NucBreak: Location of structural errors in a genome assembly by using paired-end Illumina reads

Supplementary materials

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Supplementary methods and results

1. Fragment size estimation

Only read pairs satisfying the following conditions are used for fragment size estimation:

- 1. Each read in a pair is uniquely aligned
- 2. Both reads are mapped to the same genome sequence
- 3. The reads have different orientations relative to the genome sequence
- 4. The read with the reverse orientation is located at the same position or further down on the sequence compared to the mapping locations of the forward-oriented read
- 5. The forward- and reverse-oriented reads are not soft-clipped at both sides. However, the alignments of properly mapped reads may contain short substitutions, insertions and deletions.

The fragment size is calculated by the formula:

 $frag_size = ref_end_2 - ref_st_1 + 1$, where

 ref_end_2 - the location of reverse-oriented read end at the genome chromosome ref_st_1 - the location of forward-oriented read start at the genome chromosome

The fragment sizes are sorted in ascending order, and for each fragment size the number of read pairs (#P) having the given fragment size is calculated. Then *min_frag_size* and *max_frag_size* are found:

$$\begin{split} min_frag_size &= \{frag_size_i: \#P(frag_size_i) \geq 10 \text{ and } \forall j < i \ \#P(frag_size_j) < 10 \\ and \exists k = i + 1 \dots i + 10 \ \#P(frag_size_k) \geq 10 \text{ and } \#k \geq 3 \} \end{split}$$

$$max_frag_size = \{frag_size_i: \#P(frag_size_i) \ge 10 \text{ and } \forall j > i \ \#P(frag_size_j) < 10$$
$$and \exists k = i - 11 \dots i - 1 \ \#P(frag_size_k) \ge 10 \text{ and } \#k \ge 3\}$$

If the number of corresponding read pairs is less than 10 for any fragment size, then:

 $min_frag_size = \{max(0, frag_size_i - 50): \forall k \neq i \ \#P(frag_size_i) \ge \ \#P(frag_size_k)\}$ $max_frag_size = \{frag_size_i + 50: \forall k \neq i \ \#P(frag_size_i) \ge \ \#P(frag_size_k)\}$

2. Fragment size detection between properly mapped read pairs

Since the reads from properly mapped reads pairs may be soft-clipped in the start or at the end of the read depending on the read orientation, a fragment size inside properly mapped reads is calculated by the extended formula:

$$frag_size = ref_end_2 + end_clipped_dist_2 - ref_st_1 - start_clipped_dist_1 + 1$$
, where

 ref_end_2 - the location of the reverse-oriented read end at the genome chromosome $end_clipped_dist_2$ - the number of soft-clipped bases at the end of the reverse-oriented read ref_st_1 - the location of the forward-oriented read start at the genome chromosome $start_clipped_dist_1$ - the number of soft-clipped bases in the beginning of the reverse-oriented read read

3. The Velvet, ABySS and SPAdes parameter settings used to obtain assemblies

SPAdes was run with the "-t 2 -k 33 --cov-cutoff 2" parameter settings.

ABySS was run with "k=64" parameter setting.

Velveth was run with k-mer length equal to 31.

Velvetg was run with "-ins_length 180 -scaffolding yes -min_contig_lgth 250 -cov_cutoff 5" parameter settings.

4. The NucBreak, REAPR and FRCbam parameter settings used to detect assembly errors

In the Sections 3.1 and 3.2, we used the following parameter settings for the tools:

- NucBreak was run with "--min_frag_size 620 --max_frag_size 790" parameter settings
- In case of REAPR, perfectmap was run with 700 bp average insert size
- FRCbam was run with "--pe-max-insert 776" and the value for "--genome-size" parameter was detected automatically by using python script for each modification case.

In the Section 3.3, we used the following parameter settings for the tools:

- in case of REAPR, perfectmap was run with 300 bp average insert size
- FRCbam was run with "--pe-max-insert 776 --genome-size 112000000" parameter settings

In the Section 3.4, we used the following parameter settings for the tools:

- In case of REAPR, perfectmap was run with the following average insert sizes depending on the genome dataset used:
 - Salmonella dataset 500 bp
 - Staphylococcus dataset 400 bp
 - Escherichia dataset 300 bp
 - Pseudomonas dataset 180 bp
 - Bordetella dataset 450 bp
 - Brucella dataset 500 bp
 - Klebsiella dataset 200 bp
 - Enterobacter dataset 300 bp
- FRCbam was run with the following parameter settings depending on the genome dataset used:
 - Salmonella dataset "--pe-max-insert 1060 --genome-size 4810000"
 - Staphylococcus dataset "--pe-max-insert 1040 --genome-size 2860000"
 - Escherichia dataset "--pe-max-insert 1110 --genome-size 5480000"
 - Pseudomonas dataset "--pe-max-insert 844 --genome-size 6820000"
 - Bordetella dataset "--pe-max-insert 890 --genome-size 4110000"
 - Brucella dataset "--pe-max-insert 1120 --genome-size 3300000"
 - Klebsiella dataset "--pe-max-insert 950 --genome-size 5720000"
 - Enterobacter dataset "--pe-max-insert 819 --genome-size 5040000"

5. Result evaluation

The ground truth entries may be represented as dots (e.g. in case of deletions, simple relocations or translocations) or as intervals (e.g. in case of insertion, duplications, relocations with overlap). If a ground truth entry is an interval, it may be fully covered with reads mapped back to the query sequences (e.g. in case of inversions) or remain uncovered (e.g. in case of inserted regions that are not present in the reference genome). In the first case, a tested tool is expected to mark the regions corresponding to the start- and/or end-points of the ground truth entry as breakpoints, while in the second case the whole entry is expected to be predicted as a breakpoint.

We say that if a ground truth entry coincides with an obtained breakpoint or the ground truth entry start- and/or end-points coincide with obtained breakpoints, then we have a true positive (TP). If a ground truth entry does not coincide with any of obtained breakpoints, then we have a false negative (FN). To get TPs and FNs, we have run BEDTools with the pairtopair -both' option. With this option, BEDTool reports an overlap between two intervals A and B if both ends of A overlap B. If BEDTool reports an overlap for a whole ground truth entry or for its start- and/or end-points, then we get a TP, otherwise a FN. Having obtained the number of TPs and FNs, we formula:

$$Sensitivity = \frac{\#TP}{\#TP + \#FN}$$

Unlike ground truth entries, an obtained result can correspond only to one interval: either to a whole ground truth entry or to its start- or end-point. If an obtained breakpoint does not coincide with any of the ground truth entries and with any of the ground truth entry start- and end-points, then the given obtained breakpoint is a false positive (FP). To get FP, we have run BEDTools with the "pairtopair -notboth' option. With this option, BEDTool reports an overlap between two intervals A and B, if one or neither of A's ends overlap B. If BEDTool reports an overlap for an obtained breakpoint with a whole ground truth entry or with its ends, then we get a FP. Having obtained the number of FPs, we calculate FDR by the formula:

$$FDR = \frac{FP}{FP + TP}$$

Supplementary figures

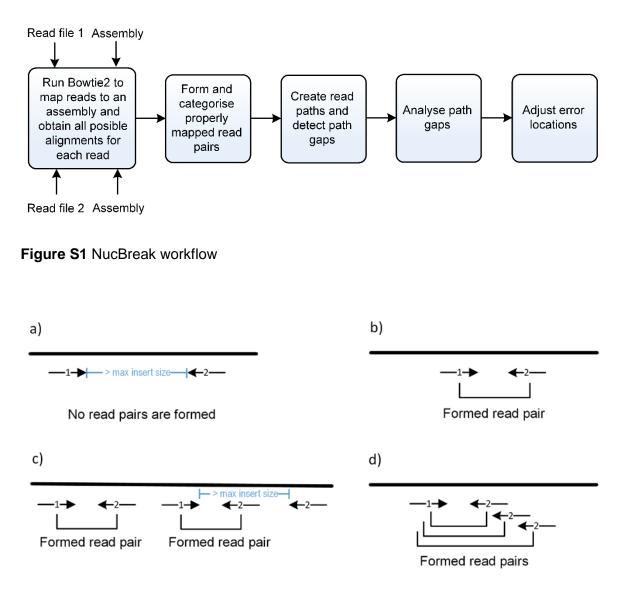


Figure S2 Properly mapped read pair formation. The black line represents an assembly. The arrows represent all possible read mapping locations. The cases a) and b) correspond to the situations when no read pairs are formed or just one read pair is formed, respectively. The cases c) and d) show examples when several read pairs are formed from two given reads. The case d) is an example of the situation when reads are mapped to a tandem repeat.

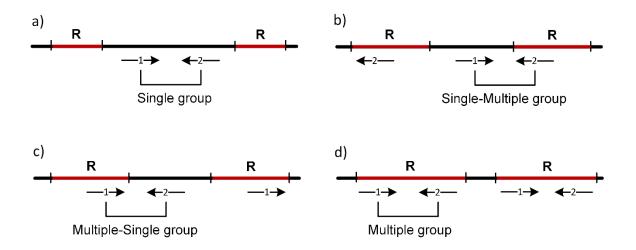


Figure S3 Properly mapped read pair categorization. The black line represents an assembly. The assembly regions marked by red colour correspond to repeated regions. The repeated regions are identical or near-identical copies of the same repeat. The arrows represent all possible read mapping locations.

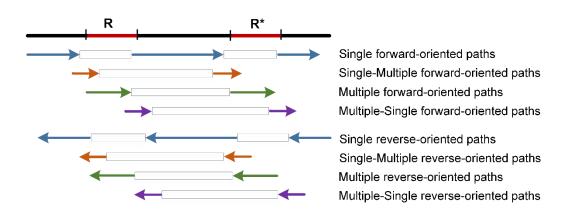


Figure S4 Read paths and path gaps. The black line represents an assembly. The assembly regions marked by red colour correspond to repeated regions. The repeated regions are identical or near-identical copies of the same repeat or copies of different repeats. The arrows represent read paths. The arrows of the same colour correspond to the read paths of the same type. The rectangles between the read paths indicate path gaps. The example demonstrates the correct order of the read paths in the absence of assembly errors.

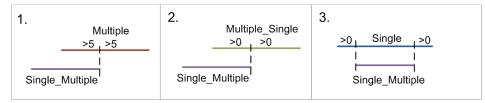
Single path

1. Single_Multiple >5 >5 I Single	2. Multiple >0 >0 Single_Multiple	3. Multiple >0 >0 Single_Multiple >0 Single	4. <u>>0</u> Multiple >0 I I Single
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Multiple path

1. Multiple_Single >5 + >5 I Multiple	2. Single >0 >0 Multiple_Single	3. Single >0 >0 Multiple_Single >0 Multiple	4. <u>>0</u> Single >0 Multiple
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Single_Multiple path



Multiple_Single path

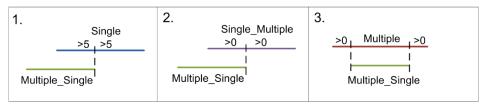


Figure S5 Possible type order and locations of read paths in the absence of breakpoints.

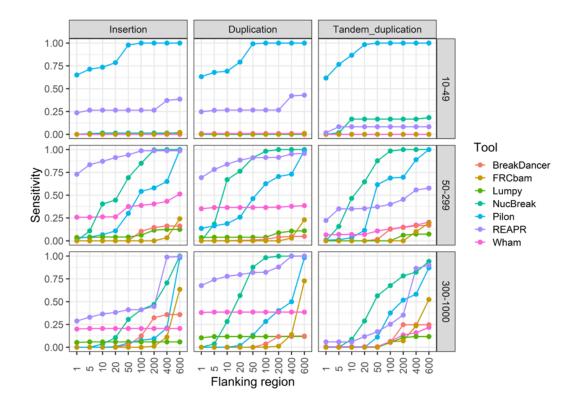


Figure S6 Sensitivity results for the insertion, duplication and tandem duplication groups, obtained using the simulated datasets.

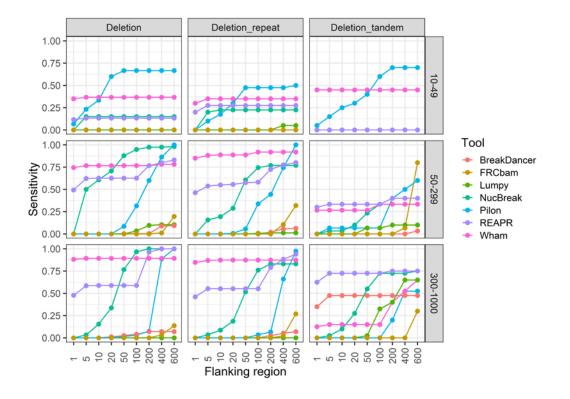


Figure S7 Sensitivity results for the deletion, deletion_repeat and deletion_tandem groups, obtained using the simulated datasets. The deletion_repeat group contains deletions of interspersed repeats or their parts. The deletion_tandem group contains deletions of tandem repeats or their parts.

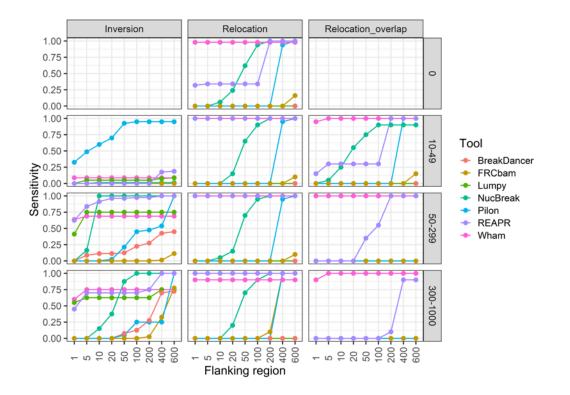


Figure S8 Sensitivity results for the inversion, relocation and relocation_overlap groups, obtained using the simulated datasets. The relocation group consists of relocations with either inserted regions between misjoined regions (size varied between 10 and 1000) or without them (size is equal to 0). The relocation_overlap group consists of relocations with overlapped misjoined regions.

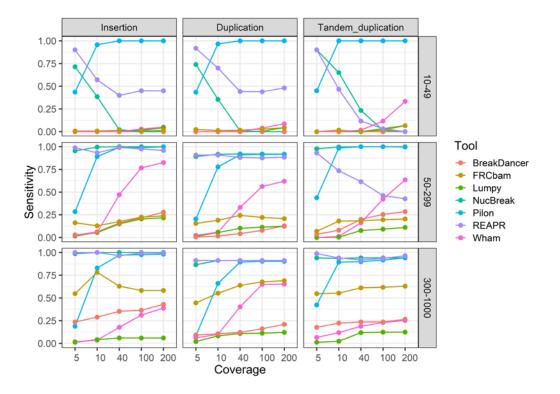


Figure S9 Sensitivity results for the insertion, duplication and tandem duplication groups, obtained using the simulated datasets.

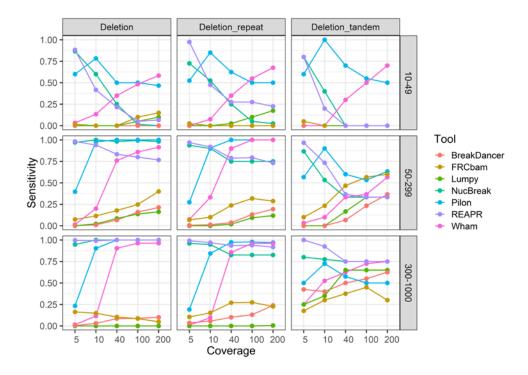


Figure S10 Sensitivity results for the deletion, deletion_repeat and deletion_tandem groups, obtained using the simulated datasets. The deletion_repeat group contains deletions of interspersed repeats or their parts. The deletion_tandem group contains deletions of tandem repeats or their parts.

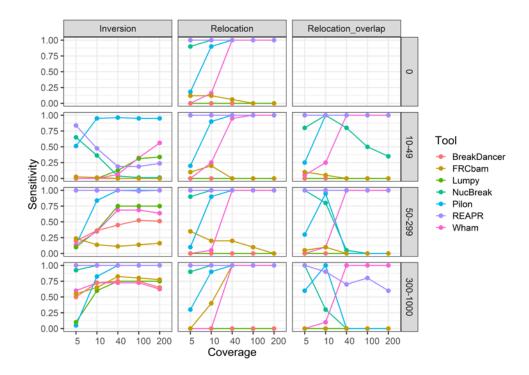


Figure S11 Sensitivity results for the inversion, relocation and relocation_overlap groups, obtained using the simulated datasets. The relocation group consists of relocations with either inserted regions between misjoined regions (size varied between 10 and 1000) or without them (size is equal to 0). The relocation_overlap group consists of relocations with overlapped misjoined regions.

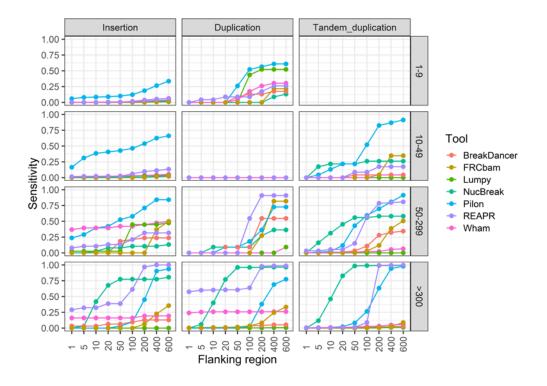


Figure S12 Sensitivity results for the insertion, duplication and tandem duplication groups, obtained using the datasets from the Assemblathon 1 project.

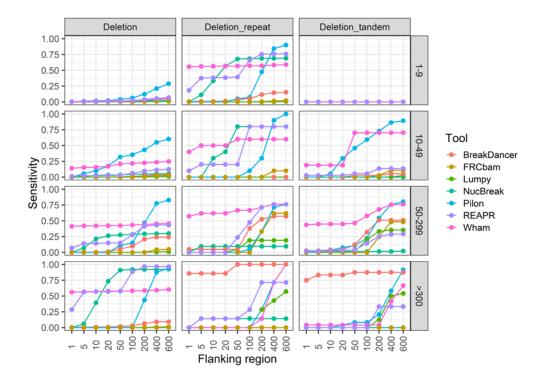


Figure S13 Sensitivity results for the deletion, deletion_repeat and deletion_tandem groups, obtained using the datasets from the Assemblathon 1 project. The deletion_repeat group contains deletions of interspersed repeats or their parts. The deletion_tandem group contains deletions of tandem repeats or their parts.

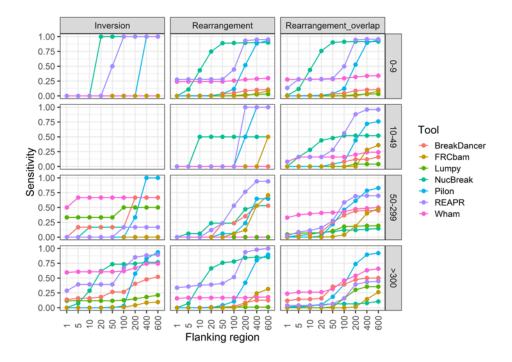


Figure S14 Sensitivity results for the inversion, rearrangement and rearrangement_overlap groups, obtained using the datasets from the Assemblathon 1 project. The rearrangement group consists of relocations and translocations with either inserted regions between misjoined regions (size varied between 1 and 1000) or without them (size is equal to 0). The rearrangement_overlap group consists of relocations and translocations and translocations with overlapped misjoined regions.

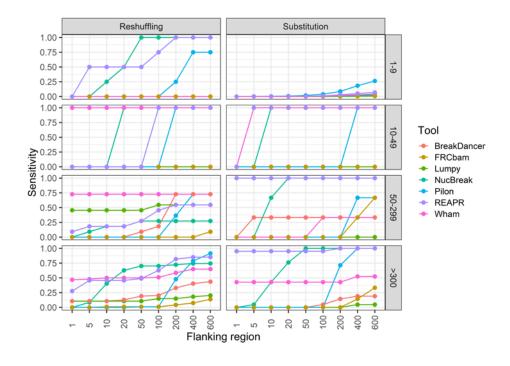


Figure S15 Sensitivity results for the reshuffling and substitution groups, obtained using the datasets from the Assemblathon 1 project.

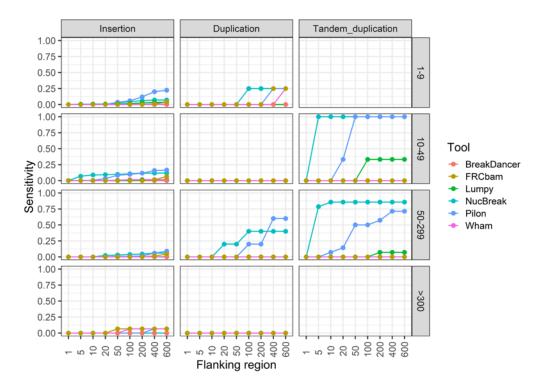


Figure S16 Sensitivity results for the insertion, duplication and tandem duplication groups obtained using the bacterial genome datasets.

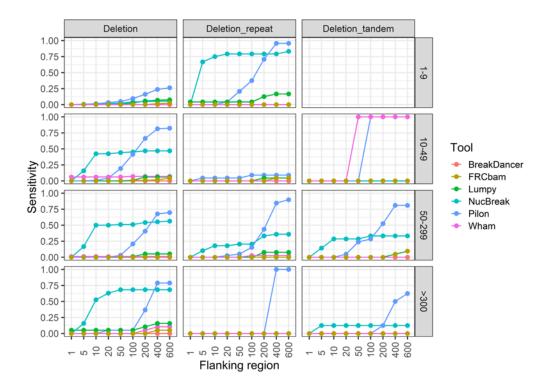


Figure S17 Sensitivity results for the deletion, deletion_repeat and deletion_tandem groups, obtained using the bacterial genome datasets. The deletion_repeat group contains deletions of interspersed repeats or their parts. The deletion_tandem group contains deletions of tandem repeats or their parts.

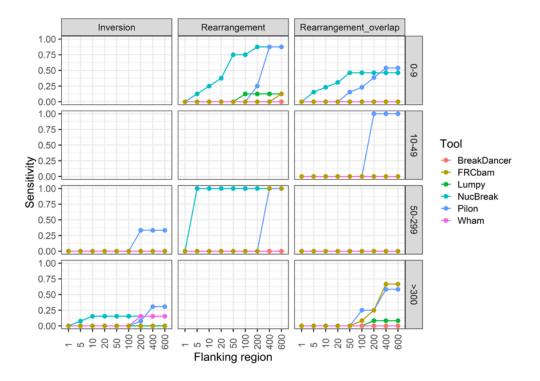


Figure S18 Sensitivity results for the inversion, rearrangement and rearrangement_overlap groups, obtained using the bacterial genome datasets. The rearrangement group consists of relocations and translocations with either inserted regions between misjoined regions (size varied between 1 and 1000) or without them (size is equal to 0). The rearrangement_overlap group consists of relocations and translocations with overlapped misjoined regions.

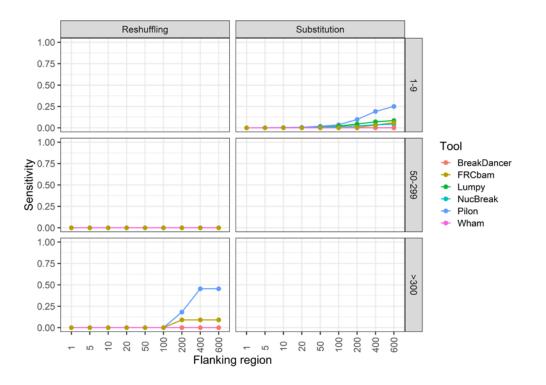


Figure S19 Sensitivity results for the reshuffling and substitution groups, obtained using the bacterial genome datasets.

Supplementary tables

Table S1 Genome modifications implemented during the simulation process. G and A denote a reference genome and assembly, respectively. All other letters denote reference genome and assembly sequence regions. Diff means difference. C' is the reverse complement of C.

46. G: DLLLLxC
A: DCLLLLxC Diff: duplication
47. G: DLLLLxTKxTKxTK A: DTLLLLxTKxTKxTK Diff: duplication
48. G: DLLLLxTKxTKxTK A: DKLLLLxTKxTKxTK Diff: duplication
49. G: DLLLLxCxCxC A: DCLLLLxCxCxC Diff: duplication
50. G: DKTKTKTKT A: DTKTKTKTKT Diff: duplication
51. G: DKTKTKTKT A: DKKTKTKTKT Diff: tandem_duplication
52. G: DCCCC A: DCCCCC Diff: tandem_duplication
53. G: DKTKTKTKT A: DTKKTKTKTKT Diff: duplication
54. G: DPPPPxTKTKTKTK A: DTPPPPxTKTKTKTK Diff: duplication
55. G: DPPPPxTKTKTKTK A: DKPPPPxTKTKTKTK Diff: duplication
56. G: DPPPPxCCCC A: DCPPPPxCCCC Diff: duplication
57. G: DPPPPxTKTKTKTK A: DKTPPPPxTKTKTKTK Diff: duplication

- 13. G: CxCxC A: CxCCxC Diff: tandem_duplication
- 14. G: RxRxRxTKTKTKTK A: RxTRxRxTKTKTKTK Diff: duplication
- 15. G: RxRxRxTKTKTKTK A: RxKRxRxTKTKTKTK Diff: duplication
- 16. G: RxRxRxTKTKTKTK A: RxTKRxRxTKTKTKTK Diff: duplication
- 17. G: RxRxRxTKTKTKTK A: RxKTRxRxTKTKTKTK Diff: duplication
- 18. G: RxRxRxCCCC A: RxCCCCRxRxCCCC Diff: duplication
- 19. G: RxRxRxTKxTKxTK A: RxTRxRxTKxTKxTK Diff: duplication
- 20. G: RxRxRxTKxTKxTK A: RxKRxRxTKxTKxTK Diff: duplication
- 21. G: RxRxRxCxCxC A: RxCRxRxCxCxC Diff: duplication
- 22. G: RxRxR A: RxRCxR Diff: insertion
- 23. G: RxRxRxC A: RxRCxRxC Diff: duplication
- 24. G: TKxTKxTK A: TKxTKTxTK Diff: duplication
- 25. G: TKxTKxTK A: TKxTKKxTK Diff: tandem_duplication
- 26. G: RxRxRxTKTKTKTK A: RxRTxRxTKTKTKTK Diff: duplication
- 27. G: RxRxRxTKTKTKTK A: RxRKxRxTKTKTKTK Diff: duplication

- 58. G: DPPPPxCCCC A: DCCCCPPPPxCCCC Diff: duplication
- 59. G: LLLLD A: LLLLCD Diff: insertion
- 60. G: LLLLDxC A: LLLLCDxC Diff: duplication
- 61. G: LLLLDxTKxTKxTK A: LLLLTDxTKxTKxTK Diff: duplication
- 62. G: LLLLDxTKxTKxTK A: LLLLKDxTKxTKxTK Diff: duplication
- 63. G: LLLLDxCxCxC A: LLLLCDxCxCxC Diff: duplication
- 64. G: TKTKTKTKD A: TKTKTKTKTD Diff: duplication
- 65. G: TKTKTKTKD A: TKTKTKTKKD Diff: tandem_duplication
- 66. G: TKTKTKTKD A: TKTKTKTKKTD Diff: duplication
- 67. G: PPPPDxTKTKTKTK A: PPPPTDxTKTKTKTK Diff: duplication
- 68. G: PPPPDxTKTKTKTK A: PPPPKDxTKTKTKTK Diff: duplication
- 69. G: PPPPDxCCCC A: PPPPCDxCCCC Diff: duplication
- 70. G: PPPPDxTKTKTKTK A: PPPPKTDxTKTKTKTK Diff: duplication
- 71. G: PPPPDxCCCC A: PPPPCCCCDxCCCC Diff: duplication
- 72. G: PPPP A: PPCPP Diff: insertion

- 28. G: RxRxRxTKTKTKTK A: RxRTKxRxTKTKTKTK Diff: duplication
- 29. G: RxRxRxTKTKTKTK A: RxRDTxRxTKTKTKTK Diff: duplication
- 30. G: RxRxRxCCCC A: RxRCCCCxRxCCCC Diff: duplication
- 31. G: RxRxRxTKxTKxTK A: RxRTxRxTKxTKxTK Diff: duplication
- 32. G: RxRxRxTKxTKxTK A: RxRKxRxTKxTKxTK Diff: duplication
- 33. G: RxRxRxCxCxC A: RxRCxRxCxCxC Diff: duplication
- 34. G: RDxRDxRD A: RDxRCDxRD Diff: insertion
- 35. G: RDxRDxRDxC A: RDxRCDxRDxC Diff: duplication
- 36. G: TKxTKxTK A: TKxTKKxTK Diff: tandem_duplication
- 37. G: RDxRDxRDxTKTKTKTK A: RDxRTDxRDxTKTKTKTK Diff: duplication
- 38. G: RDxRDxRDxTKTKTKTK A: RDxRKDxRDxTKTKTKTK Diff: duplication
- 39. G: RDxRDxRDxCCCC A: RDxRCDxRDxCCCC Diff: duplication
- 40. G: RDxRDxRDxTKTKTKTK A: RDxRKTDxRDxTKTKTKTK Diff: duplication
- 41. G: RDxRDxRDxCCCC A: RDxRCCCCDxRDxCCCC Diff: duplication
- 42. G: RDxRDxRDxTKxTKxTK A: RDxRTDxRDxTKxTKxTK Diff: duplication

- 73. G: PPPPxC A: PPCPPxC Diff: duplication
- 74. G: PPPPxTKxTKxTK A: PPTPPxTKxTKxTK Diff: duplication
- 75. G: PPPPxTKxTKxTK A: PPKPPxTKxTKxTK Diff: duplication
- 76. G: PPPPxCxCxC A: PPCPPxCxCxC Diff: duplication
- 77. G: TKTKTKTK A: TKTKKTKTK Diff: tandem_duplication
- 78. G: PPPPxTKTKTK A: PPTPPxTKTKTK Diff: duplication
- 79. G: PPPPxTKTKTK A: PPKPPxTKTKTK Diff: duplication
- 80. G: PPPPxCCC A: PPCPPxCCC Diff: duplication
- 81. G: PPPPxTKTKTK A: PPKTPPxTKTKTK Diff: duplication
- 82. G: PPPPxCCC A: PPCCCPPxCCC Diff: duplication
- 83. G: DKL A: DKTKL Diff: insertion
- 84. G: DKLxT A: DKTKLxT Diff: insertion
- 85. G: LxKLxLxT A: LxKTKLxLxT Diff: insertion
- 86. G: KLxKLxKLxT A: KLxKTKLxKLxT Diff: insertion
- 87. G: LKxLKxLKxT A: LKxLKTKxLKxT Diff: insertion

43. G: RDxRDxRDxTKxTKxTK	88. G: DCR
A: RDxRKDxRDxTKxTKxTK	A: DCCR
Diff: duplication	Diff: tandem_duplication
44. G: RDxRDxRDxCxCxC	89. G: DCR
A: RDxRCDxRDxCxCxC	A: DCCCCR
Diff: duplication	Diff: tandem_duplication
45. G: DLLLL	90. G: LxCLxL
A: DCLLLL	A: LxCCLxL
Diff: insertion	Diff: tandem_duplication
Deletions	
1. G: RCD	14. G: DTKKKK
A: RD	A: DKKKK
Diff: deletion	Diff: deletion
2. G: RxCRxR	15. G: DTKKKK
A: RxRxR	A: DKKK
Diff: deletion	Diff: deletion
3. G: KRxTKRxKR	16. G: DTKKKK
A: KRxRxKR	A: DK
Diff: deletion_repeat	Diff: deletion_tandem
4. G: RxCRxR	17. G: DTKKKKF
A: RxxR	A: DF
Diff: deletion_repeat	Diff: deletion
5. G: KxTKFxK	18. G: DTLLLLK
A: KxxK	A: D
Diff: deletion_repeat	Diff: deletion
6. G: CRxCRxCR	19. G: RTKLKLKLKL
A: CRxRxCR	A: RLKLKLKL
Diff: deletion_repeat	Diff: deletion
7. G: CxCxC	20. G: DTKTKTKTK
A: CxxC	A: DKTKTKTK
Diff: deletion_repeat	Diff: deletion
8. G: KxKTxK	21. G: DTKTKTKTK
A: KxxK	A: DTKTTKTK
Diff: deletion_repeat	Diff: deletion
9. G: KTxKTxKT	22. G: TKTKTKTKD
A: KTxKxKT	A: TKTKTKTD
Diff: deletion_repeat	Diff: deletion
10. G: RTxRTKxRT	23. G: DCCCC
A: RTxRxRT	A: DCCC
Diff: deletion_repeat	Diff: deletion_tandem
11. G: RxRCxR	24. G: RCCCCD
A: RxRxR	A: RD
Diff: deletion	Diff: deletion
12. G: KTKxK	25. G: DTTTTK
A: KxK	A: DTTT
Diff: deletion_repeat	Diff: deletion

13. G: KTK A: K Diff: deletion_repeat	26. G: DTTTTK A: D Diff: deletion
Relocations	Inversions
 G: SzV A: SCV Diff: relocation G: SzV A: SV Diff: relocation G: SCzCV A: SCV Diff: relocation_overlap 	 G: DCR A: DC'R Diff: inversion G: DCRxRxR A: DC'RxRxR Diff: inversion G: DRCxRxR A: DRC'xRxR Diff: inversion G: RCDxRCDxRCD A: RCDxRC'DxRCD Diff: inversion

In the simulated modifications, the following lengths of regions were used:

- 1. Distance between each manipulation case =2500 bp
- 2. len(H)=800 bp
- 3. len(B)=800 bp
- 4. len(x)=800 bp
- 5. len(C)={17,30,100,250,800} bp

6. $len(TK) = \{[50,70], [100,150], [250,250], [600,600]\}$ bp, where first number in a pair is len(T)

and second number in a pair is len(K)

- 7. len(R)=600 bp
- 8. len(D)=600 bp
- 9. len(L)=200 bp
- 10. len(P)=400 bp
- 11. len(F)=len(T) in len(TK)
- 12. len(S)=1500 bp
- 13. len(V)=1500 bp
- 14. len(Z)=15000 bp

Genome	Genome length, Mb	Accession number	Reads length, bp (first, second)	Coverage	Read library accession number
Bordetella pertussis str. J081	4,11	GCA_002859625.1	250 250	32x	SRR5829829
Brucella melitensis str. 1	3,30	GCA_900236405.1	243 ± 28.8 243 ± 28.7	40x	ERR2192800
Enterobacter cloacae str. AR_0136	5,04	GCA_002204775.1	233 ± 34.9 233 ± 34.8	23x	SRR4025988
<i>Escherichia coli</i> str. 2014C-3599	5,48	GCA_003018935.1	236 ± 39.0 236 ± 38.8	60x	SRR1609862
Klebsiella pneumonia str. SGH10	5,72	GCA_002813595.1	146 ± 15.8 146 ± 15.7	32x	SRR5082357
Pseudomonas aeruginosa str. AR_0095	6.82	GCA_002997005.1	229 ± 38.2 229 ± 36.9	60x	SRR3242025
Salmonella enterica str. CFSAN047866	4,81	GCA_003073535.1	244 ± 27.3 244 ± 27.3	37x	SRR3272258
Staphylococcus aureus str. CFSAN007896	2,86	GCA_003031425.1	236 ± 41.8 236 ± 41.7	28x	SRR5912676

 Table S2 List of bacterial genomes.

Table S3 Number of ground truth errors in each group.

Error type	Error size	Simulated datasets	Assemblathon 1 dataset	Bacterial genome datasets
insertion	0-9	0	6658	402
	10-49	140	892	414
	50-299	240	38	133
	>300	170	31	15
duplication	0-9	0	23	4
	10-49	380	1	12
	50-299	1510	11	5
	>300	840	287	1

tandem_duplication	0-9	0	0	0
	10-49	60	23	3
	50-299	260	93	14
	>300	170	683	0
deletion	0-9	0	6933	437
	10-49	60	1091	113
	50-299	270	307	96
	>300	270	527	19
deletion_repeat	0-9	0	424	24
	10-49	40	10	22
	50-299	160	21	39
	>300	230	7	2
deletion_tandem	0-9	0	1	0
	10-49	20	37	1
	50-299	30	147	21
	>300	40	24	8
inversion	0-9	0	2	0
	10-49	80	0	0
	50-299	80	6	3
	>300	40	94	13
relocation/ rearrangement	0-9	50	749	8
	10-49	20	2	0
	50-299	20	17	1
	>300	10	95	0
relocation_overlap/ rearrangement_overlap	0-9	0	744	13
	10-49	20	25	1
	50-299	20	152	1
	>300	10	76	12
reshuffling	0-9	0	4	0
	10-49	0	1	0
	50-299	0	11	1

	>300	0	94	11
substitution	0-9	0	225721	8000
	10-49	0	1	0
	50-299	0	3	0
	>300	0	21	0