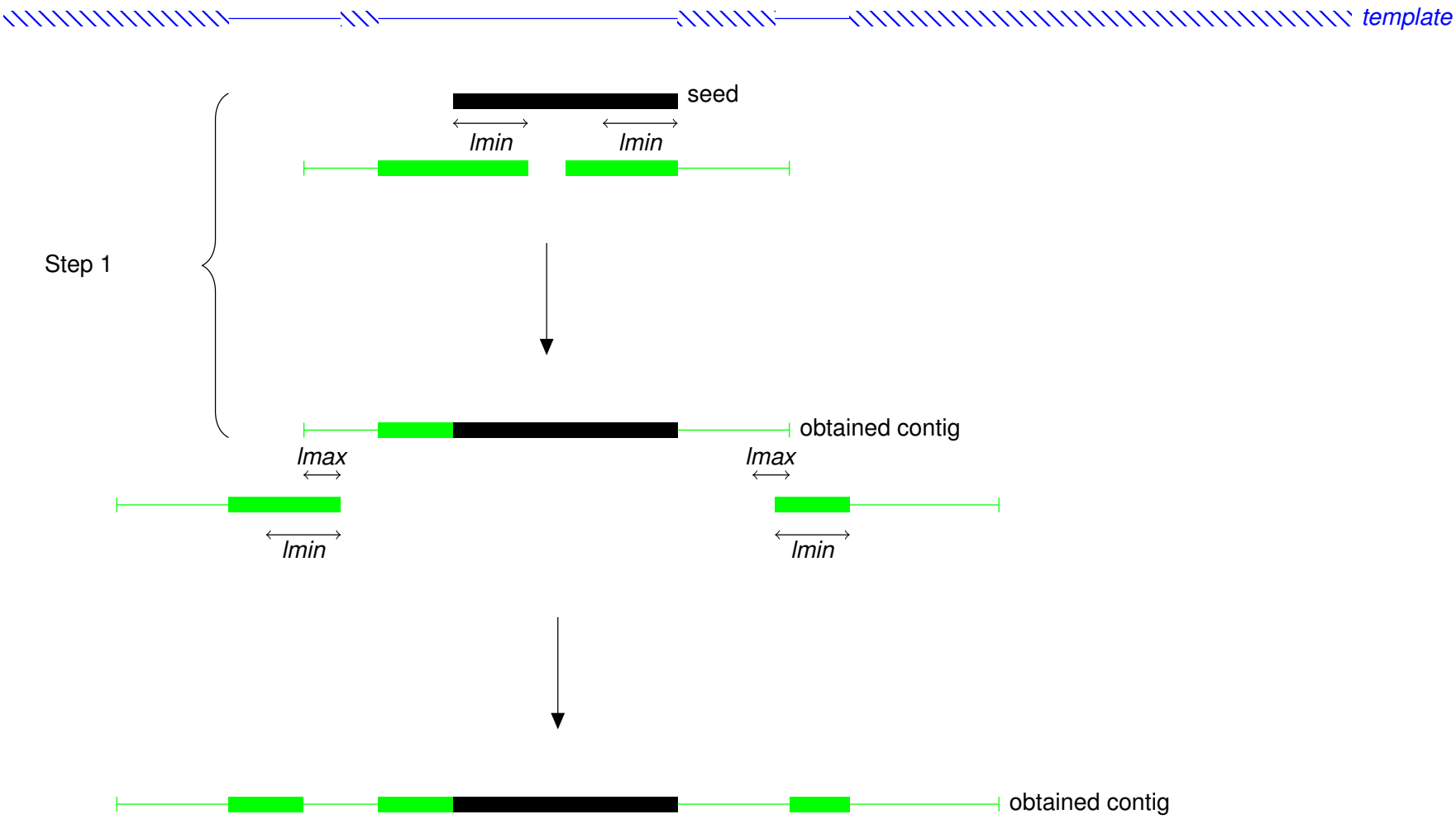
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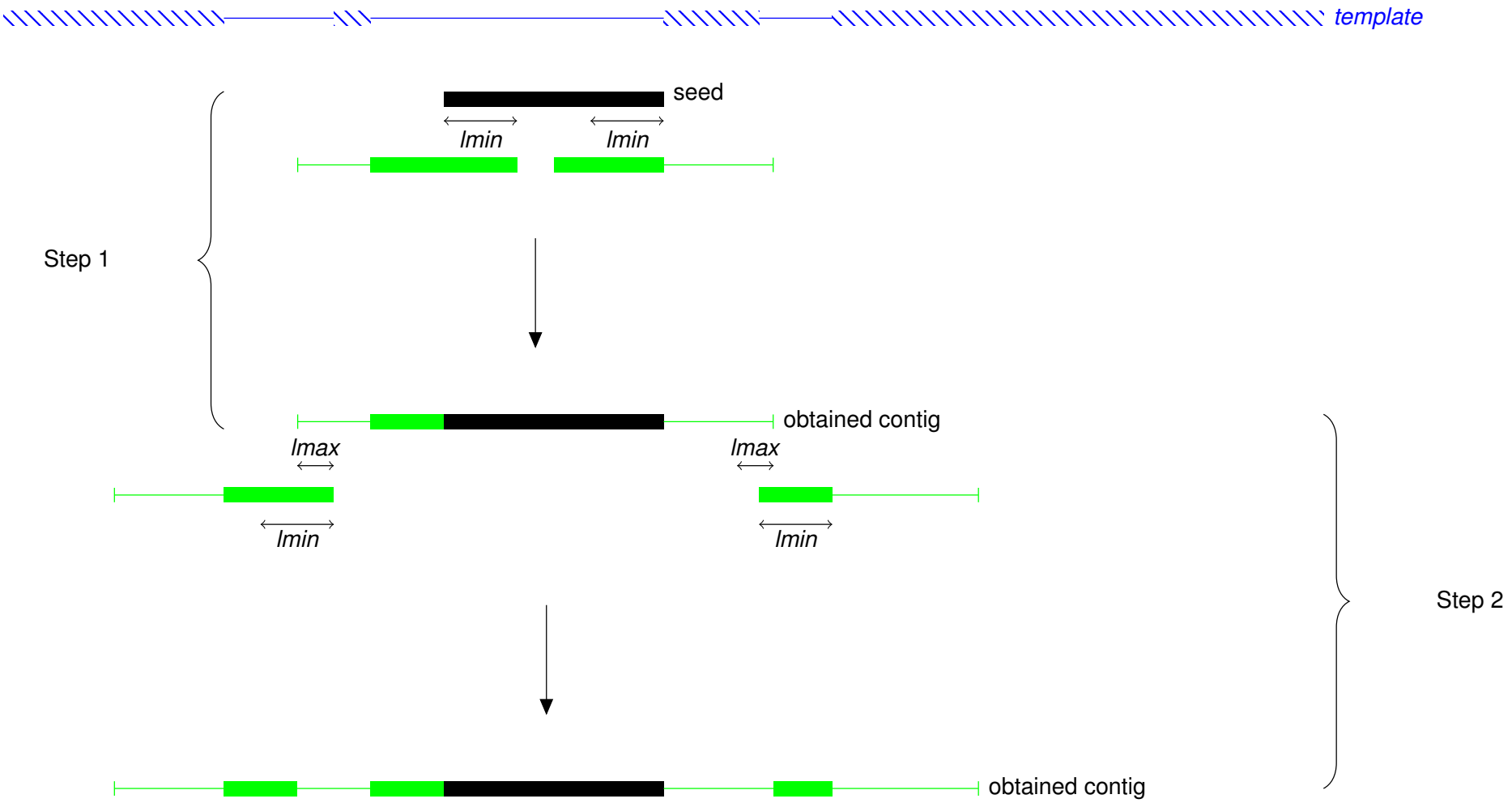
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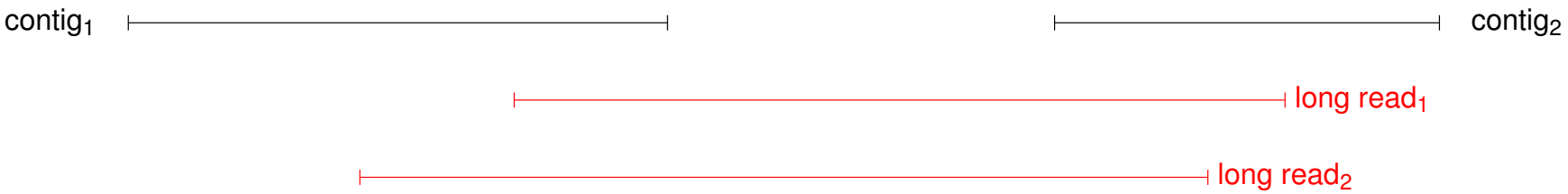

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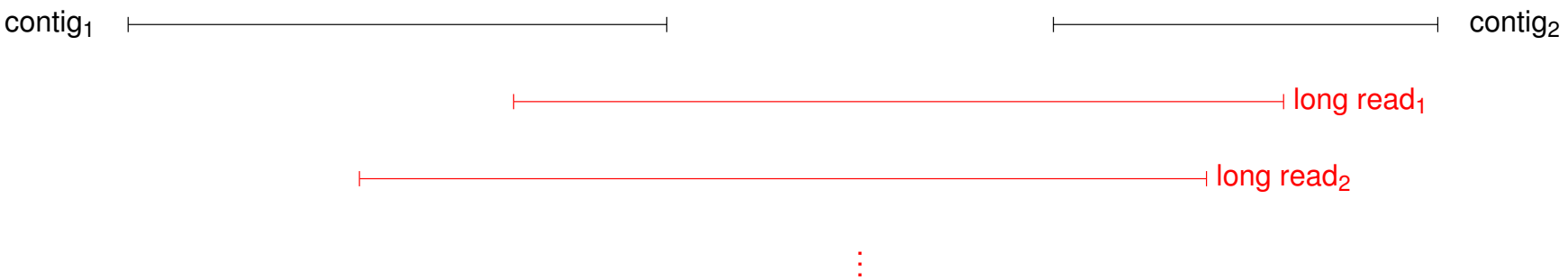

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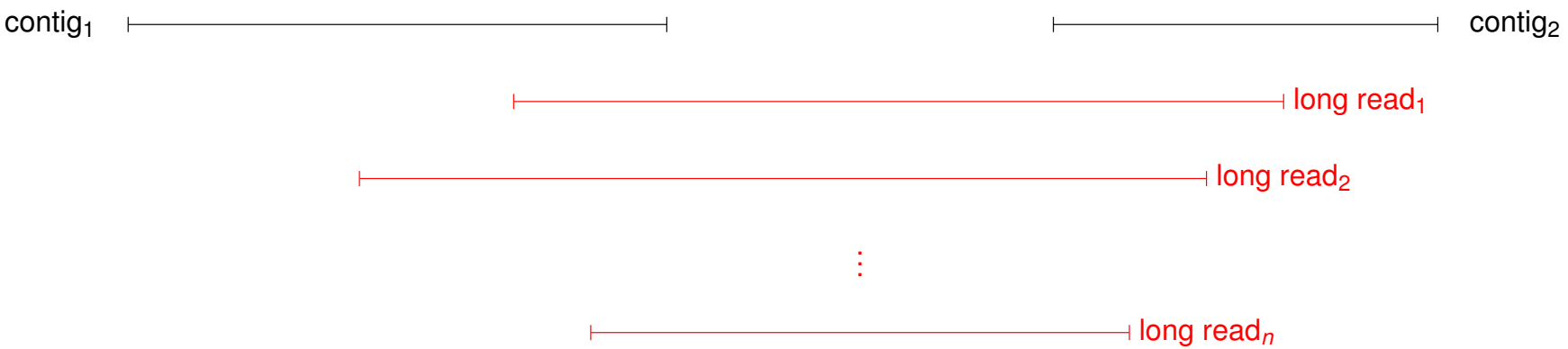

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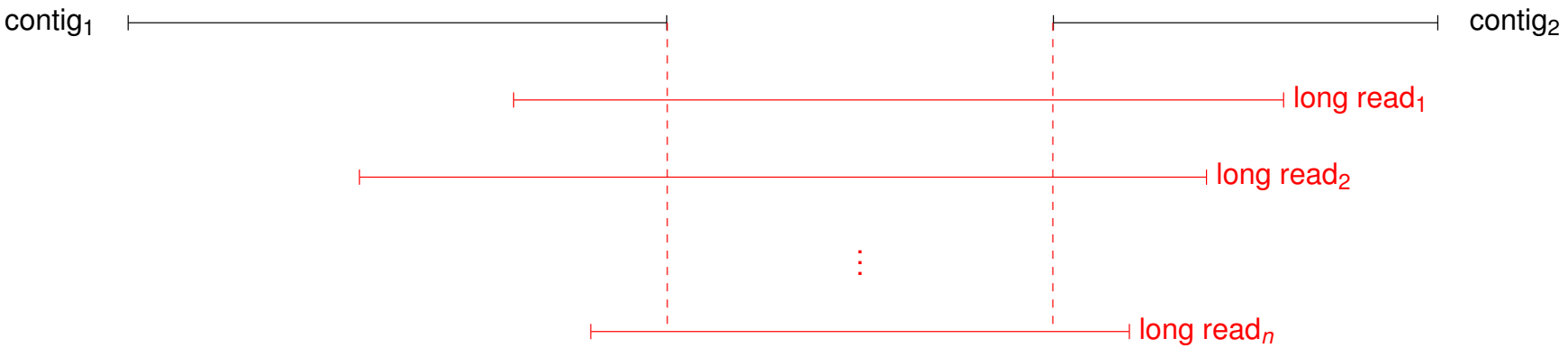

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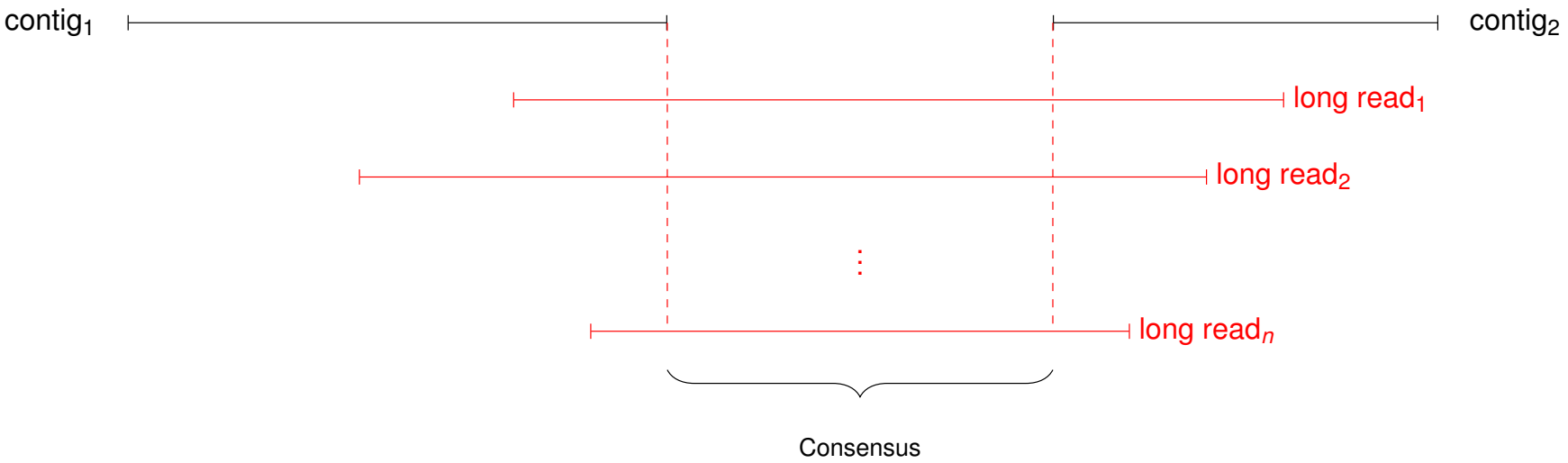
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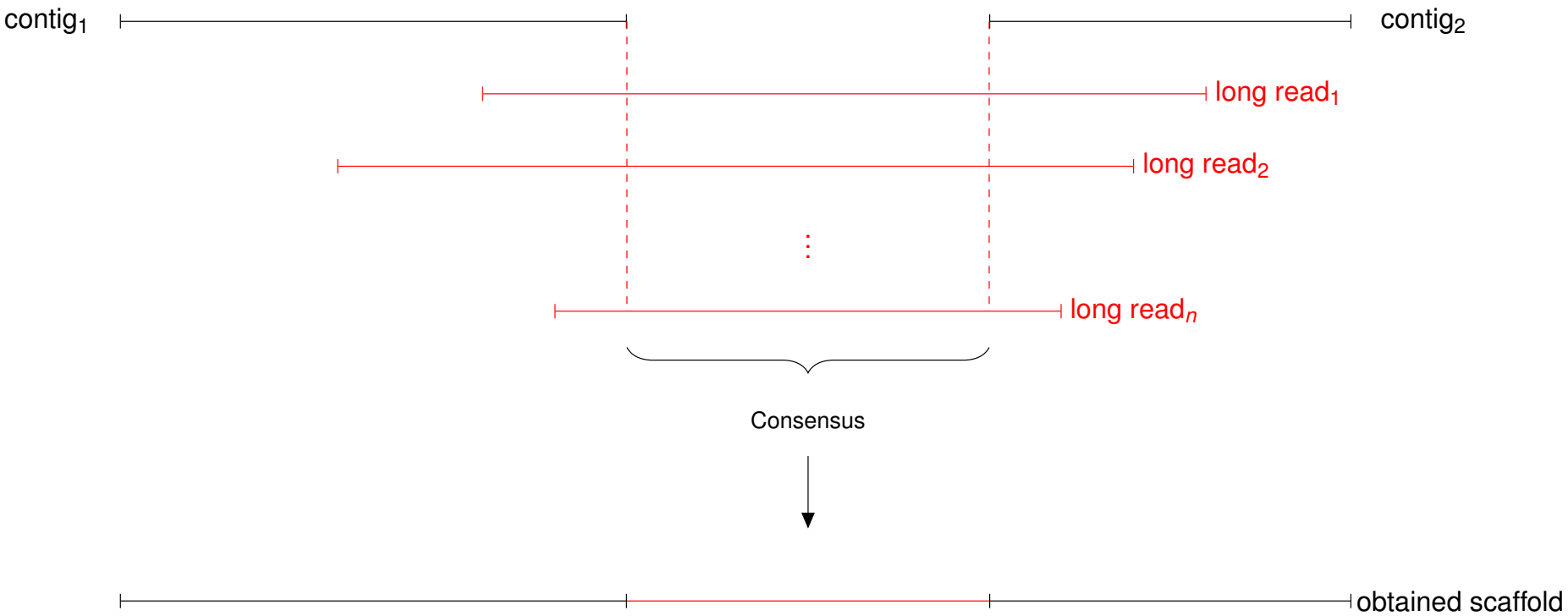
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- Useless to develop this idea any more

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- Try to allow a less fragmented assembly by assembling together short reads and long reads contigs

Tests and results

With a set of reads from ADP1 :

k-mer size	Number of k-mers	Number of k-mer in the short reads contigs
64	375 999 371	380 967
32	335 836 269	2 942 135
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$\Rightarrow$ More interesting to search for spaced k-mers ?

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We use this definition of spaced *k*-mers rather than the classical one in order to take into account indel. error instead of substitutions errors, as they are more common in long reads

Tests and results

Results on the previous dataset, allowing a gap of length at most 10 :

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$\Rightarrow$ Comparison is still not interesting, even with spaced k-mers

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- Not interesting approach
- Allow more gaps in the spaced k-mers, and not just one in the middle, could potentially yield better resultats $\Rightarrow$ Need to find an algorithm that builds a spaced suffix arrays

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5. Extension of the obtained synthetic long read, on the left (resp. right) of the leftmost (resp. rightmost) seed

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Among these requests, the third one will allow us to find perfect overlaps between k-mers

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$\Rightarrow$ Allow to look for overlaps of length $k-2$ if no overlap of length $k-1$ was found, without any need to recompute the whole index

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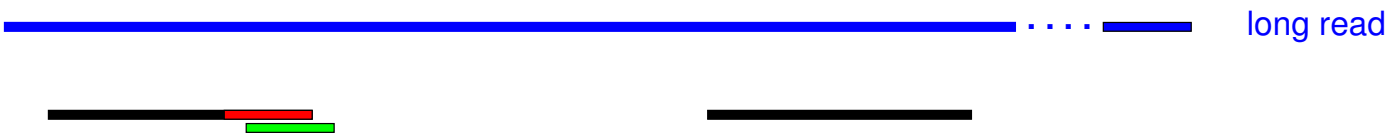

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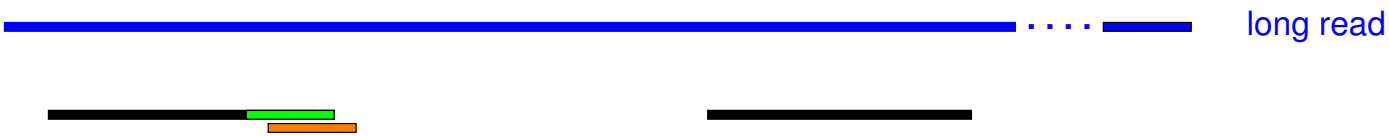

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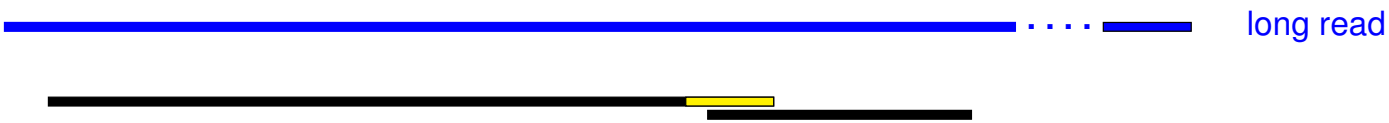

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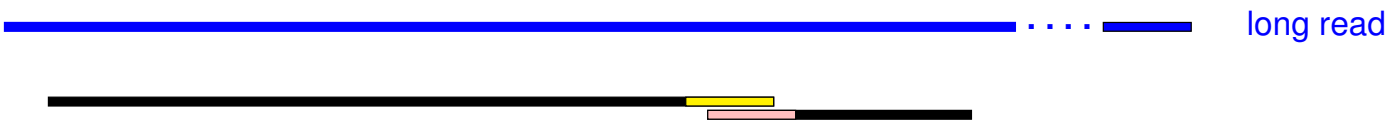

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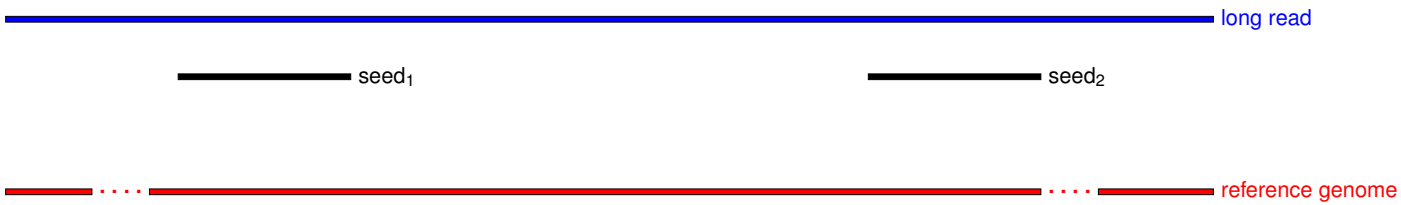

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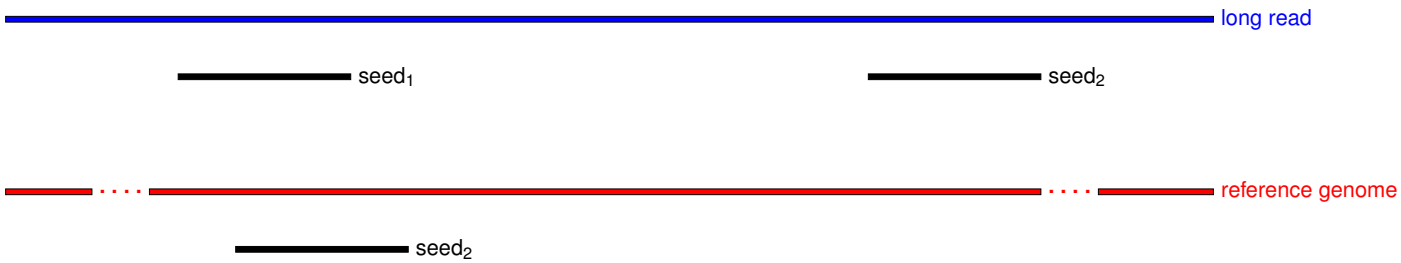

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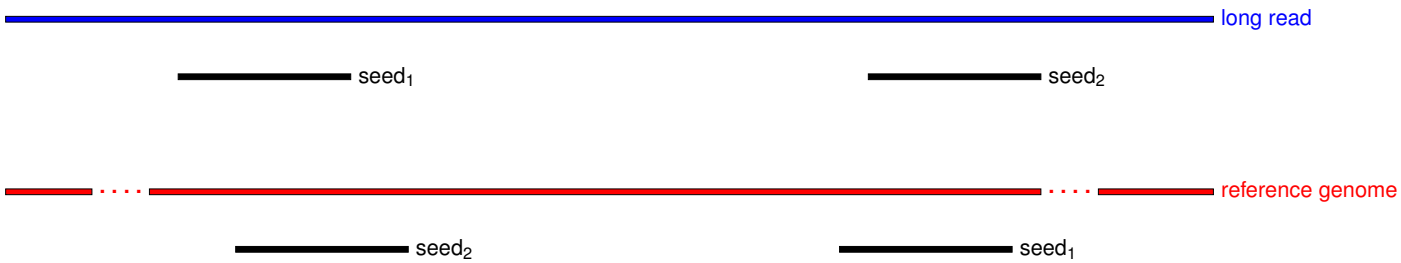

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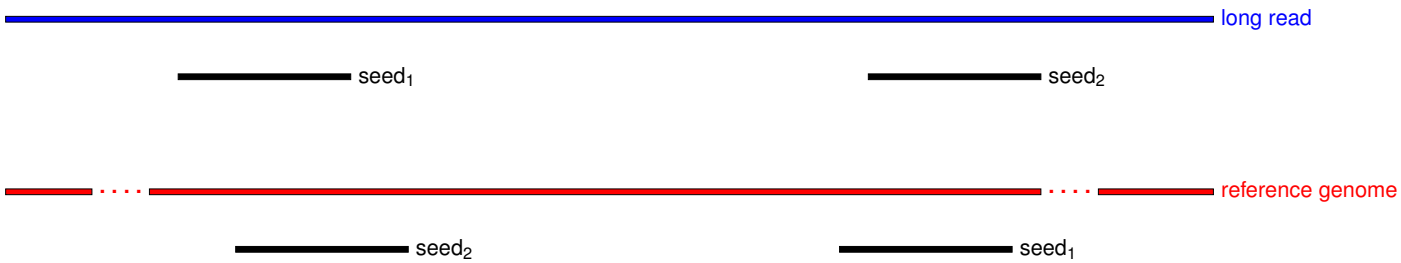

- When only one seed mapped on a given long read, we just extend this seed on both directions

Step 5

The leftmost seed doesn't always map right at the beginning of the long read, and the rightmost doesn't always reach the end

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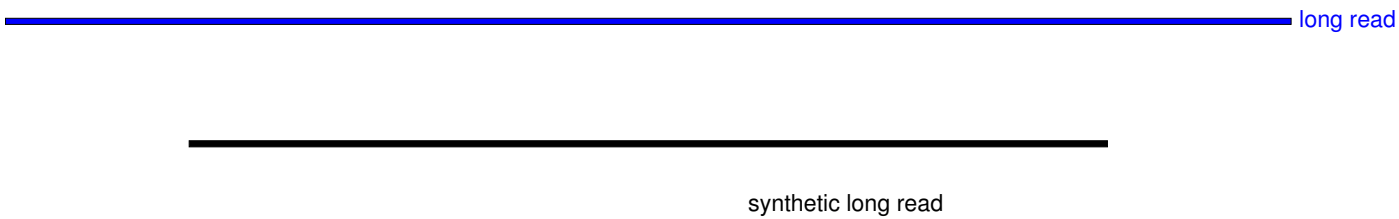
$\Rightarrow$ Once all seeds have been linked, and the synthetic long read produced, we extend, with the help of perfectly overlapping k-mers, its both ends, until the borders of the initial long reads are reached, or an ambiguity is met (multiple k-mers perfectly overlapping the currently considered one)

Step 5, first case : No ambiguity



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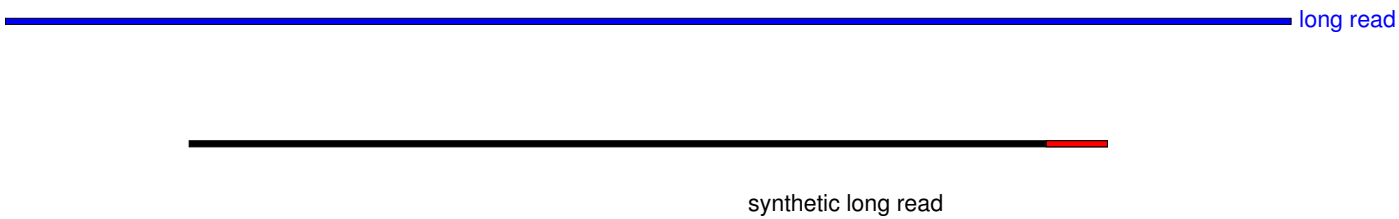

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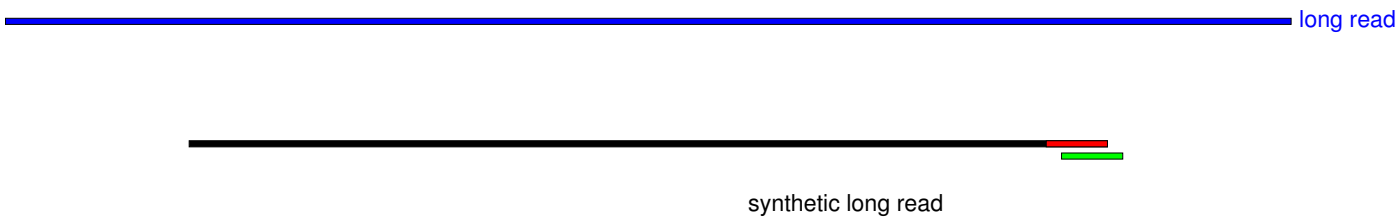

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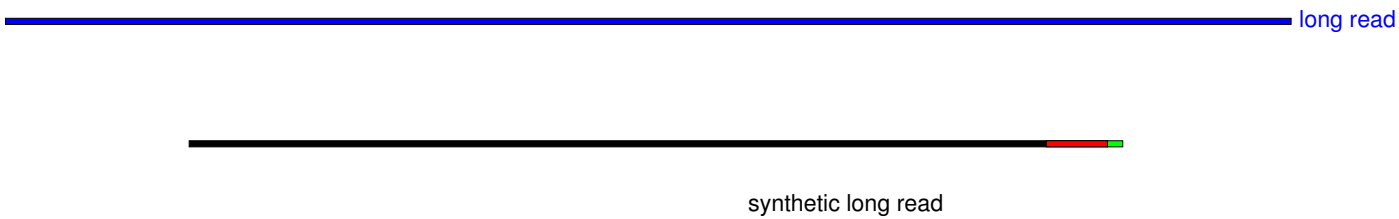

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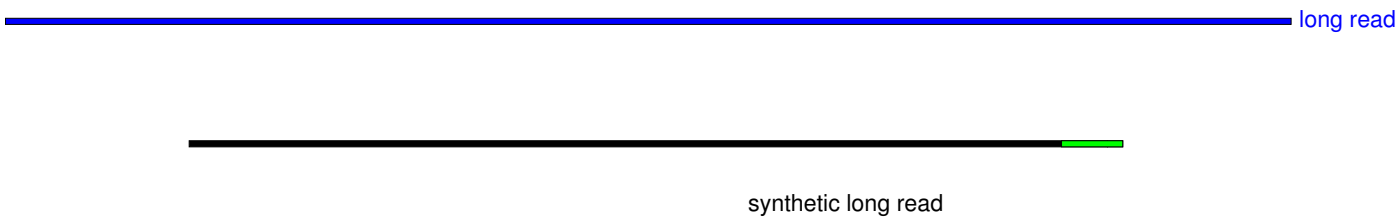

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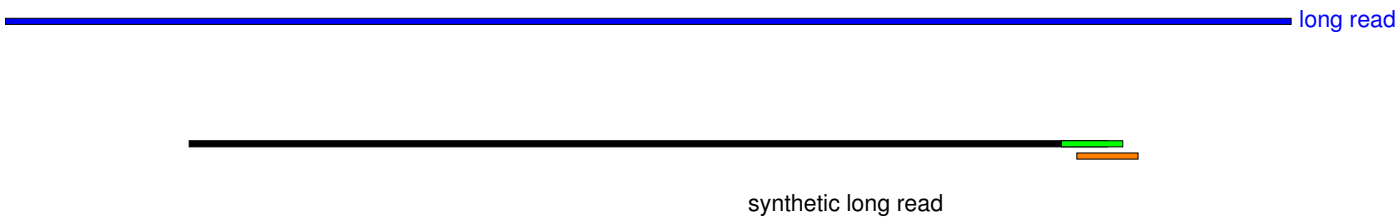

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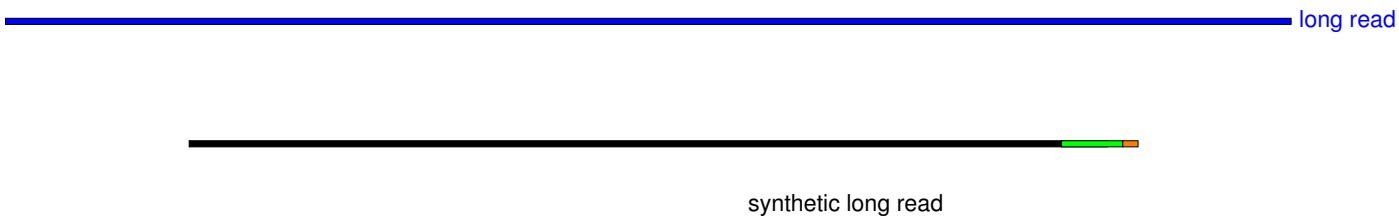

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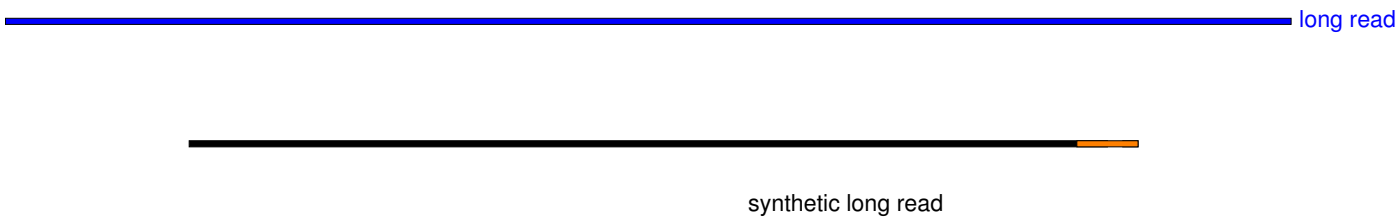

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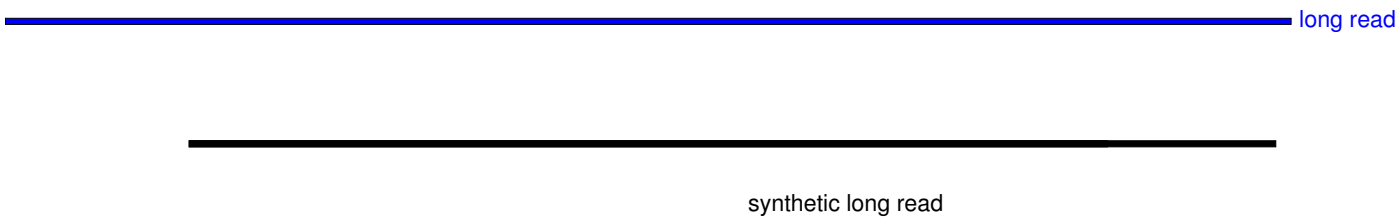

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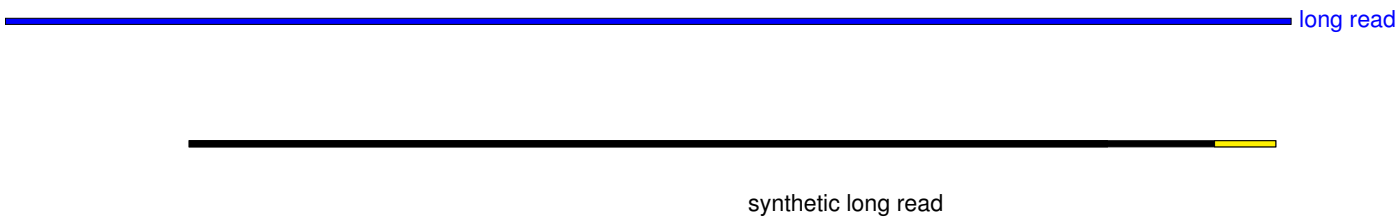

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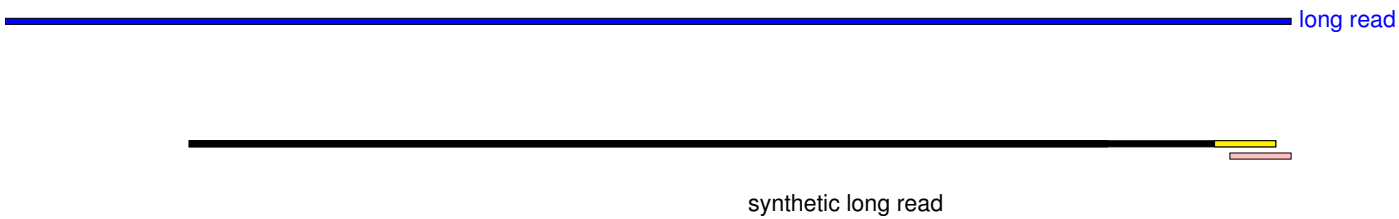

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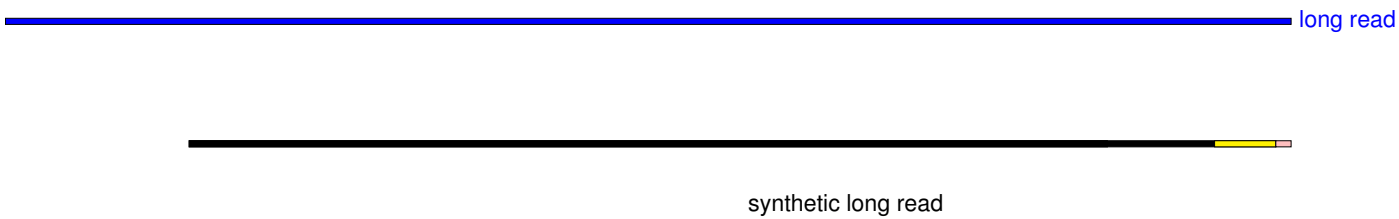

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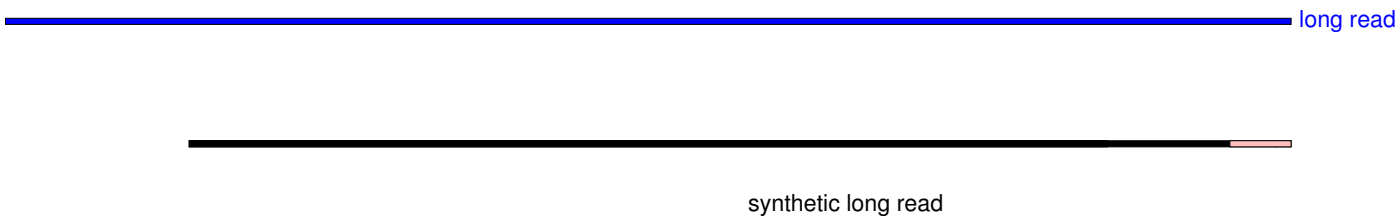

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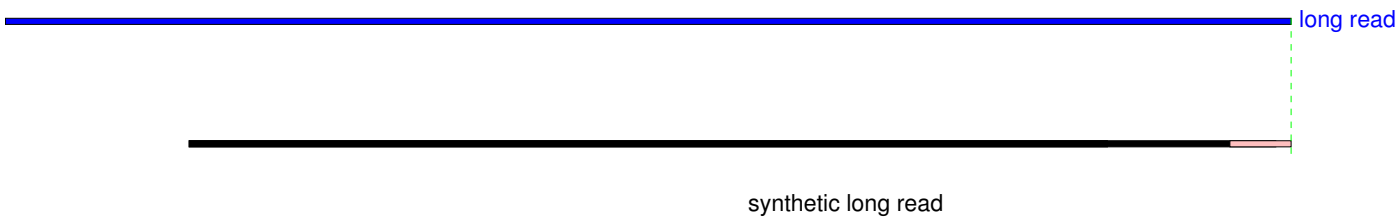

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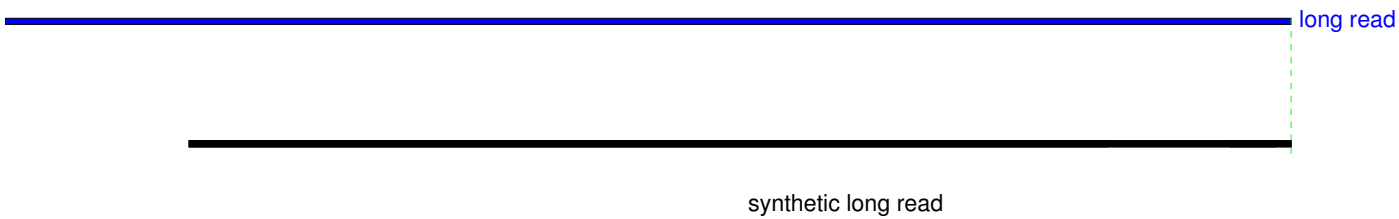

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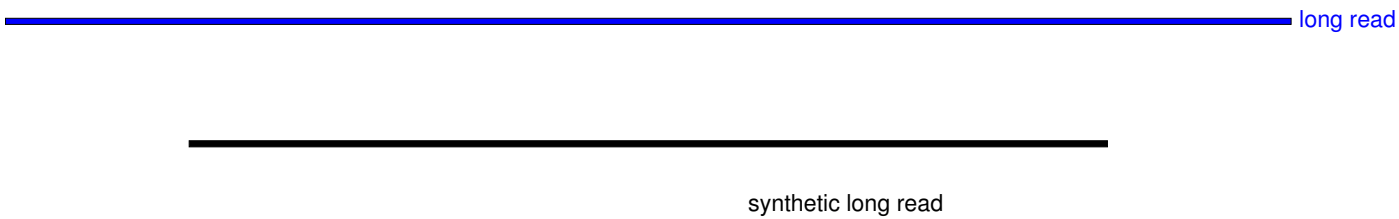

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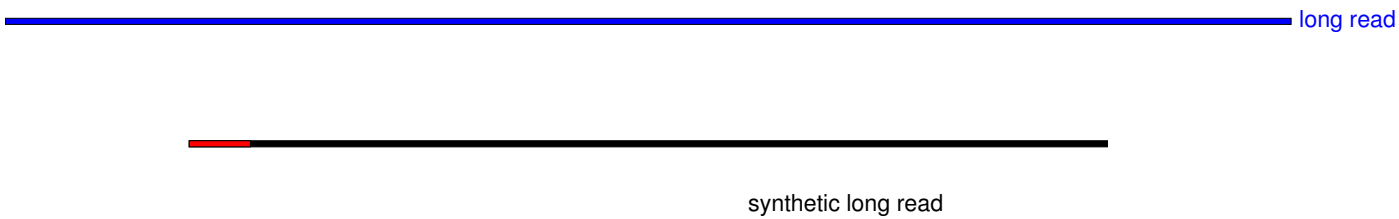

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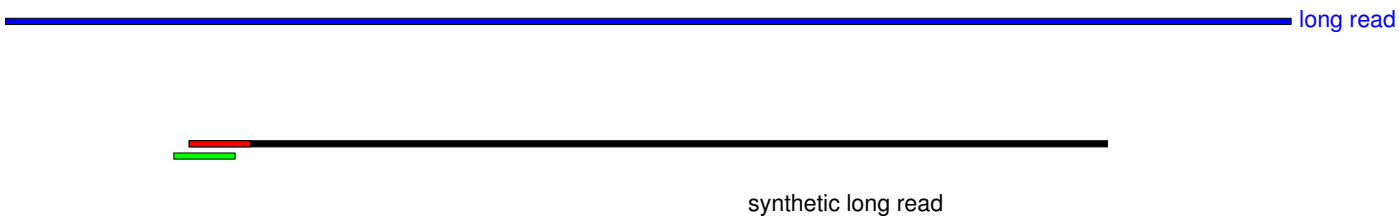

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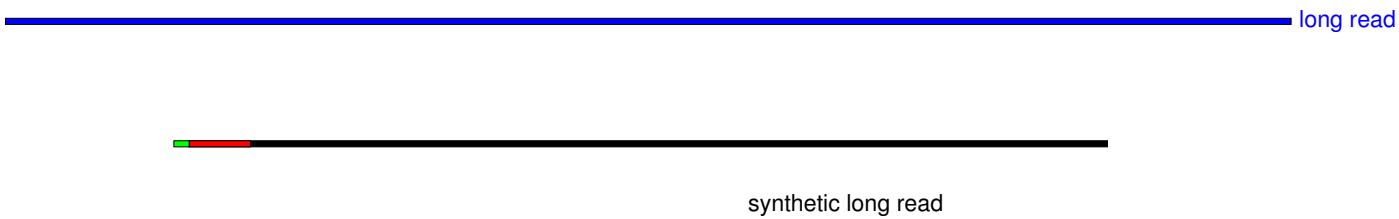

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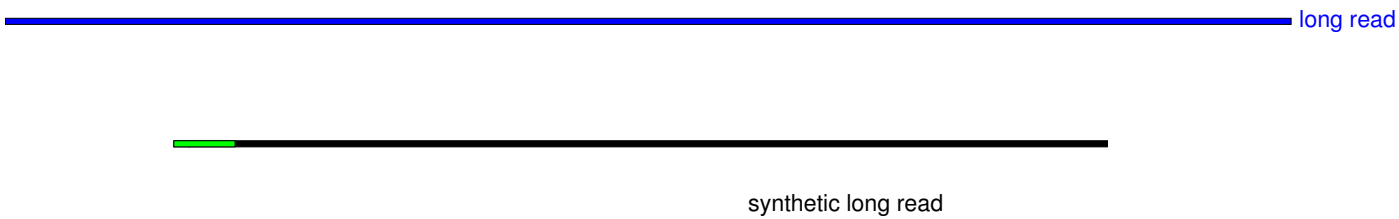

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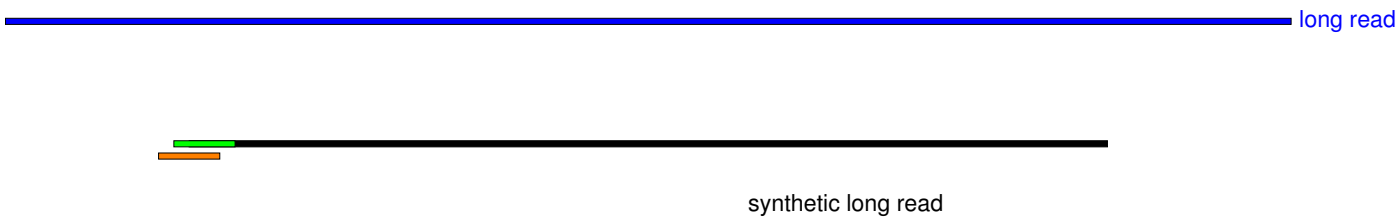

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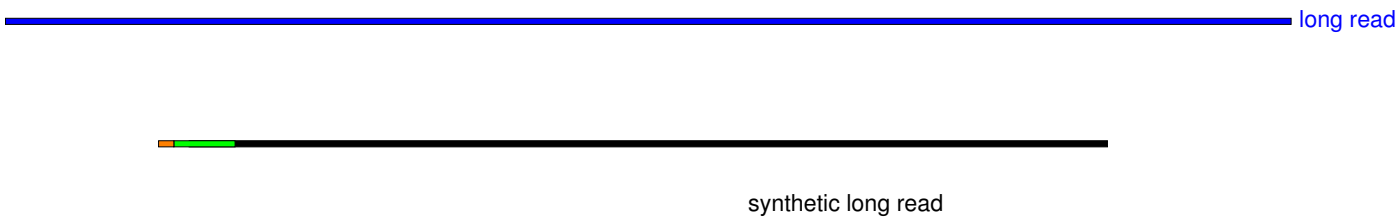

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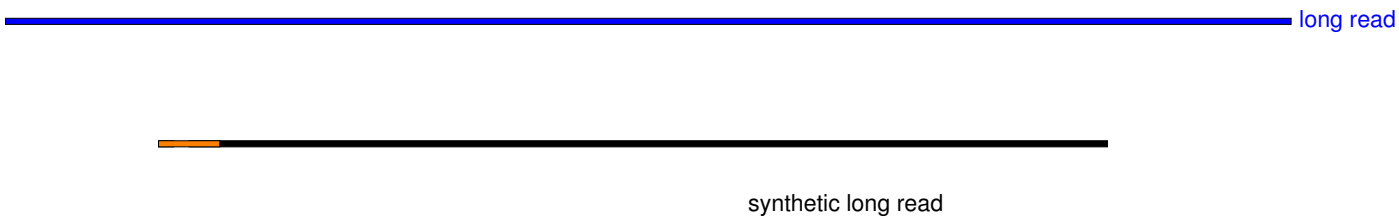

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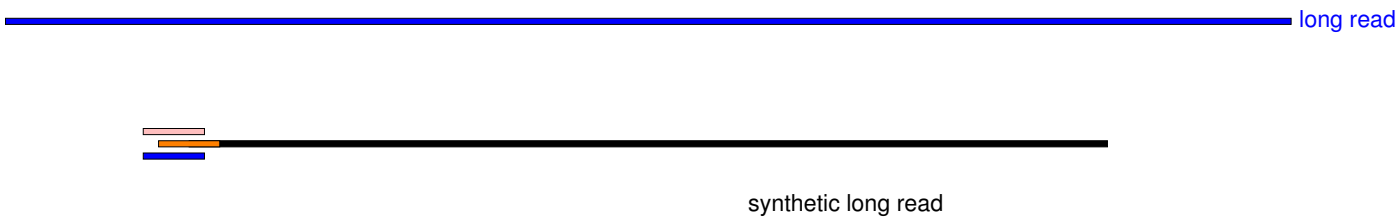

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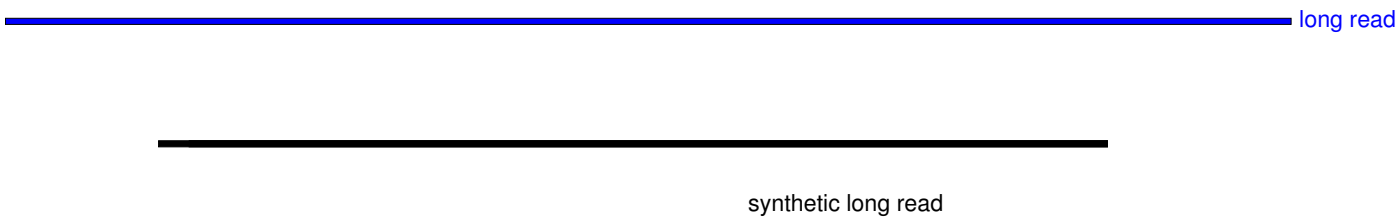

Results and comparison with NaS : Mapping

On the 6 ADP1 long reads datasets available from the Genoscope website :

	Number of reads	Average length	Cumulative size	Average identity	s **Runtime**
Raw LRs	70 314	2 530	177 869 033	3,84 %	N.A.
NaS (fast)	8 219	4 514	37 099 564	99,92 %	TODO
NaS (sensitive)	12 053	6 338	76 388 104	99,89 %	TODO
Nous	7 425 (249 fragmented)	10 250	78 739 767	99,57 %	TODO

TABLE – On the 1D long reads

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TABLE – On the 1D long reads

	Number of reads	Average length	Cumulative size	Average identity	s Runtime
Raw LRs	18 697	10 884	203 496 742	37,07 %	N.A.
NaS (fast)	15 844	11 084	175 607 625	99,78 %	TODO
NaS (sensitive)	16 439	11 871	195 138 674	99,79 %	TODO
Nous	15 575 (984 fragmented)	10 562	178 222 404	99,54 %	TODO

TABLE – On the 2D long reads

Results and comparison with NaS : Assembly

With the two 1D and 2D datasets previously corrected :

Tool	Number of reads	Number of contigs	Genome coverage	Identity
NaS (fast)	24,063	1	100 %	99.98 %
NaS (sensitive)	28,492	1	100 %	99.99 %
Our method	TODO	TODO	TODO	TODO

TABLE – Assembly results

To do

- Try to produce less fragmented synthetic long reads $\Rightarrow$ Tuning of BLASR parameters

To do

- Try to produce less fragmented synthetic long reads $\Rightarrow$ Tuning of BLASR parameters
- Allow the correction to run in parallel to reduce runtime

Méthodes existantes

- LoRDEC (2014, Hybrid, short reads DBG)
- Jabba (2016, Hybrid, short reads DBG)
- LoRMA (2016, Only LRs, long reads DBG)