

ADAM: Genomics Formats and Processing Patterns for Cloud Scale Computing

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Abstract

Current genomics applications are dominated by the movement of data to and from disk. This data movement pattern is a significant bottleneck that prevents these applications from scaling well to distributed computing clusters. In this report, we introduce a new set of data formats and programming patterns for genomics applications using in-memory MapReduce frameworks. These formats improve application performance, data storage efficiency, and programmer productivity.

1 Introduction

Although the cost of data processing has not historically been an issue for genomic studies, the falling cost of genetic sequencing will soon turn computational tasks into a dominant cost [10]. The process of transforming reads from alignment to variant-calling ready reads involves several processing stages including duplicate marking, base score quality recalibration, and local realignment. Currently, these stages have involved reading a Sequence/Binary Alignment Map (SAM/BAM) file, performing transformations on the data, and writing this data back out to disk as a new SAM/BAM file [8].

Because of the amount of time these transformations spend shuffling data to and from disk, these transformations have become the bottleneck in modern variant calling pipelines. It currently takes three days to perform these transformations on a high coverage BAM file¹. By rewriting these applications to make use of modern in-memory MapReduce frameworks like Spark [13], these transformations can now

be completed in FIXME² hours.

In this paper, we introduce ADAM, which is a programming framework and a set of data formats for cloud scale genomic processing. These frameworks and formats scale efficiently to modern cloud computing performance, which allows us to speedup read translation steps that are required between alignment and variant calling. In this paper, we provide an introduction to the data formats (§2) and pipelines used to process genomes (§3), introduce the ADAM formats and data access APIs (§4) and programming model (§5). Finally, we review the performance and compression gains we achieve (§6), and outline future enhancements to ADAM that we are working on (§7).

2 Current Genomics Storage Standards

The current de facto standard for the storage and processing of genomics data in read format is BAM. BAM is a binary file format that implements the SAM standard for read storage [8]. BAM files can be operated on in several languages, using either the SAM-tools ([8], C++), Picard ([3], Java), and Hadoop-BAM ([11], Hadoop MapReduce through Java) APIs. BAM provides efficient access and compression over the SAM file format, as it's binary encoding reduces several fields into a single byte, and eliminates text processing on load. However, the file format has been criticized as it is difficult to process — the three main APIs that implement the format each note that they do not fully implement the format due to it's complexity. Additionally, the file format is difficult to use in multiprocessing environments due to it's use of a centralized header; the Hadoop-BAM implementation notes that it's scalability is limited to distributed

¹A 250GB BAM file at 30× coverage. See §6.2 for a longer discussion

²FIXME

processing environments of less than 8 machines.

In response to the growing size of BAM files³, the CRAM format has been proposed as a standard for archival purposes [6]. This format is a binary format that implements similar fields as BAM but with better compression. Lossy compression is achieved by only storing differences from the reference, and by binning quality scores to reduce the amount of data that needs to be saved. This format provides it's own API, and has some compatibility with the existing Picard API for Java.

3 Genomic Processing Pipelines

After sequencing and alignment, there are a few common steps in modern genomic processing pipelines for producing variant call ready reads. These steps minimize the amount of erroneous data in the input read set by eliminating duplicate data, verifying the alignment of short inserts/deletions (indels), and calibrating the quality scores assigned to bases (base quality score recalibration, BQSR). The typical pipeline for variant calling is illustrated in figure 1.

Traditionally, bioinformaticians have focused on improving the accuracy of the algorithms used for alignment and variant calling. There is obvious merit to this approach — these two steps are the dominant contributors to the accuracy of the variant calling pipeline. However, the intermediate read processing stages are responsible for the majority of execution time. A breakdown of stage execution time is shown in table 1 for the version 2.7 of the Genome Analysis Toolkit (GATK), a popular variant calling pipeline [9]. The numbers in the table are derived from running on the NA12878 high-coverage human genome.

Table 1: Processing Stage Times for GATK Pipelines

Stage	GATK 2.7/NA12878
Alignment	6 hr
Sort	
Mark Duplicates	
BQSR	
Realignment	
Call Variants	

To provide the readers with a background about

³High coverage read files can be approximately 250 GB for a human genome.

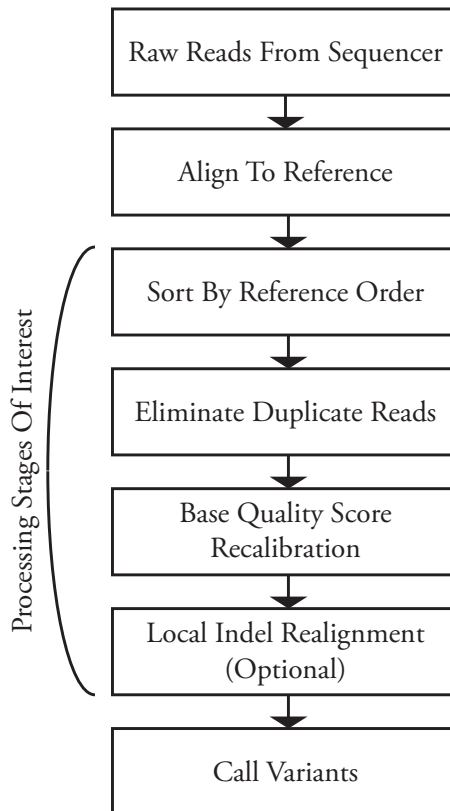


Figure 1: Variant Calling Pipeline

how the stages of this pipeline work, we will discuss the algorithms that implement the intermediate read processing stages. For a detailed discussion of these algorithms, we refer readers to DePristo et al [5].

Sorting: This phase performs a pass over the reads and sorts them by the reference position at the start of their alignment.

Duplicate Removal: Due to imperfections during the sequencing process, an unknown number of reads are optically duplicated. If these duplicate reads are not removed, they will then incorrectly bias the variant caller, and can lead to incorrect variant calls. In this stage, we review all reads mapped at a specific loci, and discard reads that have identical sequence information.

Base Quality Score Recalibration: During the sequencing process, systemic errors occur that lead to the incorrect assignment of base quality scores. In this step, a statistical model of the quality scores is

built and is then used to revise the measured quality scores.

Local Realignment: For performance reasons, all modern aligners use algorithms that provide approximate alignments. This can cause reads with evidence of indels to have slight misalignments with the reference. In this stage, we use fully accurate sequence alignment methods (Smith-Waterman algorithm [12]) to locally realign reads that contain evidence of short indels. This pipeline step is omitted in some variant calling pipelines, if the variant calling algorithm that is implemented is not susceptible to these local alignment errors.

For current implementations of these read processing steps, performance is limited by disk bandwidth. This is because the operations read in a SAM/BAM file, perform a bit of processing, and write the data to disk as a new SAM/BAM file. We address this by performing our processing iteratively in memory. The four read processing stages can then be chained together, eliminating three dumps to disk and an additional three long reads from disk.

4 Data Format and API

ADAM contains formats for storing read and reference oriented sequence information, and variant/genotype data. The read oriented sequence format is forwards and backwards compatible with BAM/SAM, and the variant/genotype data is forwards and backwards compatible with VCF. In this section, we discuss the frameworks used to store this data. We then introduce the representations, and discuss the content of each representation.

The data representation for the ADAM format is described using the open source Apache Avro data serialization system [1]. The Avro system also provides a human readable schema description language that can auto-generate the schema implementation in several common languages including Scala, Java, C/C++/C#, Python, Ruby, and php. This provides a significant cross-compatibility advantage over the BAM/SAM format, where the data format has only been implemented for C/C++ through Samtools and for Java through Picard [8, 3].

We layer this data format inside of the Parquet column store [2]. Parquet is an open source columnar storage format that was designed by Twitter, which can be used as a single flat file, a distributed file, or as a database inside of Hive, Shark, or Impala. Columnar stores like Parquet provide several signifi-

cant advantages when storing genomic data:

- Column stores enable predicate pushdown [7], which minimizes the amount of data read from disk. When using predicate pushdown, we deserialize specific fields in a record from disk, and apply them to a predicate function. We then only read the full record if it passes the predicate. This is useful when implementing filters that check read quality.
- Column stores achieve extremely high compression [4]. This reduces storage space on disk, and also improves serialization performance inside of MapReduce frameworks. We are able to achieve a $0.75\times$ lossless compression ratio when compared to BAM, and have especially impressive results on quality scores. This is discussed in more detail in §6.3.
- Varied data projections can be achieved with column stores. This means that we can choose to only read several fields from a record. This improves performance for applications that do not read all the fields of a record. Additionally, we do not pay for null fields in records that we store. This allows us to easily implement lossy compression on top of the ADAM format, and also allows us to eliminate the FASTQ standard.

By supporting varied data projections with low cost for field nullification, we can implement lossy compression on top of the ADAM format. We discuss this further in §6.3.

4.1 Read Oriented Storage

Our default read oriented data format is defined in table 2. This format provides all of the fields supported by the SAM format. To make it easier to split the file between multiple machines for distributed processing, we have eliminated the file header. Instead, the data encoded in the file header can be reproduced from every single record. Because our columnar store supports dictionary encoding and these fields are replicated across all records, replicating this data across all records has a negligible cost in terms of file size on disk.

This format is used to store all data on disk. In addition to this format, we provide an enhanced API for accessing read data.

Table 2: Read Oriented Format

Group	Field	Type
General	Reference Name	String
	Reference ID	Int
	Start	Long
	Mapping Quality	Int
	Read Name	String
	Sequence	String
	Mate Reference	String
	Mate Alignment Start	Long
	Mate Reference ID	Int
	Cigar	String
	Base Quality	String
Flags	Read Paired	Boolean
	Proper Pair	Boolean
	Read Mapped	Boolean
	Mate Mapped	Boolean
	Read Negative Strand	Boolean
	Mate Negative Strand	Boolean
	First Of Pair	Boolean
	Second Of Pair	Boolean
	Primary Alignment	Boolean
Attributes	Mismatching Positions	String
	Other Attributes	String
Read Group	Sequencing Center	String
	Description	String
	Run Date	Long
	Flow Order	String
	Key Sequence	String
	Library	String
	Median Insert	Int
	Platform	String
	Platform Unit	String
	Sample	String

4.2 Reference Oriented Storage

In addition to storing sequences as reads, we provide a storage format for reference oriented (pileup) data. This format is documented in table 3. This pileup format is also used to implement a data storage format similar to the GATK’s ReducedReads format [5].

We treat inserts as an inserted sequence range at the locus position. For bases that are an alignment match against the reference⁴, we store the read base

⁴Following the conventions for CIGAR strings, an alignment match does not necessarily correspond to a sequence match. An alignment match simply means that the base is not part of an indel. The base may not match the reference base at the loci.

Table 3: Reference Oriented Format

Group	Field	Type
General	Reference Name	String
	Reference ID	Int
	Position	Long
	Range Offset	Int
	Range Length	Int
	Reference Base	Base
	Read Base	Base
	Base Quality	Int
	Mapping Quality	Int
	Number Soft Clipped	Int
	Number Reverse Strand	Int
	Count At Position	Int
Read Group	Sequencing Center	String
	Description	String
	Run Date	Long
	Flow Order	String
	Key Sequence	String
	Library	String
	Median Insert	Int
	Platform	String
	Platform Unit	String
	Sample	String

and set the range offset and length to 0. For deletions, we perform the same operation for each reference position in the deletion, but set the read base to null. For inserts, we set the range length to the length of the insert. We step through the insert from the start of the read to the end of the read, and increment the range offset at each position.

As noted earlier, this datatype supports an operation similar to the GATK’s ReducedRead datatype. We refer to these datatypes as aggregated pileups. We perform aggregation by grouping together all bases that share a common reference position and read base. Within an insert, we group further by the position in the insert. Once the bases have been grouped together, we average the base and mapping quality scores. We also count the number of soft clipped bases that show up at this location, and the amount of bases that are mapped to the reverse strand.

4.3 Variant and Genotype Storage

Variant type is one of SNP, multiple nucleotide polymorphism (MNP), insertion, deletion, structural variant (SV), or complex.

Table 4: Genotype Format

Field	Type
Sample ID	String
Genotype	Array[Int]
Likelihood (Phred)	Array[Int]
Format	String

Table 5: Variant Format

Field	Type
Reference Name	String
Position	Long
Variant ID	String
Reference Allele	String
Alternate Alleles	Array[String]
Allele Count	Array[Int]
Chromosome Count	Int
Type	Variant Type
Info	String
Filter	String
Genotypes	Array[AdamGenotype]

5 In-Memory Programming Model

6 Performance

6.1 Microbenchmarks

6.2 Applications

6.3 Compression

7 Future Work

Beyond the initial release of the ADAM data formats, API, and read transformations, we are working on several other extensions to ADAM. These extensions strive to make ADAM accessible to more users and to more programming patterns.

7.1 Database Integration

7.2 API Support Across Languages

Currently, the ADAM API and example read processing pipeline are implemented in the Scala language. However, long term we plan to make the API acces-

sible to users of other languages. ADAM is built on top of Avro, Parquet, and Spark. Spark has bindings for Scala, Java, and Python, and Parquet implementations exist for Java and C++. As the data model is implemented on top of Avro, the data model can also be autogenerated for C/C++/C#, Python, Ruby, and php. We hope to make API implementations available for some of these languages at a later date.

8 Summary

In this technical report, we have presented ADAM which is a new data storage format and processing pipeline for genomics data. ADAM makes use of efficient columnar storage systems to improve the loss-less compression available for storing read data, and uses in-memory processing techniques to eliminate the read processing bottleneck faced by modern variant calling pipelines. On top of the file formats that we have implemented, we also present APIs that enhance developer access to read, pileup, genotype, and variant data. We are currently in the process of extending ADAM to support SQL querying of genomic data, and extending our API to more programming languages. ADAM promises to improve the development of applications that process genomic data, by removing current difficulties with the extraction and loading of data and by providing simple and performant programming abstractions for processing this data.

9 Availability

The ADAM source code is available at Github at <http://www.github.com/massie/adam>. Additionally, ADAM is deployed through Maven with the following dependency:

TBD

At publication time, the current version of ADAM is 0.5.0. ADAM is open source and is released under the Apache 2 license.

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