Mapping reads on a genomic sequence: a practical comparative analysis

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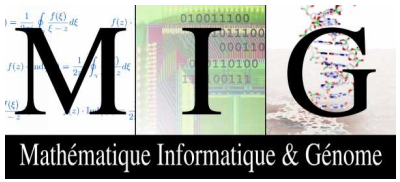


Kick-off RADIANT meeting, Manchester, January 14, 2013

Next Generation Sequencing reads mapping

- Short read mapping is the initial step of many NGS analyses (SNPs calling, RNA-Seq, CHIP-Seq, . . .)
- A lot of tools have been released between 2007 and 2012 (76 tools in the survey of Fonseca et al. (2012))
- Few complete, controlled and fully understable benchmarks

Aim of our benchmark

Controlled benchmark, simple questions :

- Are the tools capable to systematically map a read occurring exactly (with no mismatch) in the reference genome ?
- Can they always do it for a read having as many errors as the maximum number of mismatches allowed in the alignments ?
- For reads occurring at several positions, do/can they retrieve all the occurrences or only a subset ?
- Do the reads reported as unique really occur only once along the genome ?

Evaluated mappers

Mapper	Format	Algorithm	Input	Threads	Gaps
bwa	SAM	Burrows-Wheeler	nt	yes	yes
Bowtie	SAM	Burrows-Wheeler	nt & color	yes	no
SOAP2	dedicated	Burrows-Wheeler	nt	yes	no
Novoalign	SAM	hash on ref.	nt & color	yes	yes
BFAST	SAM	hash on ref.	nt & color	yes	yes
SSAHA2	SAM	hash on ref.	nt	no	no
GASSST	SAM	hash on ref.	nt	yes	yes
PerM	SAM	hash on ref.	nt & color	no	no
MPscan	dedicated	suffix tree	nt	no	no

SAM : Simple Alignment Map

nt : Nucleotide space

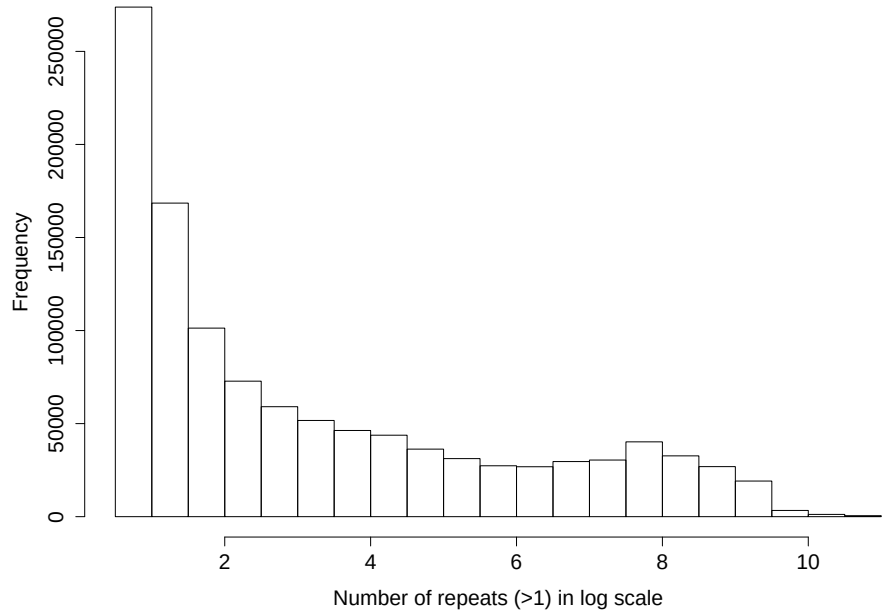
Read dataset generation : $\mathcal{H}_0$

Dataset

- Human genome (2.7 Gbp) as reference
- 10 millions of 40 bp reads
- Uniformly drawn from both strands

Characteristics

- 49 reads with 'N'
- 1 122 893 reads non unique
- Most frequent read : 53162 occurrences



Other read datasets

Human reference genome

- $\mathcal{H}_1$, $\mathcal{H}_2$ and $\mathcal{H}_3$: exactly 1, 2 and 3 mismatches uniformly generated within each read from $\mathcal{H}_0$
- $\mathcal{H}\ell_0$ and $\mathcal{H}\ell_3$: longer reads of 100 bps

Bacterial reference genome

- $\mathcal{B}_0$: 10 millions of 40bps reads drawn from 904 bacterial genomes
- $\mathcal{B}_3$: 3 mismatches uniformly generated within each read from $\mathcal{B}_0$

Results for exact mapping of $\mathcal{H}_0$ on human genome

Exact mapping of $\mathcal{H}_0$: memory usage

Software	Memory usage (Gb)	Indexing time	Mapping time	Unmapped reads	Orig. pos. not ret.
BWA	2.18	1h 36mn	1h 13mn	49	0
Novoalign	8.12	8mn	13h 24mn	632	0
Bowtie	7.36	3h 25mn	2h 42mn	49	0
SOAP2	51.87	*1h 56mn*$^{(\ddagger)}$	*56mn*$^{(\ddagger)}$	49	3 566
BFAST	9.68	18h 01mn$^{(*)}$	15h 02mn	726 332	20 026
SSAHA2	9.60	24mn	1d 1h	35 875	193 211
MPscan	2.67	1h 20mn		26	0
GASSST	57.93	*8h 45*$^{(\dagger\ddagger)}$		49	54
PerM	13.77	13h 05mn		115 871	4

Exact mapping of $\mathcal{H}_0$: computation time

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Test performed on a Intel Quad Core 2.33 GHz 16 Gb RAM, except $^{(\ddagger)}$ four Intel Six Core 2.40 GHz 132 Gb RAM

$^{(*)}$ Average indexing time per spaced seed computed on 10 seeds.

$^{(\dagger)}$ This time does not include the running time of the `gasssst_to_sam` command.

$^{(\ddagger)}$ This time is slightly over-estimated.

Exact mapping of $\mathcal{H}_0$: failures

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Exact mapping of $\mathcal{H}_0$: unique matches

		Reads uniquely retrieved		Reads with multiple hits		
Software	Unmapped reads	Nb	Orig. pos. not retr.	Nb	Nb hits mean	Orig. pos. not retr.
BWA	49	8 877 061	0	1 122 890	722.81	0
Novoalign	632	8 877 107	0	1 122 261	698.63	0
Bowtie	49	8 877 061	0	1 122 890	722.81	0
SOAP2	49	8 877 061	0	1 122 890	653.26	3566
BFAST	726 332	8 840 305	9 193	433 363	2.96	10 833
SSAHA2	35 875	8 886 204	9 847	1 077 921	79.52	183 364
MPscan	26	8 877 081	0	1 122 893	722.81	0
GASSST	49	8 877 061	0	1 122 890	722.47	54
PerM	115 871	8 877 068	3	1 007 061	126.42	1
Reference		8 877 107		1 122 893	722.81	

Exact mapping of $\mathcal{H}_0$: multiple matches

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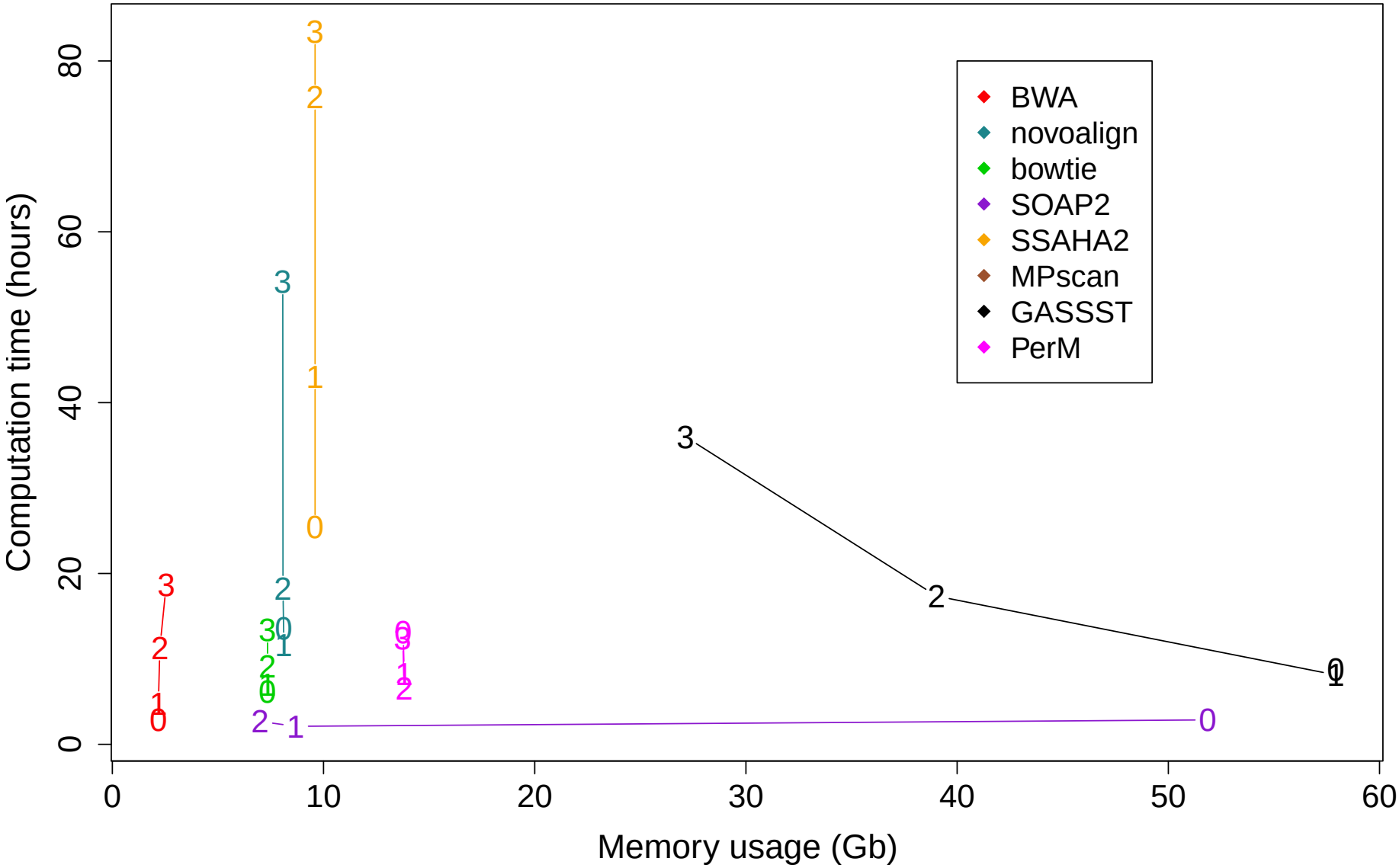
Trends as increasing the number of mismatches

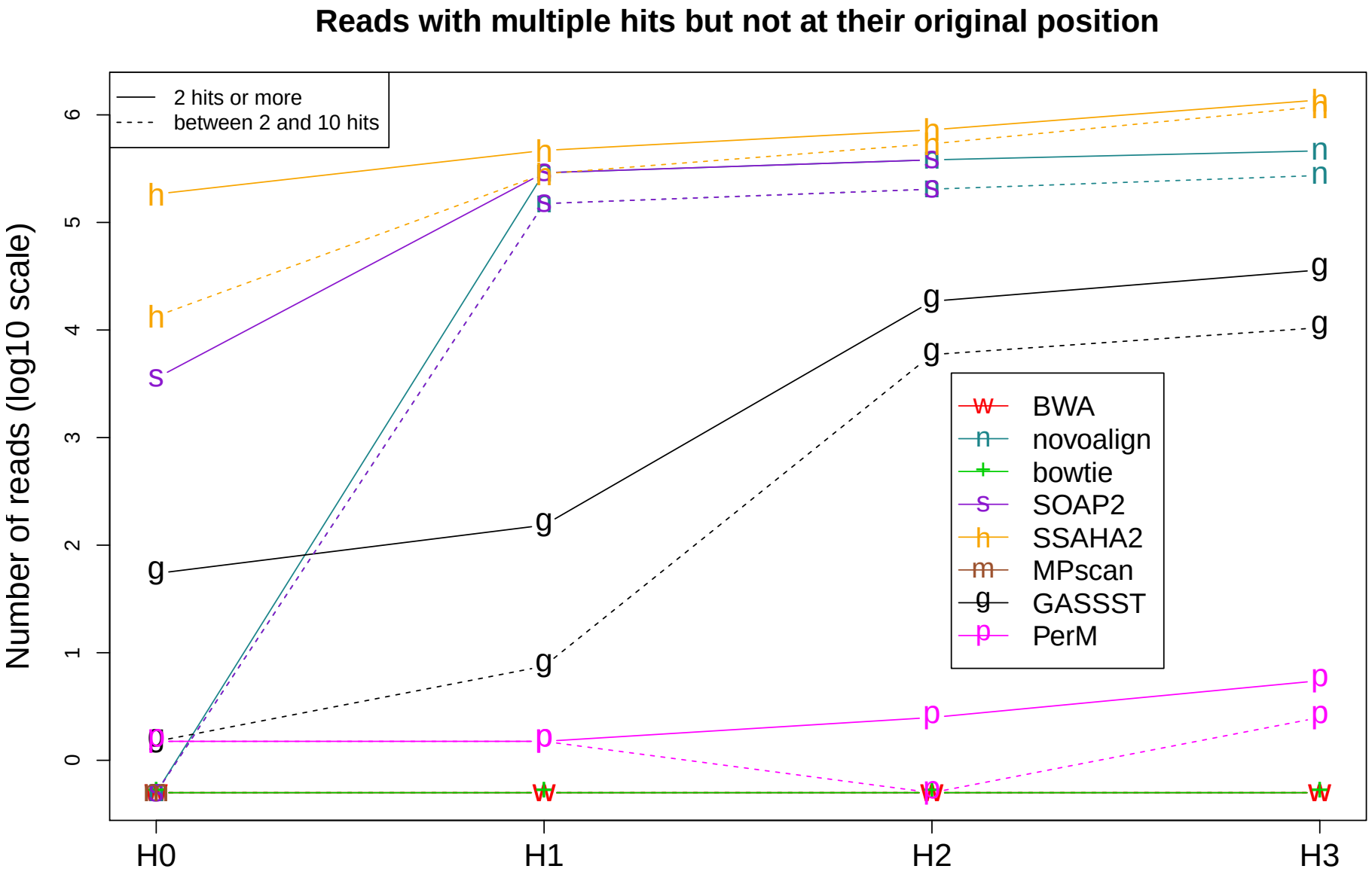
- exact mapping of $\mathcal{H}_0$ on human genome
- mapping with up to 1 mismatch of $\mathcal{H}_1$ on human genome
- mapping with up to 2 mismatches of $\mathcal{H}_2$ on human genome
- mapping with up to 3 mismatches of $\mathcal{H}_3$ on human genome

Memory usage versus Computation time



Failures for unique matches

Failures for multiple matches



Conclusions and future work

Benchmark

- Each software has specific heuristics that leads to different results, even at $\mathcal{H}_0$
- Dealing with multiple hits is a strong difference point
- Choice of software depend of the biological question
- Tuning of parameters is important
- Similar trends for the bacterial datasets.
- Two software, BWA and Bowtie seem a little ahead

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Ongoing work

- Running latest release of some software (Bowtie2, Soap3,. . .)
- paired-reads, indels

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- Valentin Loux
- Jean-François Gibrat
- Pierre Nicolas
- Jérôme Compain

Computational ressources

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Mapping Reads on a Genomic Sequence : An Algorithmic Overwiew and a Practical Comparative Analysis

Journal of Computational Biology 2012 vol. 19, pp. 796-813.

`http://genome.jouy.inra.fr/ngs/mapping`