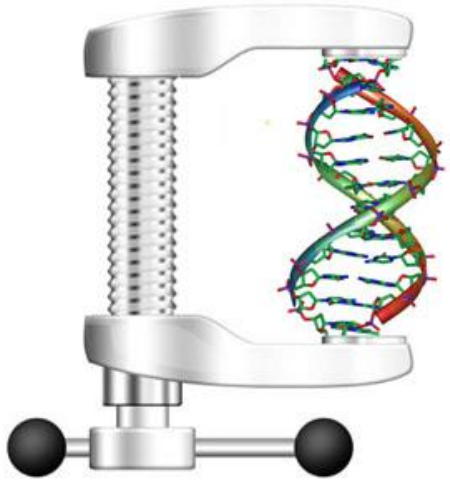
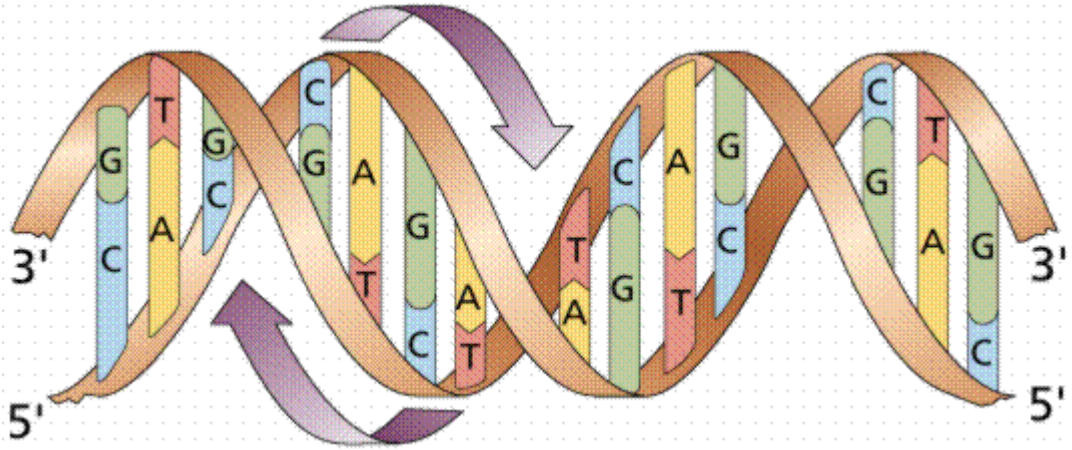
Genome Information Compression



The Human Genome

- 4 possible symbols (**bases**): A,C,G,T
- 3.2 billions base pairs for the human genome
  - 3.2 x 2 bit = 6.4 billion bits / 8 = 800 Mbytes



- So why do we need compression?

Genome sequencing

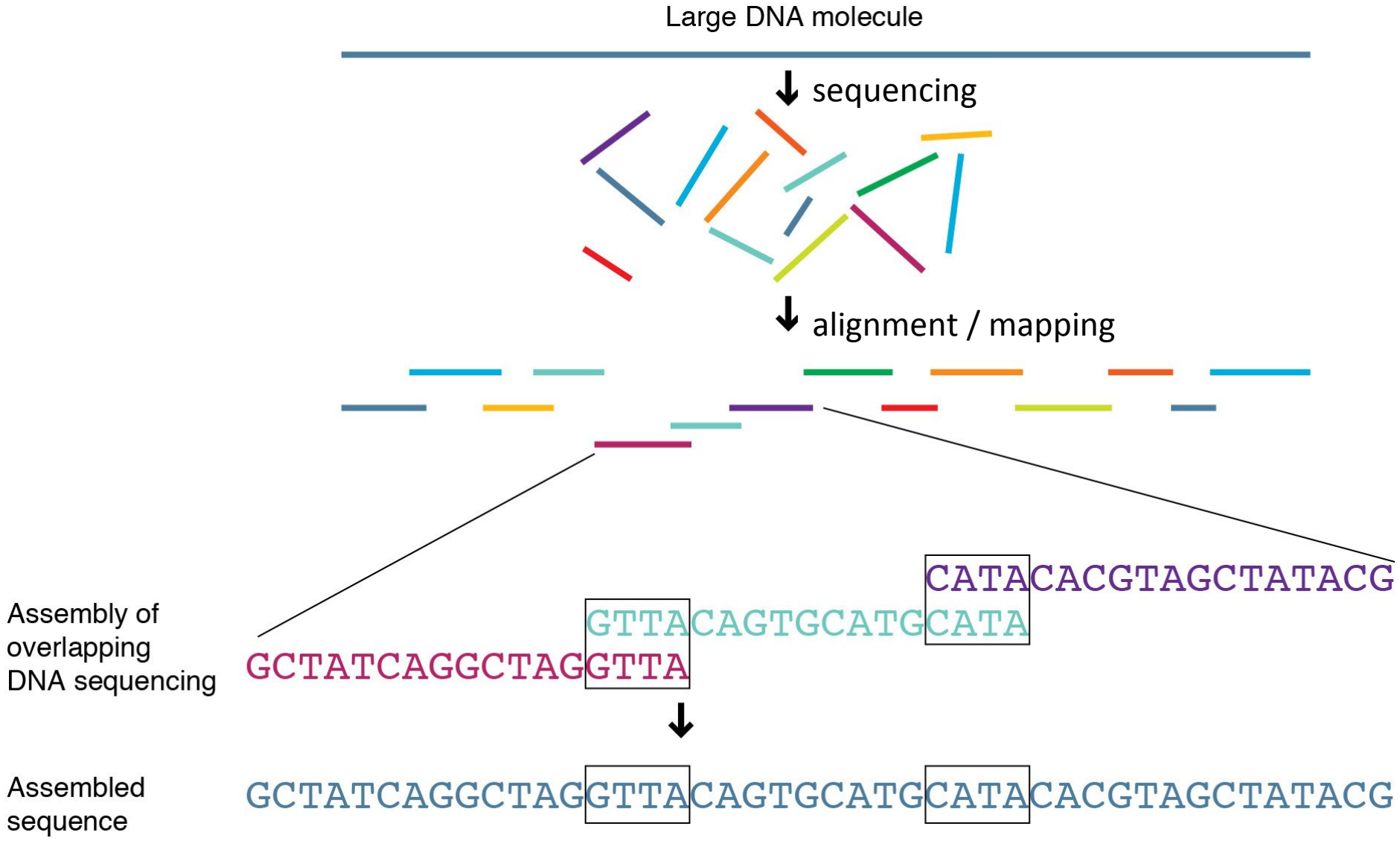
- How do we obtain a genome representation from biological samples?
- Current technology provides random fragments of genome data called “reads”
- This process is called **genome sequencing**

Short and long reads

- Different sequencing technologies provide
  - Read lengths from about 100 to 20,000+ bases
  - Single or coupled (paired) reads
  - Different accuracy levels (from 60% to 99.9%)

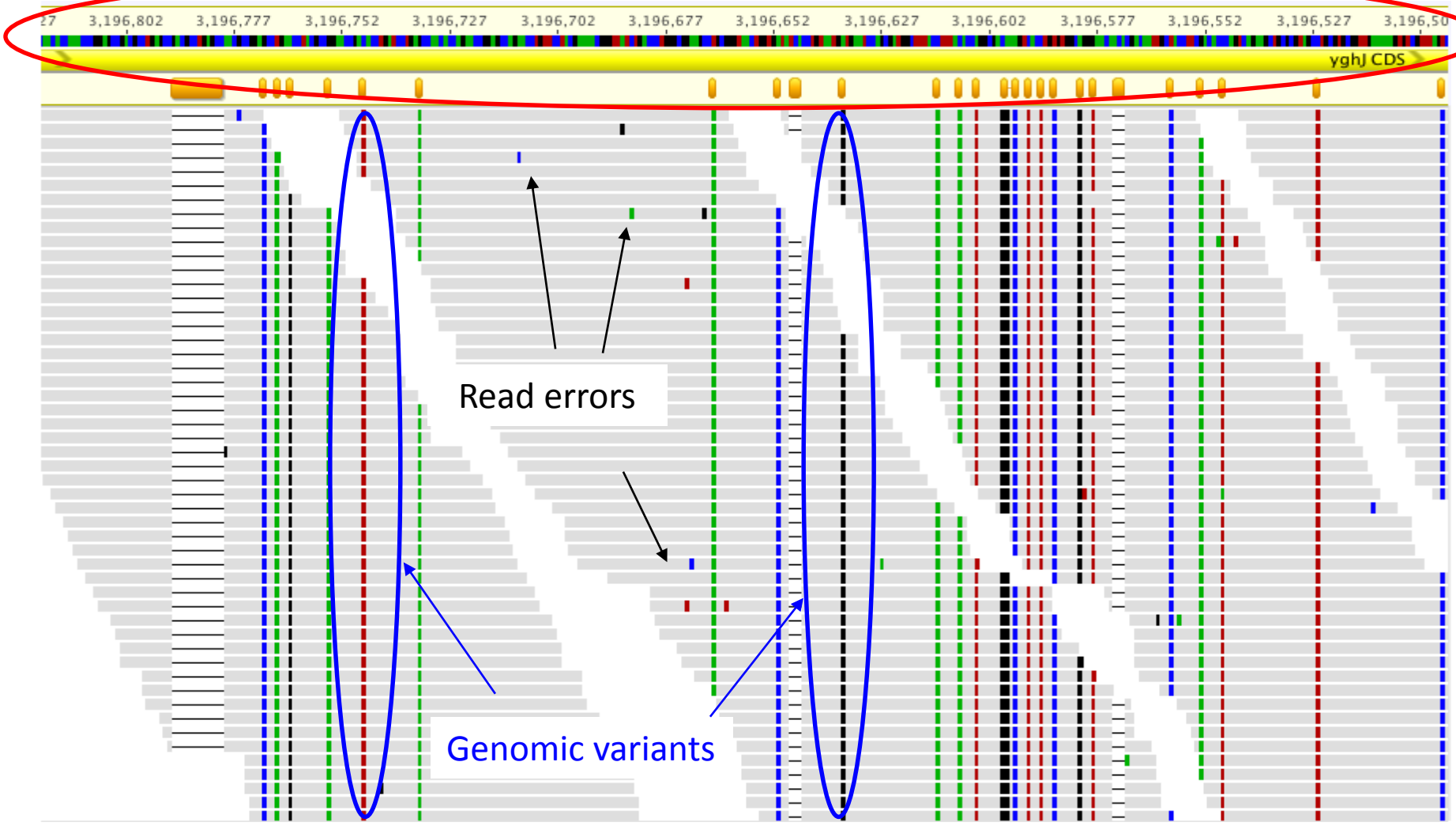
- Shorter reads are
  - more accurate (up to 99.9%)
  - produced in much larger volumes (currently up to 600 billion bases per single run)

From sequencing to assembly



Mapped reads

Reference genome



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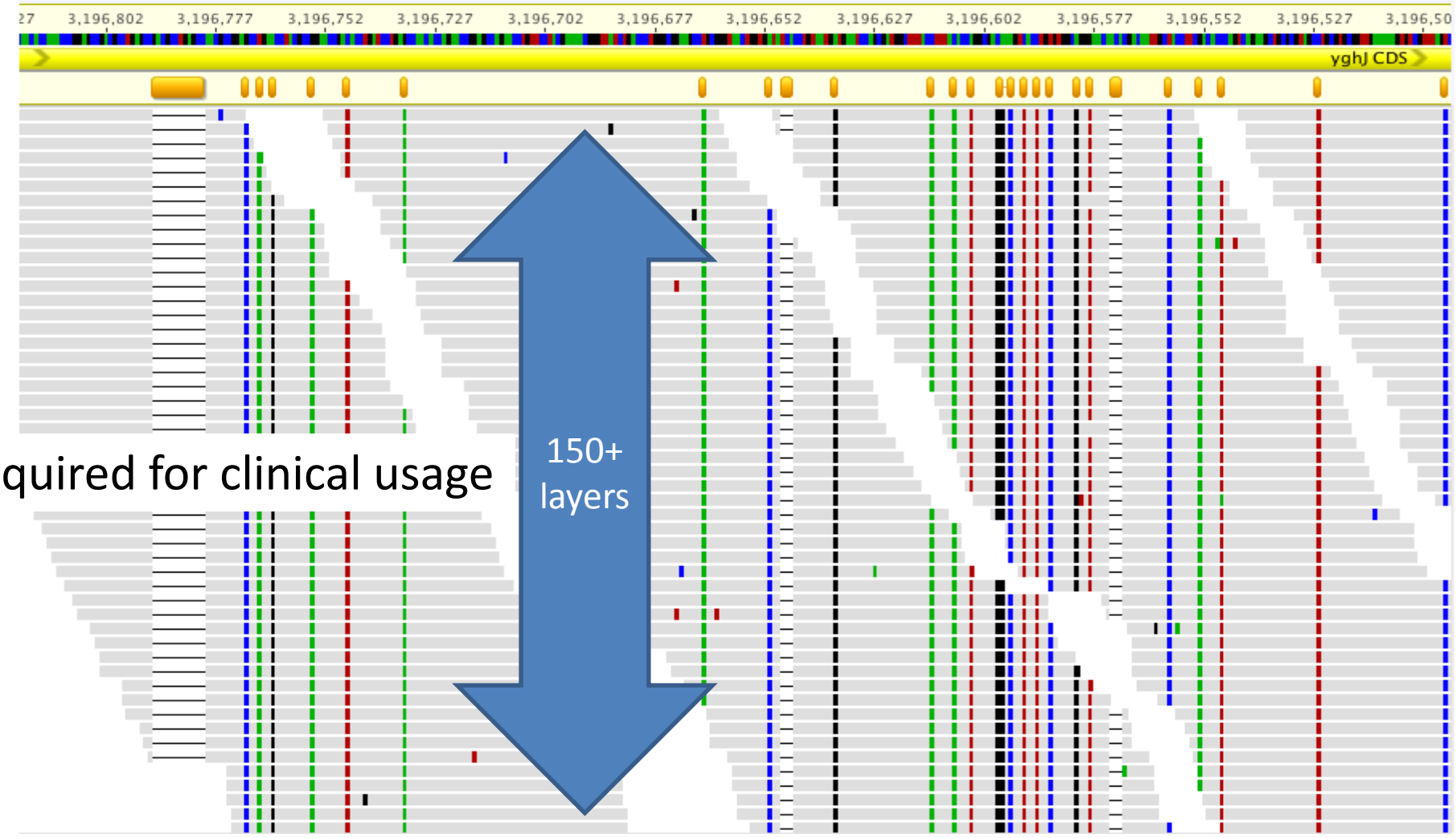
Coverage



Required for clinical usage

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All reads must be preserved

Is this reading noise or a mutation?

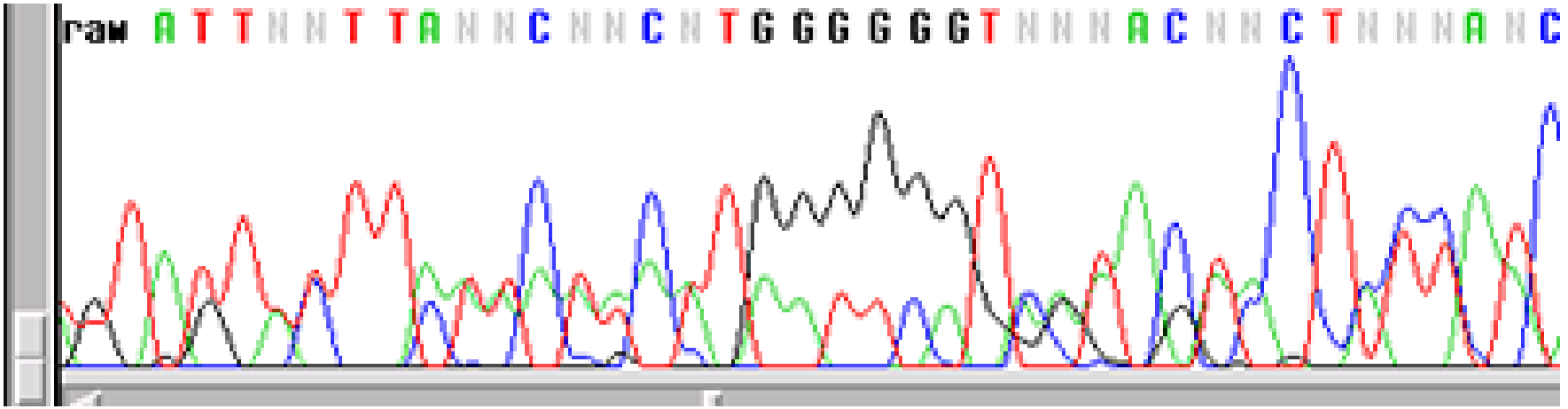
Data volumes

- 3.2 billion per genome
  - X 200+ for clinical usage (to get at least 150 layers)

- Additional information
  - 1 quality score per each base (up to 96 possible levels)

Reads quality scores

- Each base call in a read has a level of confidence



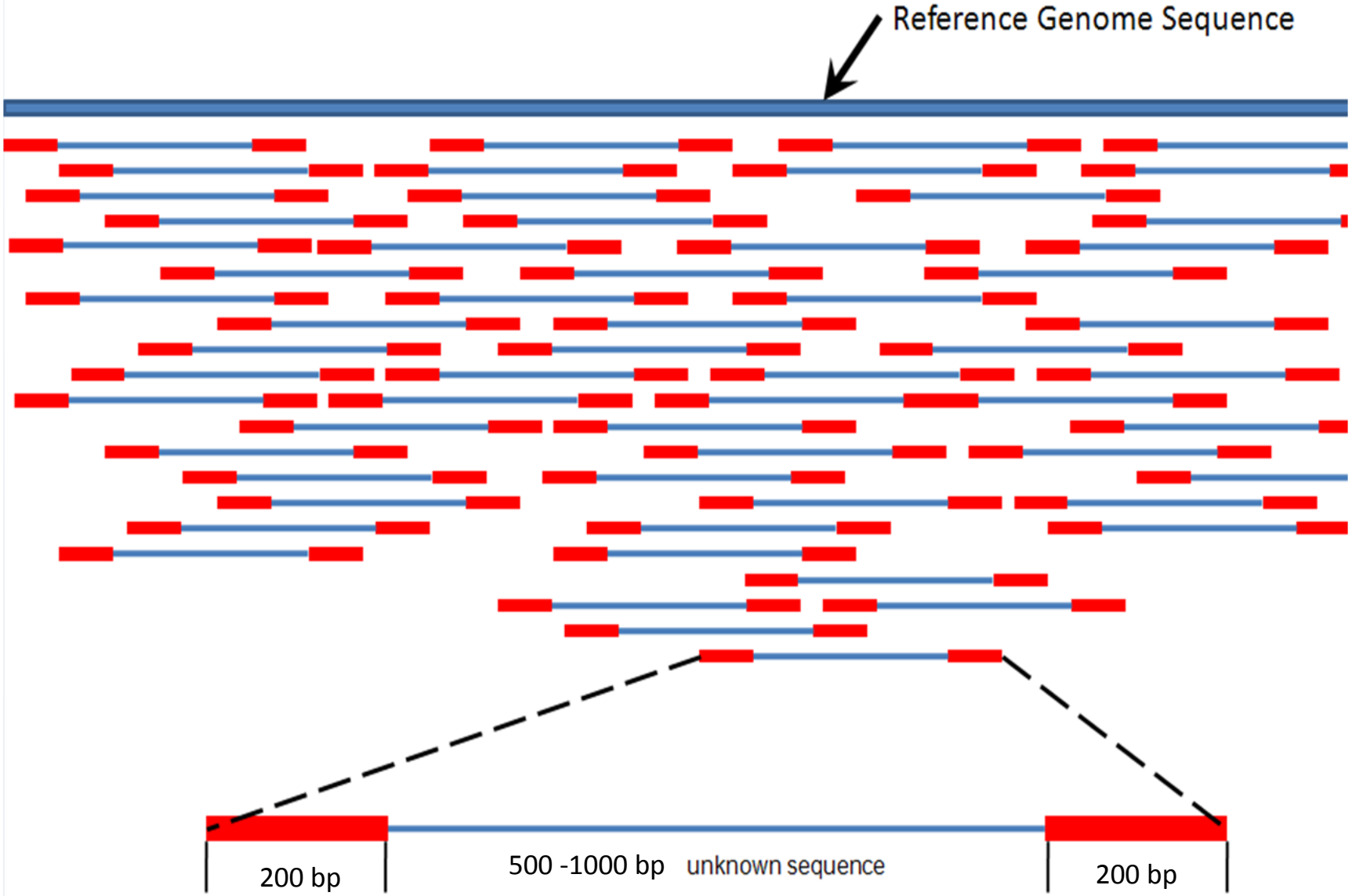
- The level of confidence is expressed as “quality score” in a range that is machine dependent represented as ASCII character.

Data volumes

- 3.2 billion per genome
  - X 200+ for clinical usage (to get at least 150 layers)

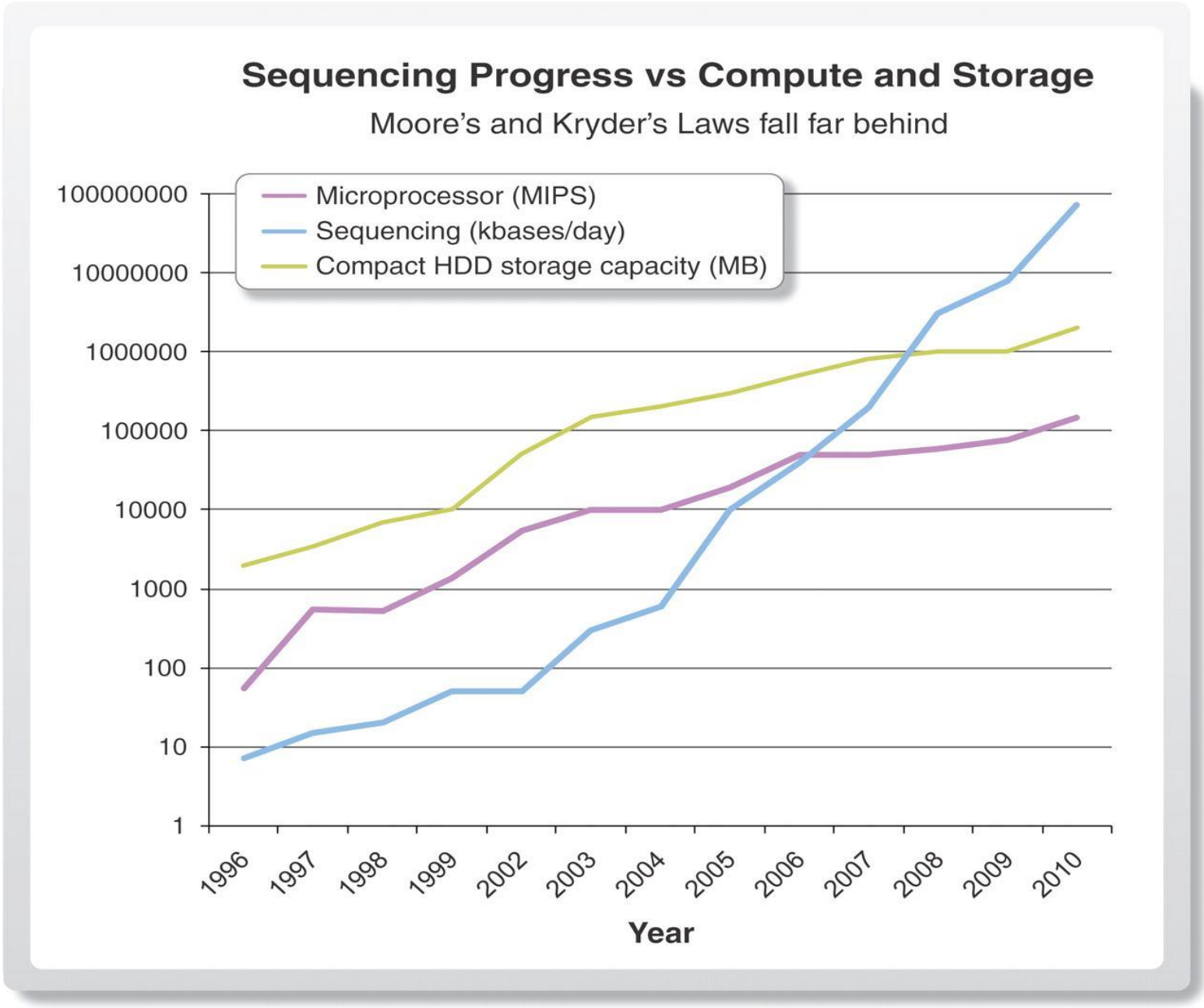
- Additional information
  - 1 quality score (ASCII char) per each base
  - pairing information for coupled reads (labelling)

Paired reads



Data volumes

- 3.2 billion per genome
  - X 200+ for clinical usage (to get at least 150 layers)
- Additional information
  - 1 quality score per each base (up to 96 possible levels)
  - pairing information for coupled reads (labelling)
- Total = 3.2GB x 200 x 2 x labelling ~= 1.5 TB
  - Labelling ~= 1.15


Sequencing Progress vs Compute and Storage
Moore's and Kryder's Laws fall far behind
Microprocessor (MIPS)
Sequencing (kbases/day)
Compact HDD storage capacity (MB)
100000000
10000000
1000000
100000
10000
1000
100
10
1
1996
1997
1998
1999
2002
2003
2004
2005
2006
2007
2008
2009
2010
Year

Raw data format

FASTQ	Field	FASTA
@HWUSI-EAS100R:6:73:941:1973#0/1	*Header (Unique ID plus other information). Only the first character is standard.*	**>HWUSI-EAS100R:6:73:941:1973#0/1**
GATTTGGGGT…..	*Nucleotides sequence*	**GATTTGGGGT……**
+SRR001666.1 071112_SLXA-EAS1_s_7	*Optional description. Only the first character is standard. This is becoming obsolete*	Not present
!''*((((*+)**	*Quality scores*	Not present

Example

One read:

```
HS2000-1240_45:1:1234:6966:12500
AAATATTTTTTAAAATTAGCCAGGTGTGGTGGTGTGTGCCTATAGTTCCAACTAGTTGTAAAGCTGAAACATAAGGACCACTTGGGTACAGGAGTTCCAA
+
CCCFFFFFHHHHHIJIIJIIJIJJFHGGIFHHHIIJJJIJIHIJJFIJJIIJJJHIIIIGIIIIIIFHGGGHFFFFF?BBEECDD?CCCECDD?AC;5@
```

Example

One read:

```
HS2000-1240_45:1:1234:6966:12500/1
AAATATTTTTTAAAATTAGCCAGGTGTGGTGGTGTGTGCCTATAGTTCCAACTAGTTGTAAAGCTGAAACATAAGGACCACTTGGGTACAGGAGTTCCAA
+
CCCFFFFFHHHHHIJIIJIIJIJJFHGGIFHHHIIJJJIJIHIJJFIJJIIJJJHIIIIGIIIIIIFHGGGHFFFFF?BBEECDD?CCCECDD?AC;5@


HS2000-1240_45:1:1234:6966:12500/2
ATCAGATGTATAATTTGCAAATAGTTTCTCTCATTCTTTTTTTTTTTTTTTTAGACAGGGTCTCACTGTATTGCCCAGGCTGGAGTGCAGTGGTGCAATC
+
CCCFFFFFHHHHHJJJJJJJJIIJJJIJJJJIJIJJJIJJJJJJJJHFDD@##################################################
```

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Example

- A read aligned onto a section of the chromosome 1 of the reference genome.

- Chr1 39999220 39999240 39999260 39999280 39999300 39999320 39999340
- . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | .
|
- AATGGTGCAGTCACAGCTGTCTACAAAAATATTTTTTAAAATTAGCCAGGTGTGGTGGTGTGTGCCTATAGTTCCAACTAGTTGTAAAGCTGAAACATAAGGACCACTTGGGTACAGGAGTTCCA AGACTGTGGTGAG
- ..........AAATATTTTTTAAAATTAGCCAGGTGTGGTGGTGTGTGCCTATAGTTCCAACTAGTTGTAAAGCTGAAACATAAGGACCACTTGGGTACAGGAGTTCCAA.....

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Example

- A read aligned onto a section of the chromosome 1 of the reference genome.

```
 Chr1          39999220            39999240            39999260            39999280            39999300            39999320
39999340
                 .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .
|
AATGGTGCAGTCACAGCTGTCTACAAAAATATTTTTTAAAATTAGCCAGGTGTGGTGGTGTGTGCCTATAGTTCCAACTAGTTGTAAAGCTGAAACATAAGGACCACTTGGGTACAGGAGTTCCA AGACTGTGGTGAG
.........................AAATATTTTTTAAAATTAGCCAGGTGTGGTGGTGTGTGCCTATAGTTCCAACTAGTTGTAAAGCTGAAACATAAGGACCACTTGGGTACAGGAGTTCCAA............
```

- A second read, known to be associated with the first read.

```
39999340            39999360            39999380            39999400            39999420            39999440            39999460
  .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |
GTGGTGAGCTGTGATTGCACCACTGCACTCCAGCCTGGGCAATACAGTGAGACCCTGTCTAAAAAAAAAAAAAAAAAAGAATGAGAGAAACTATTTGCAAATTATACATCTGATAAGAGACCTGTAT CTA
............GTTTTGCCCCCCTCACCCCAGCCTGGGGAATAAAGGGGGGCCCTTTCTAAAAAAAAAAAAAAAAAAGAATGAGAGAAACTATTTGCAAATTATACATCTGAT.............
```

Example

- A read aligned onto a section of the chromosome 1 of the reference genome.

```
 Chr1          39999220            39999240            39999260            39999280            39999300            39999320
39999340
                .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .
|
AATGGTGCAGTCACAGCTGTCTACAAAAATATTTTTTAAAATTAGCCAGGTGTGGTGGTGTGTGCCTATAGTTCCAACTAGTTGTAAAGCTGAAACATAAGGACCACTTGGGTACAGGAGTTCCA AGACTGTGGTGAG
.........................AAATATTTTTTAAAATTAGCCAGGTGTGGTGGTGTGTGCCTATAGTTCCAACTAGTTGTAAAGCTGAAACATAAGGACCACTTGGGTACAGGAGTTCCAA............
```

- A second read, known to be associated with the first read.

```
39999340            39999360            39999380            39999400            39999420            39999440            39999460
  .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |
GTGGTGAGCTGTGATTGCACCACTGCACTCCAGCCTGGGCAATACAGTGAGACCCTGTCTAAAAAAAAAAAAAAAAAAGAATGAGAGAAACTATTTGCAAATTATACATCTGATAAGAGACCTGTAT CTA
............GTTTTGCCCCCCTCACCCCAGCCTGGGGAATAAAGGGGGGCCCTTTCTAAAAAAAAAAAAAAAAAAGAATGAGAGAAACTATTTGCAAATTATACATCTGAT.............
```

HS2000-1240_45:1:1234:6966:12500/2
ATCAGATGTATAATTTGCAAATAGTTTCTCTCATTCTTTTTTTTTTTTTTTTAGACAGGGTCTCACTGTATTGCCCAGGCTGGAGTGCAGTGGTGCAATC

Note that the original sequence of the second read had to be reverse complemented to match the genome.

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Example

- A read aligned onto a section of the chromosome 1 of the reference genome.

```
 Chr1          39999220            39999240            39999260            39999280            39999300            39999320
39999340
                .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .
|
AATGGTGCAGTCACAGCTGTCTACAAAAATATTTTTTAAAATTAGCCAGGTGTGGTGGTGTGTGCCTATAGTTCCAACTAGTTGTAAAGCTGAAACATAAGGACCACTTGGGTACAGGAGTTCCA AGACTGTGGTGAG
..........................>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>> >............
```

- A second read, known to be associated with the first read.

```
39999340            39999360            39999380            39999400            39999420            39999440            39999 460
  .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |
GTGGTGAGCTGTGATTGCACCACTGCACTCCAGCCTGGGCAATACAGTGAGACCCTGTCTAAAAAAAAAAAAAAAAGAATGAGAGAAACTATTTGCAAATTATACATCTGATAAGAGACCTGTAT CTA
............<T<<TGC<<C<CT<<<C<<<<<<<<<<G<<<<A<<G<G<G<<<<T<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<.............. ...
```

Note that the sequence obtained may not reflect exactly the genomic sequence.

Example

- A read aligned onto a section of the chromosome 1 of the reference genome.

```
 Chr1          39999220            39999240            39999260            39999280            39999300            39999320
39999340
                 .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .
|
AATGGTGCAGTCACAGCTGTCTACAAAAATATTTTTTAAAATTAGCCAGGTGTGGTGGTGTGTGCCTATAGTTCCAACTAGTTGTAAAGCTGAAACATAAGGACCACTTGGGTACAGGAGTTCCA AGACTGTGGTGAG
..........................>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>
                               CCCFFFFFHHHHHIJIIJIIJIJJFHGGIFHHHIIJJJIJIHIJJFIJJIIJJJJHIIIIGIIIIIIFHGGGHFFFFF?BBEECDD?CCCECDD?AC;5@
```

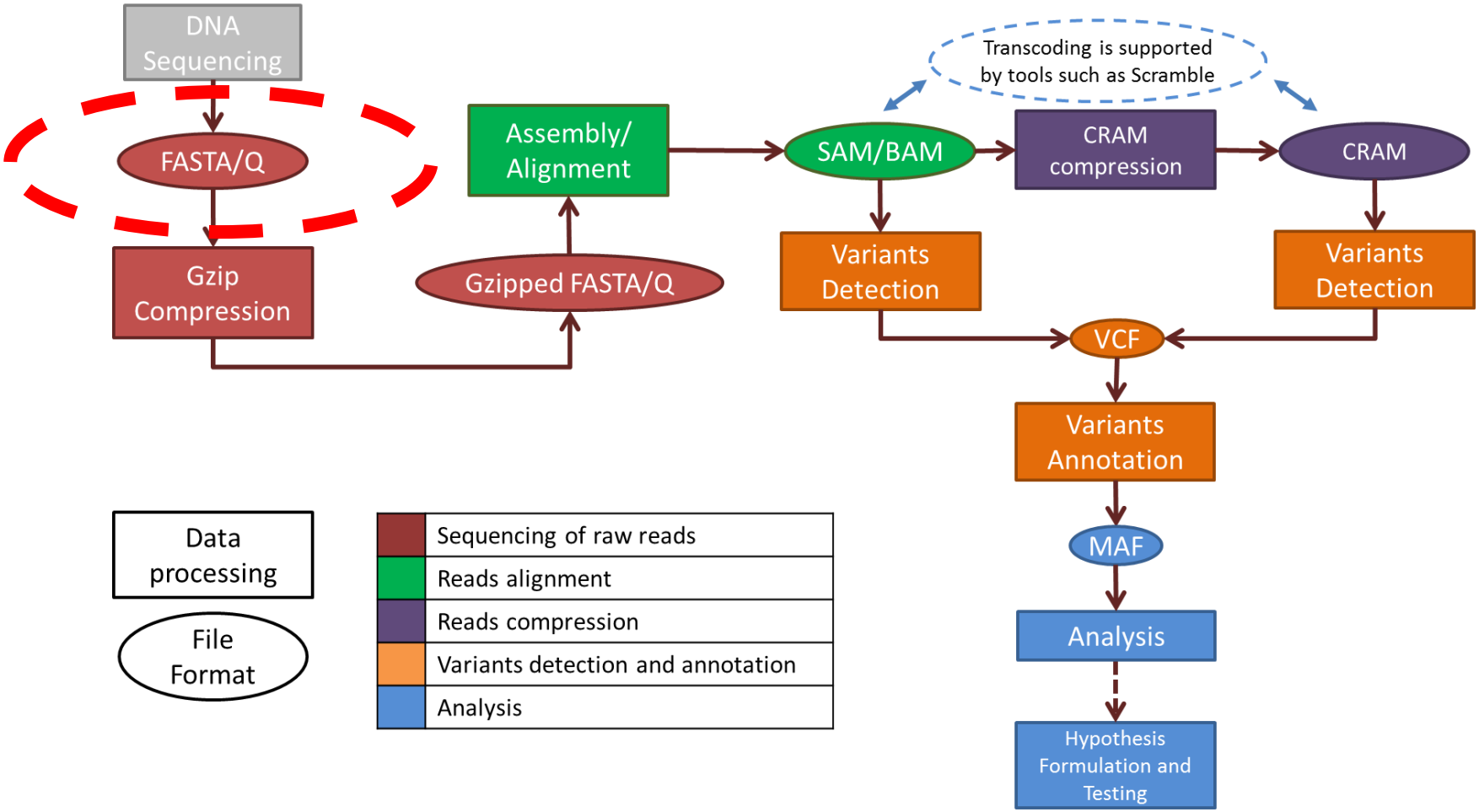
- A second read, known to be associated with the first read.

```
39999340            39999360            39999380            39999400            39999420            39999440            39999460
  .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |    .    |
GTGGTGAGCTGTGATTGCACCACTGCACTCCAGCCTGGGCAATACAGTGAGACCCTGTCTAAAAAAAAAAAAAAAAGAATGAGAGAAACTATTTGCAAATTATACATCTGATAAGAGACCTGTAT CTA
............<T<<TGC<<C<CT<<<C<<<<<<<<<<G<<<<A<<G<G<G<<<<T<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<................
            ################################################@DDFHJJJJJJJIJJJIJIJJJJIJJJJIIJJJJJJJHHHHHFFFFFCCC
```

Here, the quality of the sequence obtained, associated to each nucleotide has been flagged as poor in the region where it does not match well the reference genome.

```
@SRR000921.1 E7OAHBI01AQMFC length=41
GGGGGGGTGTAGAAAAGATGTGAGATACCTTTCCTCACCCT
+
::::555GFFGC66;;=GHHHHHHHHHHHFFFFFFGC955C
@SRR000921.3 E7OAHBI01A9JXR length=126
GGGGTGGTATGGAGAGACAATGGGCGATGTTTCTCAGGGCTGCTTCAAGCGGGATTAGGGGCAGCGTGGGAAGCTAGAGTGGGAGAGATTAAGCTGAAGG
+
0777=GFFFFFFFFFFFFIIIIIIIIIIIIIIIIIIIIIIIIIIIFFFFFFFFFFFFCCCCFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF
@SRR000921.7 E7OAHBI01A9IFH length=173
GGGGGGGGGGGGTTGGGCATGTGGGACCCCCTCCATGTTGACAGTCGAGGCATACGGCCTGCAGGTCCACGCTTACTTGCTGTCCATGCTGTCGGTGTCA
+
//////////////88FFFFFFFFEFEFFFFFEEEFFFGGGGGIIIIFFFFFFFFFFFFFFFFFFFFFFFFFFFFEEEFFFFFFFFFFFFFFFFFFFFFF
@SRR000921.9 E7OAHBI01B333T length=153
GGGGGTTTCCTGGTGGGGTTAGAGGCGGGACGTGAGAAACGTGGCAGGTGGTGGCCAGGCTGTGGGGGAGCCAGGGTATTTCTTGATGGGGTTAGATGGG
+
0000055FFFFFFF;=??EEHGHHHHIIIIIIIIIIIIIIIIIIFFFFFFFFFFFFFFFFFF@@@??GFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF
@SRR000921.10 E7OAHBI01D6JUW length=87
GGGGGTGCCTCCCAGTTAGGCTGCTCAGGGGTCAGGGGTCAGGGACCCGCTTGAGGAGGCAGTCTGCCCATTCTCAGATCTCCAGCC
+
00000=CFFFFFFFFFFFIIIIIIIIIIIIIIIIIIIIIIIIIIIFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF
@SRR000921.11 E7OAHBI01C8DW7 length=162
GGGGCAATTGAGTTGGGCATTGATGGCCAAGGAGTTCCGGGGAAACCATGTTGAAGCTGGGAGAGTAGAACACCTGAAATCCTGTGAAATCCATAAAATT
+
BBBBFFFFFFFFFFFFFIIIIHHHHHHIIIIIIIIIIIIIIIIIFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF
@SRR000921.16 E7OAHBI01EFO7A length=84
GGGGGACAAAATTCAGTCCATAGTACATGCACGATCTCATTTGATCTTCCAGAACCCCATGACATAGTTTCCATTTGAAGATGA
+
////58@DDDDDDDDDDDIIIIIIIIIIIIIIIIIIIIIIIIIIIDDDDDDDCCAAAADDDDDDDDDDDDDDDDDDDDDD
@SRR000921.17 E7OAHBI01BRP08 length=148
GGGGGGGTCAGCCCCCCCGCCCGGCCAGCCGCCCCATCCAGGAGGTGAGGGGCACCTCTGCCCGGCCGCCCCTACTGGGAAGTGAGGAGCCCCTCTGCCC
+
4440000<@@<///////5+++AADDEECCC====CEEEEFFHHICCCCCCCCCCCCCCC===CCCCCCCCCCCGCCCCCCHCCCCCCCCCCCCCCCCC
@SRR000921.18 E7OAHBI01BAECM length=67
GGGGGCGCCTCTTAACACACCAGCTGGTGGACTGTGAATCATTCTGCAGCAGGAAGCGCATGCATGG
+
A@@@@FFFFFFFFFFFFIIIIIIIIIIIIIIIIIIIHHHHHHHGFFFFFFFFFFFFFFFFFFFFF
```

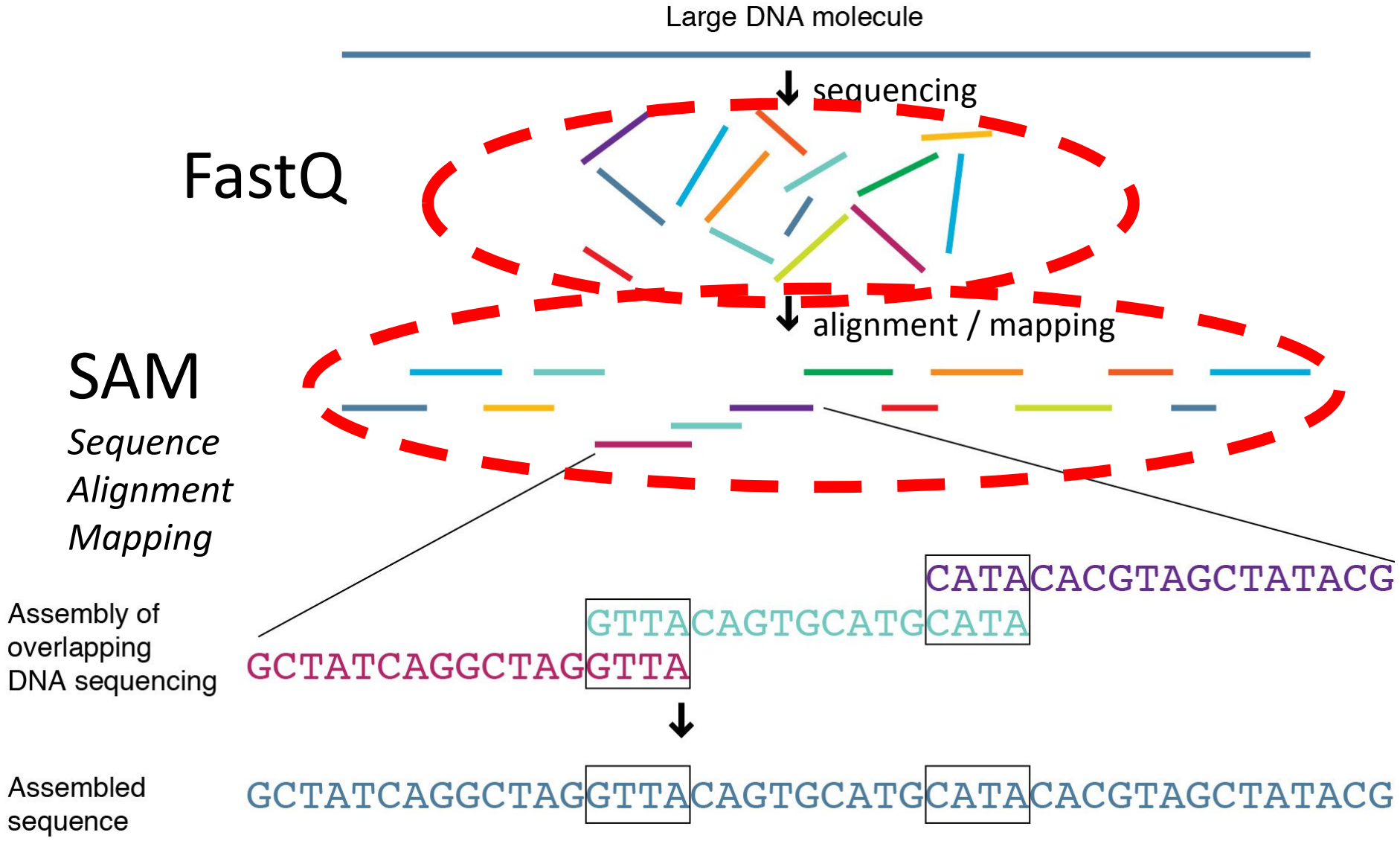
Genome processing pipeline



FastQ compression today

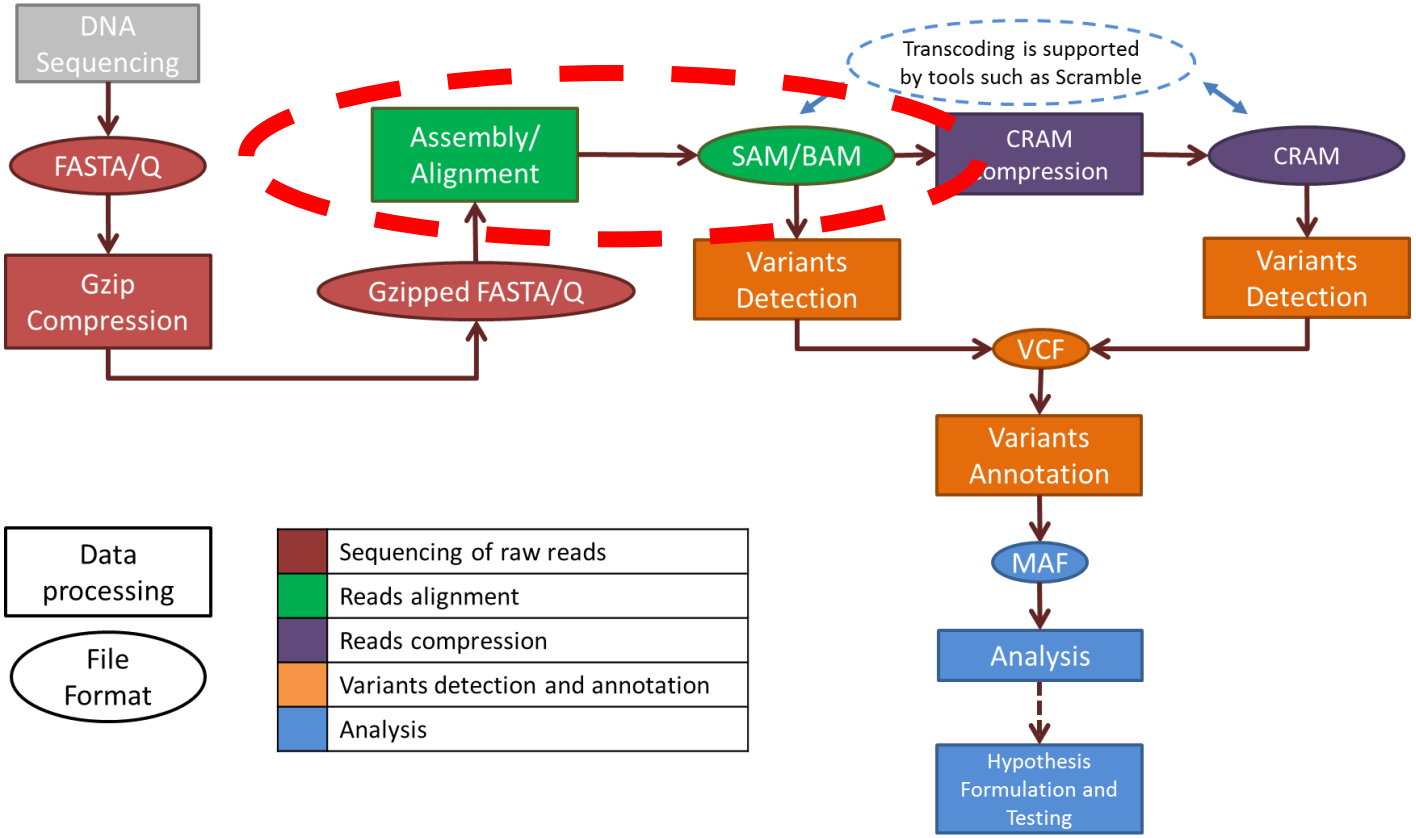
- Gzip of the entire txt file (sometimes split into several files)
- Compression ratio : 3 to 5
- According to the coverage 1 genome can take up to 2 TB

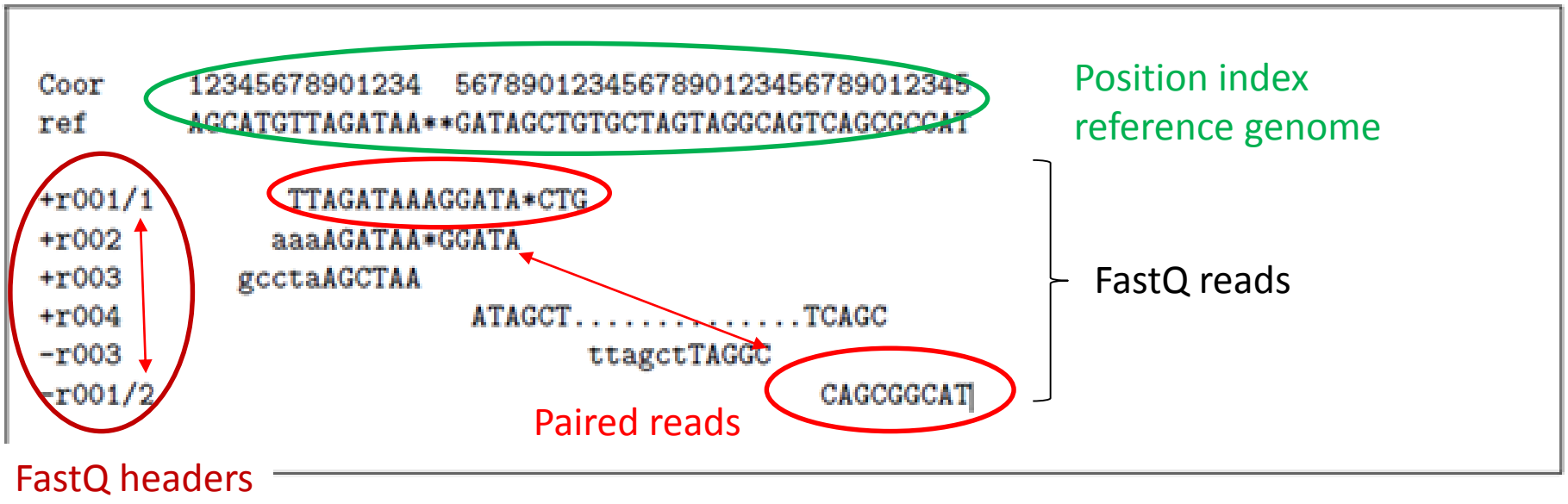
From sequencing to assembly

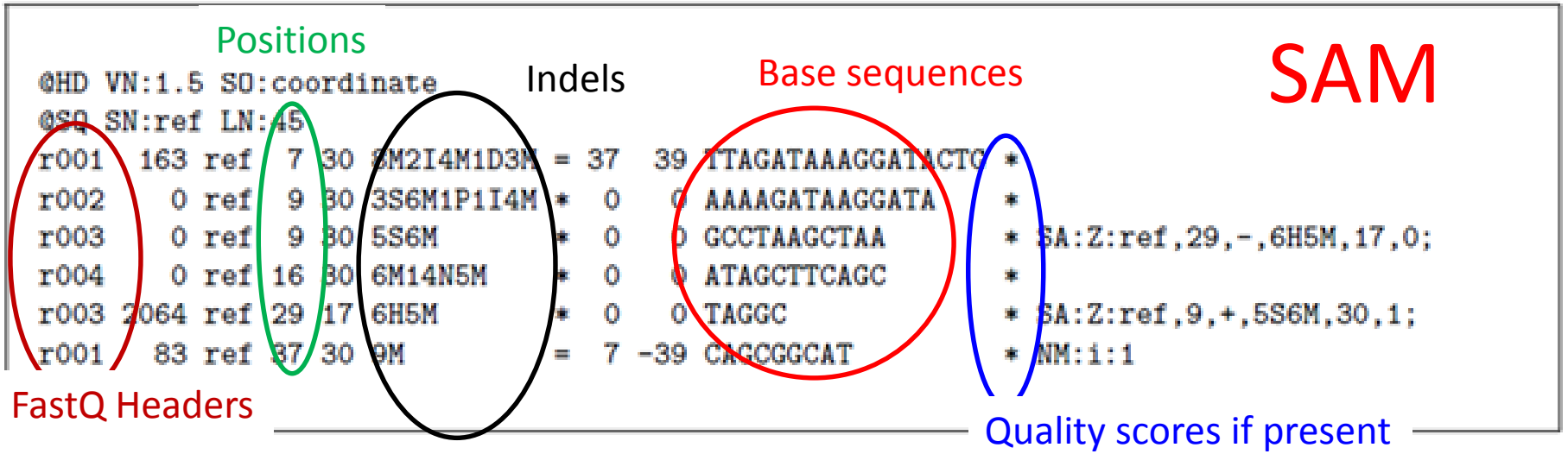


Alignment / mapping

- Raw data + alignment information




Coor 12345678901234 5678901234567890123456789012345
ref AGCATGTTAGATAA**GATAGCTGTGCTAGTAGGCAGTCAGCGCCAT
+r001/1
+r002
+r003
+r004
-r003
-r001/2
TTAGATAAAGGATA*CTG
aaaAGATAA*GGATA
gcctaAGCTAA
ATAGCT..............TCAGC
ttagctTAGGC
CAGCGGCAT
Position index
reference genome
FastQ reads
Paired reads
FastQ headers


Positions
Indels
Base sequences
SAM
@HD VN:1.5 SO:coordinate
@SQ SN:ref LN:45
r001 163 ref 7 30 8M2I4M1D3M = 37 39 TTAGATAAAGGATACTG *
r002 0 ref 9 30 3S6M1P1I4M * 0 0 AAAAGATAAGGATA *
r003 0 ref 9 30 5S6M * 0 0 GCCTAAGCTAA * SA:Z:ref,29,-,6H5M,17,0;
r004 0 ref 16 30 6M14N5M * 0 0 ATAGCTTCAGC *
r003 2064 ref 29 17 6H5M * 0 0 TAGGC * SA:Z:ref,9,+,5S6M,30,1;
r001 83 ref 37 30 9M = 7 -39 CAGCGGCAT * NM:i:1
FastQ Headers
Quality scores if present

Compressed SAM = BAM

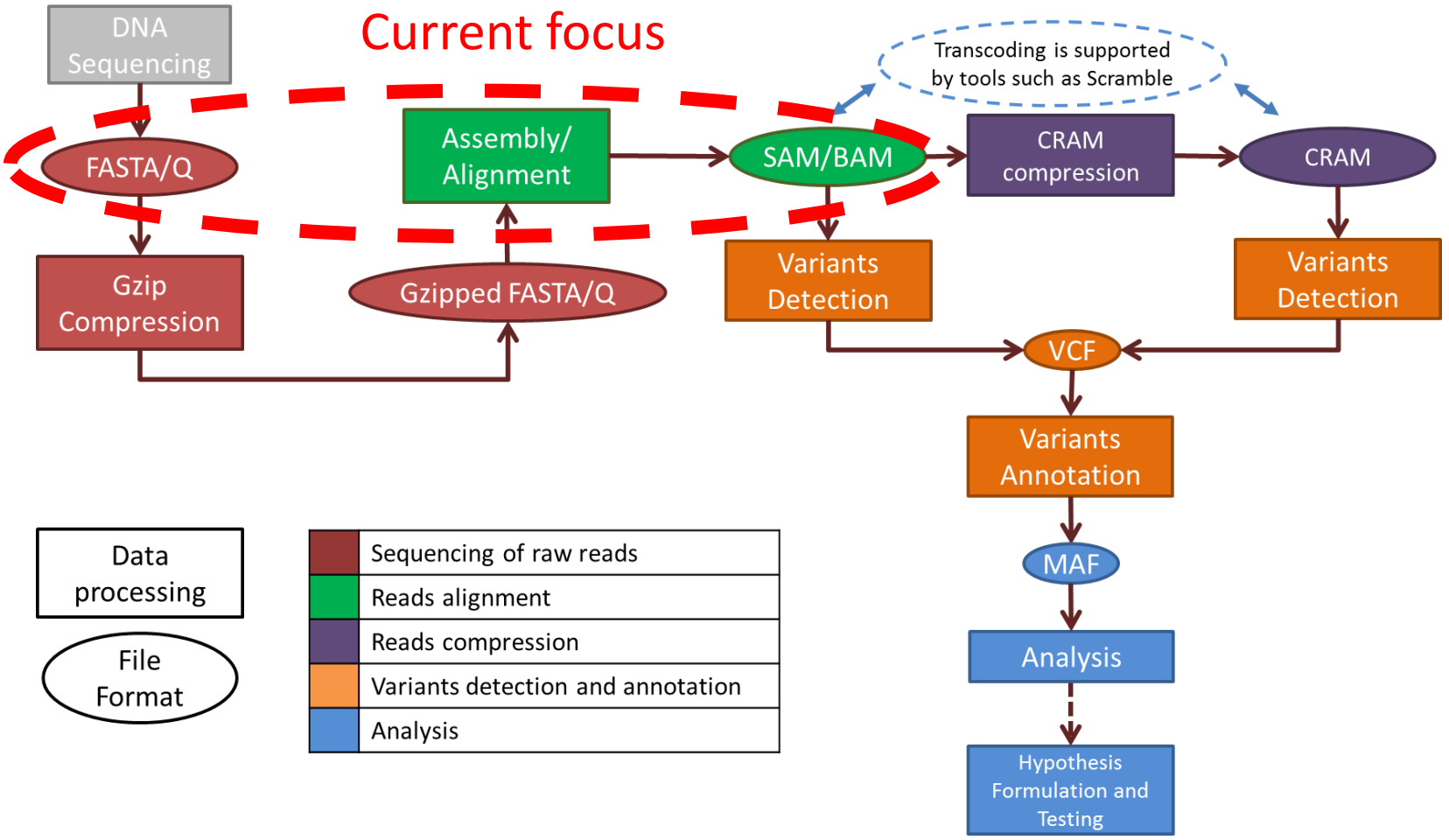
- BAM = Block based zipped SAM
- Indexable for random access
- Compression ratio over textual SAM ~= 4 to 6

- Example (coverage 200x)
  - Fastq = 1.5 TB
    - Fastq.gz = 370 GB
    - Fastq.bzip = 255 GB
    - quip = 205 GB (best compression tool for FastQ)
  - SAM = ~3 TB
  - BAM = 500 GB

SAM/BAM view demo

- Human sample from the MPEG dataset
  - /human/illumina/LowCoverage/NA21144.chrom11
- Chromosome 11
  - Reads length: 100 bases
  - No. of reads: ~10.1 millions
  - Unaligned data: 2.2 GB
  - Aligned SAM: 4.5 GB
  - Compressed BAM: 1 GB

Raw sequence data + Aligned data



Thank you