CRAM format specification (version 3.0)

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The master version of this document can be found at `https://github.com/samtools/hts-specs`.
This printing is version 99f471c from that repository, last modified on the date shown above.

1 Overview

This specification describes the CRAM 3.0 format.

CRAM has the following major objectives:

1. Significantly better lossless compression than BAM
2. Full compatibility with BAM
3. Effortless transition to CRAM from using BAM files
4. Support for controlled loss of BAM data

The first three objectives allow users to take immediate advantage of the CRAM format while offering a smooth transition path from using BAM files. The fourth objective supports the exploration of different lossy compression strategies and provides a framework in which to effect these choices. Please note that the CRAM format does not impose any rules about what data should or should not be preserved. Instead, CRAM supports a wide range of lossless and lossy data preservation strategies enabling users to choose which data should be preserved.

Data in CRAM is stored either as CRAM records or using one of the general purpose compressors (gzip, bzip2). CRAM records are compressed using a number of different encoding strategies. For example, bases are reference compressed by encoding base differences rather than storing the bases themselves.[1]

2 Data types

CRAM specification uses logical data types and storage data types; logical data types are written as words (e.g. int) while physical data types are written using single letters (e.g. i). The difference between the two is that storage data types define how logical data types are stored in CRAM. Data in CRAM is stored either as bits or bytes. Writing values as bits and bytes is described in detail below.

2.1 Logical data types

Byte
: Signed byte (8 bits).

[1] Markus Hsi-Yang Fritz, Rasko Leinonen, Guy Cochrane, and Ewan Birney, **Efficient storage of high throughput DNA sequencing data using reference-based compression**, *Genome Res.* 2011 21: 734–740; doi:10.1101/gr.114819.110; PMID:21245279.

Integer
Signed 32-bit integer.

Long
Signed 64-bit integer.

Array
An array of any logical data type: <type>[ ]

2.2 Writing bits to a bit stream

A bit stream consists of a sequence of 1s and 0s. The bits are written most significant bit first where new bits are stacked to the right and full bytes on the left are written out. In a bit stream the last byte will be incomplete if less than 8 bits have been written to it. In this case the bits in the last byte are shifted to the left.

Example of writing to bit stream

Let's consider the following example. The table below shows a sequence of write operations:

Operation order	Buffer state before	Written bits	Buffer state after	Issued bytes
1	0x0	1	0x1	-
2	0x1	0	0x2	-
3	0x2	11	0xB	-
4	0xB	0000 0111	0x7	0xB0

After flushing the above bit stream the following bytes are written: 0xB0 0x70. Please note that the last byte was 0x7 before shifting to the left and became 0x70 after that:

```
> echo "obase=16; ibase=2; 00000111" | bc
7

> echo "obase=16; ibase=2; 01110000" | bc
70
```

And the whole bit sequence:

```
> echo "obase=2; ibase=16; B070" | bc
1011000001110000
```

When reading the bits from the bit sequence it must be known that only 12 bits are meaningful and the bit stream should not be read after that.

Note on writing to bit stream

When writing to a bit stream both the value and the number of bits in the value must be known. This is because programming languages normally operate with bytes (8 bits) and to specify which bits are to be written requires a bit-holder, for example an integer, and the number of bits in it. Equally, when reading a value from a bit stream the number of bits must be known in advance. In case of prefix codes (e.g. Huffman) all possible bit combinations are either known in advance or it is possible to calculate how many bits will follow based on the first few bits. Alternatively, two codes can be combined, where the first contains the number of bits to read.

2.3 Writing bytes to a byte stream

The interpretation of byte stream is straightforward. CRAM uses *little endianness* for bytes when applicable and defines the following storage data types:

Boolean (bool)
Boolean is written as 1-byte with 0x0 being 'false' and 0x1 being 'true'.

Integer (int32)
Signed 32-bit integer, written as 4 bytes in little-endian byte order.

Long (int64)
Signed 64-bit integer, written as 8 bytes in little-endian byte order.

ITF-8 integer (itf8)
This is an alternative way to write an integer value. The idea is similar to UTF-8 encoding and therefore this encoding is called ITF-8 (Integer Transformation Format - 8 bit).

The most significant bits of the first byte have special meaning and are called 'prefix'. These are 0 to 4 true bits followed by a 0. The number of 1's denote the number of bytes to follow. To accommodate 32 bits such representation requires 5 bytes with only 4 lower bits used in the last byte 5.

LTF-8 long (ltf8)
See ITF-8 for more details. The only difference between ITF-8 and LTF-8 is the number of bytes used to encode a single value. To do so 64 bits are required and this can be done with 9 byte at most with the first byte consisting of just 1s or 0xFF value.

Array ([ ])
Array length is written first as integer (itf8), followed by the elements of the array.

Encoding
Encoding is a data type that specifies how data series have been compressed. Encodings are defined as encoding<type> where the type is a logical data type as opposed to a storage data type.

An encoding is written as follows. The first integer (itf8) denotes the codec id and the second integer (itf8) the number of bytes in the following encoding-specific values.

Subexponential encoding example:

Value	Type	Name
0x7	itf8	codec id
0x2	itf8	number of bytes to follow
0x0	itf8	offset
0x1	itf8	K parameter

The first byte "0x7" is the codec id.

The next byte "0x2" denotes the length of the bytes to follow (2).

The subexponential encoding has 2 parameters: integer (itf8) offset and integer (itf8) K.

offset = 0x0 = 0

K = 0x1 = 1

Map
A map is a collection of keys and associated values. A map with N keys is written as follows:

size in bytes	N	key 1	value 1	key ...	value ...	key N	value N

Both the size in bytes and the number of keys are written as integer (itf8). Keys and values are written according to their data types and are specific to each map.

String
A string is represented as byte arrays using UTF-8 format. Read names, reference sequence names and tag values with type 'Z' are stored as UTF-8.

3 Encodings

Encoding is a data structure that captures information about compression details of a data series that are required to uncompress it. This could be a set of constants required to initialize a specific decompression algorithm or statistical properties of a data series or, in case of data series being stored in an external block, the block content id.

Encoding notation is defined as the keyword 'encoding' followed by its data type in angular brackets, for example 'encoding<byte>' stands for an encoding that operates on a data series of data type 'byte'.

Encodings may have parameters of different data types, for example the EXTERNAL encoding has only one parameter, integer id of the external block. The following encodings are defined:

Codec	ID	Parameters	Comment
NULL	0	none	series not preserved
EXTERNAL	1	int block content id	the block content identifier used to associate external data blocks with data series
Deprecated (GOLOMB)	2	int offset, int M	Golomb coding
HUFFMAN	3	int array, int array	coding with int/byte values
BYTE_ARRAY_LEN	4	encoding<int> array length, encoding<byte> bytes	coding of byte arrays with array length
BYTE_ARRAY_STOP	5	byte stop, int external block content id	coding of byte arrays with a stop value
BETA	6	int offset, int number of bits	binary coding
SUBEXP	7	int offset, int K	subexponential coding
Deprecated (GOLOMB_RICE)	8	int offset, int $\log_2$m	Golomb-Rice coding
GAMMA	9	int offset	Elias gamma coding

See section 13 for more detailed descriptions of all the above coding algorithms and their parameters.

4 Checksums

The checksumming is used to ensure data integrity. The following checksumming algorithms are used in CRAM.

4.1 CRC32

This is a cyclic redundancy checksum 32-bit long with the polynomial 0x04C11DB7. Please refer to ITU-T V.42 for more details. The value of the CRC32 hash function is written as an integer.

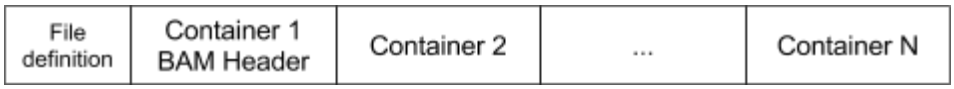
4.2 CRC32 sum

CRC32 sum is a combination of CRC32 values by summing up all individual CRC32 values modulo 2^{32}.

5 File structure

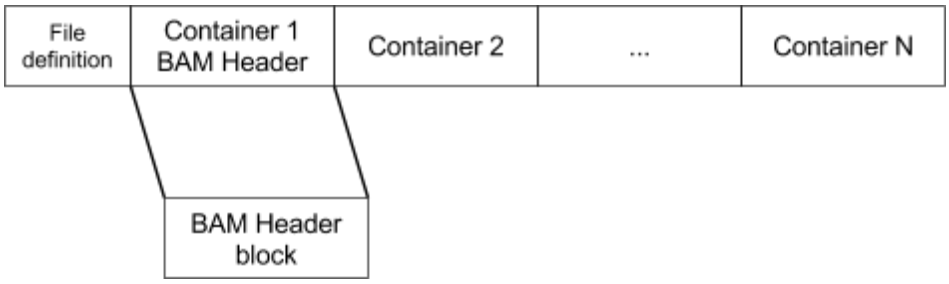
The overall CRAM file structure is described in this section. Please refer to other sections of this document for more detailed information.

A CRAM file starts with a fixed length file definition followed by one or more containers. The BAM header is stored in the first container.



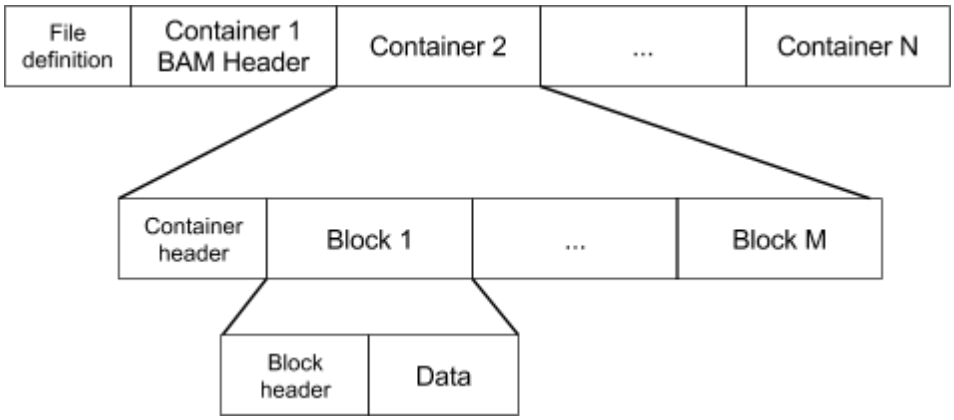
Pic.1 CRAM file starts with a file definition followed by the BAM header and other containers.

Containers consist of one or more blocks. By convention, the BAM header is stored in the first container within a single block. This is known as the BAM header block.



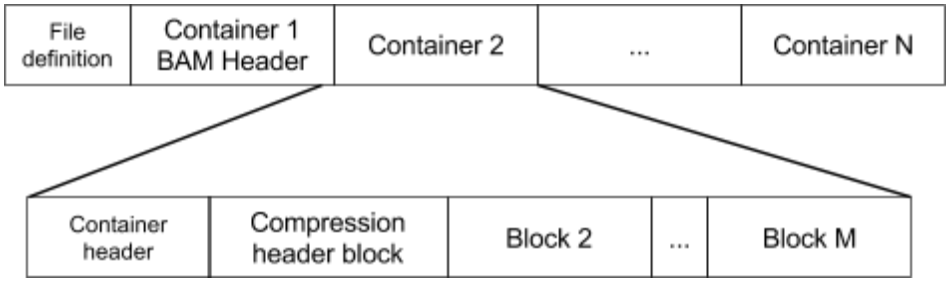
Pic.2 The BAM header is stored in the first container.

Each container starts with a container header followed by one or more blocks. Each block starts with a block header. All data in CRAM is stored within blocks after the block header.



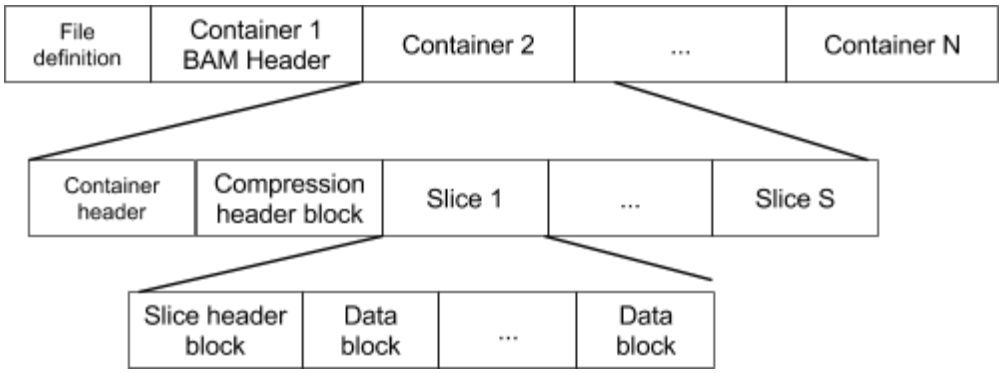
Pic.3 Container and block structure. All data in CRAM files is stored in blocks.

The first block in each container is the compression header block:



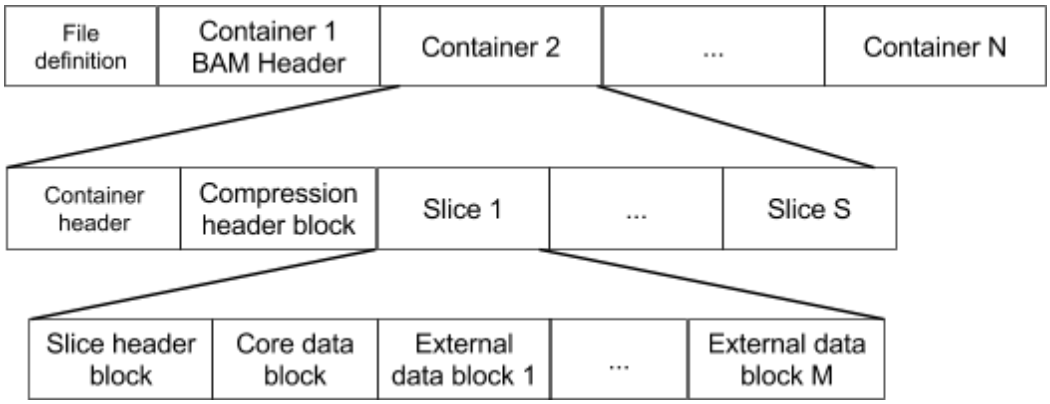
Pic.4 Compression header is the first block in the container.

The blocks after the compression header are organised logically into slices. One slice may contain, for example, a contiguous region of alignment data. Slices begin with a slice header block and are followed by one or more data blocks:



Pic.5 Containers are logically organised into slices.

Data blocks are divided into core and external data blocks. Each slice must have at least one core data block immediately after the slice header block. The core data block may be followed by one or more external data blocks.



Pic.5 Data blocks are divided into core and external data blocks.

6 File definition

Each CRAM file starts with a fixed length (26 bytes) definition with the following fields:

Data type	**Name**	**Value**
byte[4]	format magic number	CRAM (0x43 0x52 0x41 0x4d)
unsigned byte	major format number	3 (0x3)
unsigned byte	minor format number	0 (0x0)
byte[20]	file id	CRAM file identifier (e.g. file name or SHA1 checksum)

Valid CRAM *major.minor* version numbers are as follows:

1.0 The original public CRAM release.

2.0 The first CRAM release implemented in both Java and C; tidied up implementation vs specification differences in *1.0*.

2.1 Gained end of file markers; compatible with *2.0*.

3.0 Additional compression methods; header and data checksums; improvements for unsorted data.

7 Container header structure

The file definition is followed by one or more containers with the following header structure where the container content is stored in the 'blocks' field:

Data type	Name	Value
int32	length	the sum of the lengths of all blocks in this container (headers and data); equal to the total byte length of the container minus the byte length of this header structure
itf8	reference sequence id	reference sequence identifier or -1 for unmapped reads -2 for multiple reference sequences. All slices in this container must have a reference sequence id matching this value.
itf8	starting position on the reference	the alignment start position or 0 if the container is multiple-reference or contains unmapped unplaced reads
itf8	alignment span	the length of the alignment or 0 if the container is multiple-reference or contains unmapped unplaced reads
itf8	number of records	number of records in the container
ltf8	record counter	1-based sequential index of records in the file/stream.
ltf8	bases	number of read bases
itf8	number of blocks	the total number of blocks in this container
itf8[ ]	landmarks	the locations of slices in this container as byte offsets from the end of this container header, used for random access indexing. The landmark count must equal the slice count. Since the block before the first slice is the compression header, landmarks[0] is equal to the byte length of the compression header.
int	crc32	CRC32 hash of the all the preceding bytes in the container.
byte[ ]	blocks	The blocks contained within the container.

7.1 CRAM header in the first container

The first container in the CRAM file contains the BAM header in an optionally compressed block. Only gzip is allowed as compression method for this block. BAM header is terminated with \0 byte and any extra bytes in the block can be used to expand the BAM header. For example when updating @SQ records additional space may be required for the BAM header. It is recommended to reserve 50% more space in the CRAM header block than it is required by the BAM header.

8 Block structure

Containers consist of one or more blocks. Block compression is applied independently and in addition to any encodings used to compress data within the block. The block have the following header structure with the data stored in the 'block data' field:

Data type	Name	Value
byte	method	the block compression method: 0: raw (none)* 1: gzip 2: bzip2 3: lzma 4: rans
byte	block content type id	the block content type identifier
itf8	block content id	the block content identifier used to associate external data blocks with data series
itf8	size in bytes*	size of the block data after applying block compression
itf8	raw size in bytes*	size of the block data before applying block compression
byte[ ]	block data	the data stored in the block: • bit stream of CRAM records (core data block) • byte stream (external data block) • additional fields (header blocks)
byte[4]	CRC32	CRC32 hash value for all preceding bytes in the block

* Note on raw method: both compressed and raw sizes must be set to the same value.

8.1 Block content types

CRAM has the following block content types:

Block content type	Block content type id	Name	Contents
FILE_HEADER	0	BAM header block	BAM header
COMPRESSION_HEADER	1	Compression header block	See specific section
SLICE_HEADER[a]	2	Slice header block	See specific section
	3		reserved
EXTERNAL_DATA	4	external data block	data produced by external encodings
CORE_DATA	5	core data block	bit stream of all encodings except for external encodings

[a] Formerly MAPPED_SLICE_HEADER. Now used by all slice headers regardless of mapping status.

8.2 Block content id

Block content id is used to distinguish between external blocks in the same slice. Each external encoding has an id parameter which must be one of the external block content ids. For external blocks the content id is a positive integer. For all other blocks content id should be 0. Consequently, all external encodings must not use content id less than 1.

Data blocks

Data is stored in data blocks. There are two types of data blocks: core data blocks and external data blocks.The difference between core and external data blocks is that core data blocks consist of data series that are compressed using bit encodings while the external data blocks are byte compressed. One core data block and any number of external data blocks are associated with each slice.

Writing to and reading from core and external data blocks is organised through CRAM records. Each data series is associated with an encoding. In case of external encodings the block content id is used to identify the block where the data series is stored. Please note that external blocks can have multiple data series associated with them; in this case the values from these data series will be interleaved.

8.3 BAM header block

The BAM header is stored in a single block within the first container.

The following constraints apply to the BAM header:

- The SQ:MD5 checksum is required unless the reference sequence has been embedded into the file.

8.4 Compression header block

The compression header block consists of 3 parts: preservation map, data series encoding map and tag encoding map.

Preservation map

The preservation map contains information about which data was preserved in the CRAM file. It is stored as a map with byte[2] keys:

Key	Value data type	Name	Value
RN	bool	read names included	true if read names are preserved for all reads
AP	bool	AP data series delta	true if AP data series is delta, false otherwise
RR	bool	reference required	true if reference sequence is required to restore the data completely
SM	byte[5]	substitution matrix	substitution matrix
TD	byte[ ]	tag ids dictionary	a list of lists of tag ids, see tag encoding section

Data series encodings

Each data series has an encoding. These encoding are stored in a map with byte[2] keys and are decoded in approximately this order[2]:

[2]The precise order is defined in section 10.

Key	Value data type	Name	Value
BF	encoding<int>	BAM bit flags	see separate section
CF	encoding<int>	CRAM bit flags	see specific section
RI	encoding<int>	reference id	record reference id from the BAM file header
RL	encoding<int>	read lengths	read lengths
AP	encoding<int>	in-seq positions	if **AP-Delta** = true: 0-based alignment start delta from the AP value in the previous record. Note this delta may be negative, for example when switching references in a multi-reference slice. When the record is the first in the slice, the previous position used is the slice alignment-start field (hence the first delta should be zero for single-reference slices, or the AP value itself for multi-reference slices). if **AP-Delta** = false: encodes the alignment start position directly
RG	encoding<int>	read groups	read groups. Special value '-1' stands for no group.
RN[a]	encoding<byte[ ]>	read names	read names
MF	encoding<int>	next mate bit flags	see specific section
NS	encoding<int>	next fragment reference sequence id	reference sequence ids for the next fragment
NP	encoding<int>	next mate alignment start	alignment positions for the next fragment
TS	encoding<int>	template size	template sizes
NF	encoding<int>	distance to next fragment	number of records to the next fragment[b]
TL[c]	encoding<int>	tag ids	list of tag ids, see tag encoding section
FN	encoding<int>	number of read features	number of read features in each record
FC	encoding<byte>	read features codes	see separate section
FP	encoding<int>	in-read positions	positions of the read features
DL	encoding<int>	deletion lengths	base-pair deletion lengths
BB	encoding<byte[ ]>	stretches of bases	bases
QQ	encoding<byte[ ]>	stretches of quality scores	quality scores
BS	encoding<byte>	base substitution codes	base substitution codes
IN	encoding<byte[ ]>	insertion	inserted bases
RS	encoding<int>	reference skip length	number of skipped bases for the 'N' read feature
PD	encoding<int>	padding	number of padded bases
HC	encoding<int>	hard clip	number of hard clipped bases
SC	encoding<byte[ ]>	soft clip	soft clipped bases
MQ	encoding<int>	mapping qualities	mapping quality scores
BA	encoding<byte>	bases	bases
QS	encoding<byte>	quality scores	quality scores

[a] Note RN this is decoded after MF if the record is detached from the mate and we are attempting to auto-generate read names.

[b] The count is reset for each slice so NF can only refer to a record later within this slice.

[c] TL is followed by decoding the tag values themselves, in order of appearance in the tag dictionary.

Tag encodings

The tag dictionary (TD) describes the unique combinations of tag id / type that occur on each alignment record. For example if we search the id / types present in each record and find only two combinations – X1:i BC:Z SA:Z: and X1:i: BC:Z – then we have two dictionary entries in the TD map.

Let $L_i = \{T_{i0}, T_{i1}, \ldots, T_{ix}\}$ be a list of all tag ids for a record R_i, where i is the sequential record index and T_{ij} denotes j-th tag id in the record. The list of unique L_i is stored as the TD value in the preservation map. Maintaining the order is not a requirement for encoders (hence "combinations"), but it is permissible and thus different permutations, each encoded with their own elements in TD, should be supported by the decoder. Each L_i element in TD is assigned a sequential integer number starting with 0. These integer numbers are referred to by the TL data series. Using TD, an integer from the TL data series can be mapped back into a list of tag ids. Thus per alignment record we only need to store tag values and not their ids and types.

The TD is written as a byte array consisting of L_i values separated with \0. Each L_i value is written as a concatenation of 3 byte T_{ij} elements: tag id followed by BAM tag type code (one of A, c, C, s, S, i, I, f, F, Z, H or B, as described in the SAM specification). For example the TD for tag lists X1:i BC:Z SA:Z and X1:i BC:Z may be encoded as X1CBCZSAZ\0X1CBCZ\0, with X1C indicating a 1 byte unsigned value for tag X1.

Tag values

The encodings used for different tags are stored in a map. The key is 3 bytes formed from the BAM tag id and type code, matching the TD dictionary described above. Unlike the Data Series Encoding Map, the key is stored in the map as an ITF8 encoded integer, constructed using $(char1 << 16) + (char2 << 8) + type$. For example, the 3-byte representation of OQ:Z is {0x4F, 0x51, 0x5A} and these bytes are intepreted as the integer key 0x004F515A, leading to an ITF8 byte stream {0xE0, 0x4F, 0x51, 0x5A}.

Key	**Value data type**	**Name**	**Value**
TAG ID 1:TAG TYPE 1	encoding<byte[ ]>	read tag 1	tag values (names and types are available in the data series code)
...		...	...
TAG ID N:TAG TYPE N	encoding<byte[ ]>	read tag N	...

Note that tag values are encoded as array of bytes. The routines to convert tag values into byte array and back are the same as in BAM with the exception of value type being captured in the tag key rather in the value. Hence consuming 1 byte for types 'C' and 'c', 2 bytes for types 'S' and 's', 4 bytes for types 'I', 'i' and 'f', and a variable number of bytes for types 'H', 'Z' and 'B'.

8.5 Slice header block

The slice header block is never compressed (block method=raw). For reference mapped reads the slice header also defines the reference sequence context of the data blocks associated with the slice. Mapped reads can be stored along with **placed unmapped**[3] reads on the same reference within the same slice.

Slices with the Multiple Reference flag (-2) set as the sequence ID in the header may contain reads mapped to multiple external references, including unmapped[3] reads (placed on these references or unplaced), but multiple embedded references cannot be combined in this way. When multiple references are used, the RI data series will be used to determine the reference sequence ID for each record. This data series is not present when only a single reference is used within a slice.

The Unmapped (-1) sequence ID in the header is for slices containing only unplaced unmapped[3] reads.

A slice containing data that does not use the external reference in any sequence may set the reference MD5 sum to zero. This can happen because the data is unmapped or the sequence has been stored verbatim instead of via reference-differencing. This latter scenario is recommended for unsorted or non-coordinate-sorted data.

The slice header block contains the following fields.

[3]Unmapped reads can be *placed* or *unplaced*. By placed unmapped read we mean a read that is unmapped according to bit 0x4 of the BF (BAM bit flags) data series, but has position fields filled in, thus "placing" it on a reference sequence. In contrast, unplaced unmapped reads have have a reference sequence ID of -1 and alignment position of 0.

Data type	Name	Value
itf8	reference sequence id	reference sequence identifier or -1 for unmapped reads -2 for multiple reference sequences. This value must match that of its enclosing container.
itf8	alignment start	the alignment start position. 0 if the slice is multiple-reference or contains unmapped unplaced reads
itf8	alignment span	the length of the alignment. 0 if the slice is multiple-reference or contains unmapped unplaced reads
itf8	number of records	the number of records in the slice
ltf8	record counter	1-based sequential index of records in the file/stream
itf8	number of blocks	the number of blocks in the slice
itf8[ ]	block content ids	block content ids of the blocks in the slice
itf8	embedded reference bases block content id	block content id for the embedded reference sequence bases or -1 for none
byte[16]	reference md5	MD5 checksum of the reference bases within the slice boundaries. If this slice has reference sequence id of -1 (unmapped) or -2 (multi-ref) the MD5 should be 16 bytes of \0. For embedded references, the MD5 can either be all-zeros or the MD5 of the embedded sequence.
byte[]	optional tags	a series of tag,type,value tuples encoded as per BAM auxiliary fields.

The optional tags are encoded in the same manner as BAM tags. I.e. a series of binary encoded tags concatenated together where each tag consists of a 2 byte key (matching [A-Za-z][A-Za-z0-9]) followed by a 1 byte type ([AfZHcCsSiIB]) followed by a string of bytes in a format defined by the type.

Tags starting in a capital letter are reserved while lowercase ones or those starting with X, Y or Z are user definable. Any tag not understood by a decoder should be skipped over without producing an error.

At present no tags are defined.

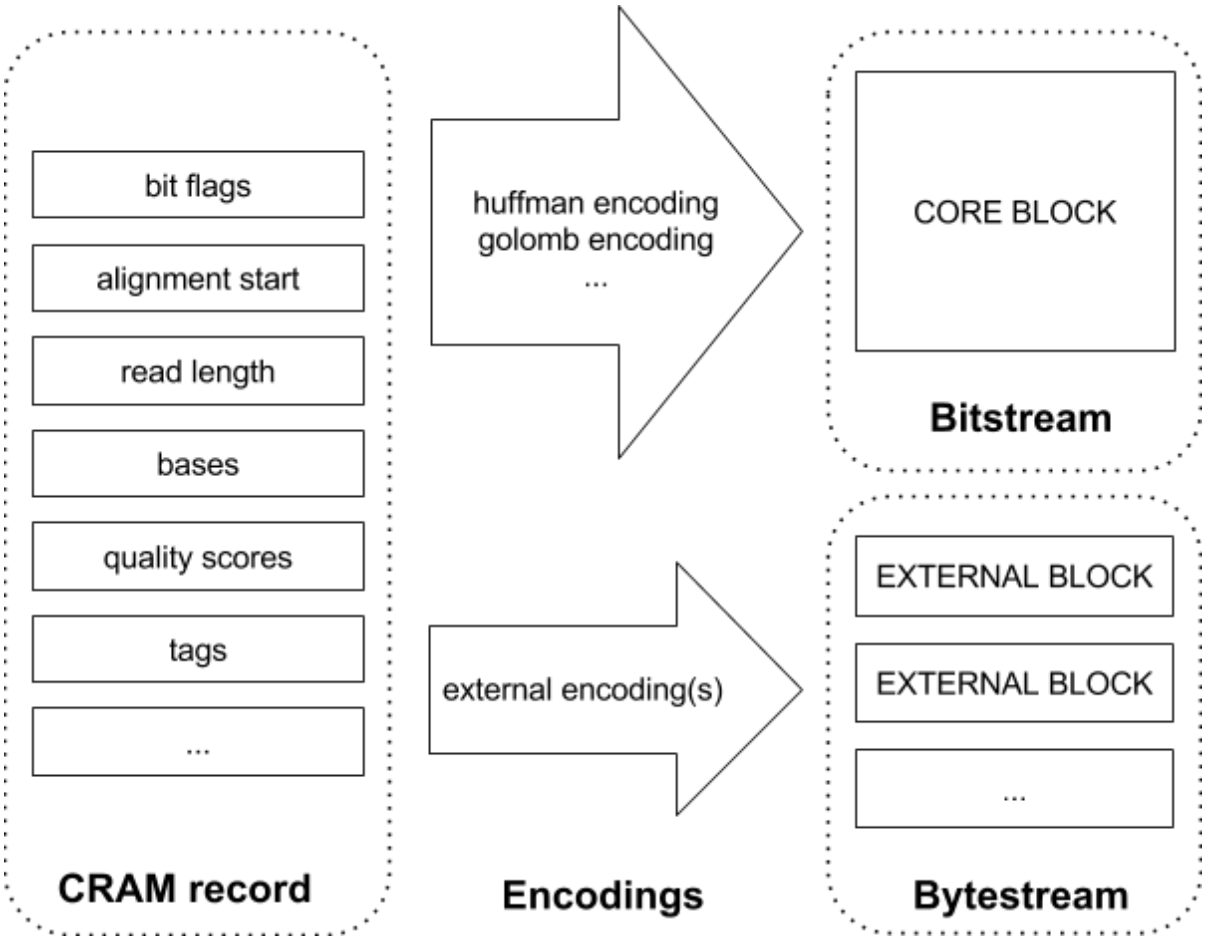
8.6 Core data block

A core data block is a bit stream (most significant bit first) consisting of one or more CRAM records. Please note that one byte could hold more then one CRAM record as a minimal CRAM record could be just a few bits long. The core data block has the following fields:

Data type	Name	Value
bit[ ]	CRAM record 1	The first CRAM record
...	...	...
bit[ ]	CRAM record N	The Nth CRAM record

8.7 External data block

Relationship between core data block and external data blocks is shown in the following picture:



Pic.3 Relationship between core data block and external data blocks.

The picture shows how a CRAM record (on the left) is partially written to core data block while the other fields are stored in two external data blocks. The specific encodings are presented only for demonstration purposes, the main point here is to distinguish between bit encodings whose output is always stored in a core data block, and external encodings which store bytes in external data blocks.

9 End of file marker

A special container is used to mark the end of a file or stream. It is required in version 3 or later. The idea is to provide an easy and a quick way to detect that a CRAM file or stream is complete. The marker is basically an empty container with ref seq id set to -1 (unaligned) and alignment start set to 4542278.

Here is a complete content of the EOF container explained in detail:

hex bytes	data type	decimal value	field name
Container header			
0f 00 00 00	integer	15	size of blocks data
ff ff ff ff 0f	itf8	-1	ref seq id
e0 45 4f 46	itf8	4542278	alignment start
00	itf8	0	alignment span
00	itf8	0	number of records
00	itf8	0	global record counter
00	itf8	0	bases
01	itf8	1	block count
00	array	0	landmarks
05 bd d9 4f	integer	1339669765	container header CRC32
Compression header block			
00	byte	0 (RAW)	compression method
01	byte	1 (COMPRESSION_HEADER)	block content type
00	itf8	0	block content id
06	itf8	6	compressed size
06	itf8	6	uncompressed size
Compression header			
01	itf8	1	preservation map byte size
00	itf8	0	preservation map size
01	itf8	1	encoding map byte size
00	itf8	0	encoding map size
01	itf8	1	tag encoding byte size
00	itf8	0	tag encoding map size
ee 63 01 4b	integer	1258382318	block CRC32

When compiled together the EOF marker is 38 bytes long and in hex representation is:

0f 00 00 00 ff ff ff ff 0f e0 45 4f 46 00 00 00 00 01 00 05 bd d9 4f 00 01 00 06 06 01 00 01 00 01 00 ee 63 01 4b

10 Record structure

CRAM record is based on the SAM record but has additional features allowing for more efficient data storage. In contrast to BAM record CRAM record uses bits as well as bytes for data storage. This way, for example, various coding techniques which output variable length binary codes can be used directly in CRAM. On the other hand, data series that do not require binary coding can be stored separately in external blocks with some other compression applied to them independently.

As CRAM data series may be interleaved within the same blocks[4] understanding the order in which CRAM data series must be decoded is vital.

The overall flowchart is below, with more detailed description in the subsequent sections.

10.1 CRAM record

Both mapped and unmapped reads start with the following fields. Please note that the data series type refers to the logical data type and the data series name corresponds to the data series encoding map.

[4]Interleaving can sometimes provide better compression, however it also adds dependency between types of data meaning it is not possible to selectively decode one data series if it co-locates with another data series in the same block.

Data series type	Data series name	Field	Description
int	BF	BAM bit flags	see BAM bit flags below
int	CF	CRAM bit flags	see CRAM bit flags below
-	-	Positional data	See section 10.2
-	-	Read names	See section 10.3
-	-	Mate records	See section 10.4
-	-	Auxiliary tags	See section 10.5
-	-	Sequences	See sections 10.6 and 10.7

BAM bit flags (BF data series)

The following flags are duplicated from the SAM and BAM specification, with identical meaning. Note however some of these flags can be derived during decode, so may be omitted in the CRAM file and the bits computed based on both reads of a pair-end library residing within the same slice.

Bit flag	Comment	Description
0x1		template having multiple segments in sequencing
0x2		each segment properly aligned according to the aligner
0x4		segment unmapped[a]
0x8	calculated[b] or stored in the mate's info	next segment in template unmapped
0x10		SEQ being reverse complemented
0x20	calculated[b] or stored in the mate's info	SEQ of the next segment in the template being reversed
0x40		the first segment in the template[c]
0x80		the last segment in the template[c]
0x100		secondary alignment
0x200		not passing quality controls
0x400		PCT or optical duplicate
0x800		Supplementary alignment

[a] Bit 0x4 is the only reliable place to tell whether the read is unmapped. If 0x4 is set, no assumptions may be made about bits 0x2, 0x100 and 0x800.

[b] For segments within the same slice.

[c] Bits 0x40 and 0x80 reflect the read ordering within each template inherent in the sequencing technology used, which may be independent from the actual mapping orientation. If 0x40 and 0x80 are both set, the read is part of a linear template (one where the template sequence is expected to be in a linear order), but it is neither the first nor the last read. If both 0x40 and 0x80 are unset, the index of the read in the template is unknown. This may happen for a non-linear template (such as one constructed by stitching together other templates) or when this information is lost during data processing.

CRAM bit flags (CF data series)

The CRAM bit flags (also known as compression bit flags) expressed as an integer represent the CF data series. The following compression flags are defined for each CRAM read record:

Bit flag	Name	Description
0x1	quality scores stored as array	quality scores can be stored as read features or as an array similar to read bases.
0x2	detached	mate information is stored verbatim (e.g. because the pair spans multiple slices or the fields differ to the CRAM computed method)
0x4	has mate downstream	tells if the next segment should be expected further in the stream
0x8	decode sequence as "*"	informs the decoder that the sequence is unknown and that any encoded reference differences are present only to recreate the CIGAR string.

The following pseudocode describes the general process of decoding an entire CRAM record. The sequence data itself is in one of two encoding formats depending on whether the record is aligned (mapped).

Decode pseudocode

```
1: procedure DecodeRecord
2:     BAM_flags  ← ReadItem(BF, Integer)
3:     CRAM_flags ← ReadItem(CF, Integer)
4:     DecodePositions                          ▷ See section 10.2
5:     DecodeNames                              ▷ See section 10.3
6:     DecodeMateData                           ▷ See section 10.4
7:     DecodeTagData                            ▷ See section 10.5

8:     if (BF AND 4) ≠ 0 then                   ▷ Unmapped flag
9:         DecodeMappedRead                     ▷ See section 10.6
10:    else
11:        DecodeUnmappedRead                   ▷ See section 10.7
12:    end if
13: end procedure
```

10.2 CRAM positional data

Following the bit-wise BAM and CRAM flags, CRAM encodes positional related data including reference, alignment positions and length, and read-group. Positional data is stored for both mapped and unmapped sequences, as unmapped data may still be "placed" at a specific location in the genome (without being aligned). Typically this is done to keep a sequence pair (paired-end or mate-pair sequencing libraries) together when one of the pair aligns and the other does not.

For reads stored in a position-sorted slice, the AP-delta flag in the compression header preservation map should be set and the AP data series will be delta encoded, using the slice alignment-start value as the first position to delta against. Note for multi-reference slices this may mean that the AP series includes negative values, such as when moving from an alignment to the end of one reference sequence to the start of the next or to unmapped unplaced data. When the AP-delta flag is not set the AP data series is stored as a normal integer value.

Data series type	Data series name	Field	Description
int	RI	ref id	reference sequence id (only present in multiref slices)
int	RL	read length	the length of the read
int	AP	alignment start	the alignment start position
int	RG	read group	the read group identifier expressed as the N^{th} record in the header, starting from 0 with -1 for no group

```
1: procedure DecodePositions
2:     if slice_header.reference_sequence_id = −2 then
```

```
        reference_id ← ReadItem(RI, Integer)
    else
        reference_id ← slice_header.reference_sequence_id
    end if
    read_length ← ReadItem(RL, Integer)
    if container_pmap.AP_delta ≠ 0 then
        if first_record_in_slice then
            last_position ← slice_header.alignment_start
        end if
        alignment_position ← ReadItem(AP, Integer) + last_position
        last_position ← alignment_position
    else
        alignment_position ← ReadItem(AP, Integer)
    end if
    read_group ← ReadItem(RG, Integer)
end procedure
```

10.3 Read names (RN data series)

Read names can be preserved in the CRAM format, but this is optional and is governed by the `RN` preservation map key in the container compression header. See section 8.4. When read names are not preserved the CRAM decoder should generate names, typically based on the file name and a numeric ID of the read using the record counter field of the slice header block. Note read names may still be preserved even when the `RN` compression header key indicates otherwise, such as where a read is part of a read-pair and the pair spans multiple slices. In this situation the record will be marked as detached (see the CF data series) and the mate data below (section 10.4) will contain the read name.

Data series type	Data series name	Field	Description
byte[]	RN	read names	read names

```
procedure DecodeNames
    if container_pmap.read_names_included = 1 then
        read_name ← ReadItem(RN, Byte[])
    else
        read_name ← GenerateName
    end if

end procedure
```

10.4 Mate record

There are two ways in which mate information can be preserved in CRAM: number of records downstream (distance, within this slice) to the next fragment in the template and a special mate record if the next fragment is not in the current slice. In the latter case the record is labelled as "detached", see the CF data series.

For mates within the slice only the distance is captured, and only for the first record. The mate has neither detached nor downstream flags set in the CF data series.

Data series type	Data series name	Description
int	NF	the number of records to the next fragment

In the above case, the NS (mate reference name), NP (mate position) and TS (template size) fields for both records should be derived once the mate has also been decoded. Mate reference name and position are obvious and simply copied from the mate. The template size is computed using the method described in the SAM specification; the inclusive distance from the leftmost to rightmost mapped bases with the sign being positive for the leftmost record and negative for the rightmost record.

If the next fragment is not found within this slice then the following structure is included into the CRAM record. Note there are cases where read-pairs within the same slice may be marked as detached and use this structure, such as to store mate-pair information that does not match the algorithm used by CRAM for computing the mate data on-the-fly.

Data series type	Data series name	Description
int	MF	next mate bit flags, see table below
byte[ ]	RN	the read name (if and only if not known already)
int	NS	mate reference sequence identifier
int	NP	mate alignment start position
int	TS	the size of the template (insert size)

Next mate bit flags (MF data series)

The next mate bit flags expressed as an integer represent the MF data series. These represent the missing bits we excluded from the BF data series (when compared to the full SAM/BAM flags). The following bit flags are defined:

Bit flag	Name	Description
0x1	mate negative strand bit	the bit is set if the mate is on the negative strand
0x2	mate mapped bit	the bit is set if the mate is mapped

Decode mate pseudocode

In the following pseudocode we are assuming the current record is *this* and its mate is $next\_frag$.

```
1: procedure DecodeMateData
2:     if CF AND 2 then                                          ▷ Detached from mate
3:         mate_flags ← ReadItem(MF,Integer)
4:         if mate_flags AND 1 then
5:             bam_flags ← bam_flags OR 0x20                     ▷ Mate is reverse-complemented
6:         end if
7:         if mate_flags AND 2 then
8:             bam_flags ← bam_flags OR 0x08                     ▷ Mate is unmapped
9:         end if
10:        if container_pmap.read_names_included ≠ 1 then
11:            read_name ← ReadItem(RN, Byte[])
12:        end if
13:        mate_ref_id  ← ReadItem(NS, Integer)
14:        mate_position ← ReadItem(NP, Integer)
15:        template_size ← ReadItem(TS, Integer)
16:    else if CF AND 4 then                                     ▷ Mate is downstream
17:        if next_frag.bam_flags AND 0x10 then
18:            this.bam_flags ← this.bam_flags OR 0x20           ▷ next segment reverse complemented
19:        end if
20:        if next_frag.bam_flags AND 0x04 then
21:            this.bam_flags ← this.bam_flags OR 0x08           ▷ next segment unmapped
22:        end if
23:        next_frag ← ReadItem(NF,Integer)
24:        Resolve mate_ref_id for this record and this + next_frag once both have been decoded
25:        Resolve mate_position for this record and this + next_frag once both have been decoded
26:        Find leftmost and rightmost mapped coordinate in records this and this + next_frag.
27:        For leftmost of this and this + next_frag record: template_size ← rightmost − leftmost + 1
28:        For rightmost of this and this + next_frag record: template_size ← −(rightmost − leftmost + 1)
29:    end if
30: end procedure
```

Note as with the SAM specification a template may be permitted to have more than two alignment records. In this case the "mate" for each record is considered to be the next record, with the mate for the last record

being the first to form a circular list. The above algorithm is a simplification that does not deal with this scenario. The full method needs to observe when record $this + NF$ is also labelled as having an additional mate downstream. One recommended approach is to resolve the mate information in a second pass, once the entire slice has been decoded. The final segment in the mate chain needs to set bam_flags fields 0x20 and 0x08 accordingly based on the first segment. This is also not listed in the above algorithm, for brevity.

10.5 Auxiliary tags

Tags are encoded using a tag line (TL data series) integer into the tag dictionary (TD field in the compression header preservation map, see section 8.4). See section 8.4 for a more detailed description of this process.

Data series type	Data series name	Field	Description
int	TL	tag line	an index into the tag dictionary (TD)
*	???	tag name/type	3 character key (2 tag identifier and 1 tag type), as specified by the tag dictionary

```
1: procedure DecodeTagData
2:     tag_line ← ReadItem(TL,Integer)
3:     for all ele ∈ container_pmap.tag_dict(tag_line) do
4:         name ← first two characters of ele
5:         tag(type) ← last character of ele
6:         tag(name) ← ReadItem(ele, Byte[])
7:     end for
8: end procedure
```

In the above procedure, *name* is a two letter tag name and *type* is one of the permitted types documented in the SAM/BAM specification. Type is `c` (signed 8-bit integer), `C` (unsigned 8-bit integer), `s` (signed 16-bit integer), `S` (unsigned 16-bit integer), `i` (signed 32-bit integer), `I` (unsigned 32-bit integer), `f` (32-bit float), `Z` (nul-terminated string), `H` (nul-terminated string of hex digits) and `B` (binary data in array format with the first byte being one of c,C,s,S,i,I,f using the meaning above, a 32-bit integer for the number of array elements, followed by array data encoded using the specified format). All integers are little endian encoded.

For example a SAM tag `MQ:i` has name `MQ` and type `i` and will be decoded using one of MQc, MQC, MQs, MQS, MQi and MQI data series depending on size and sign of the integer value.

10.6 Mapped reads

Read feature records

Read features are used to store read details that are expressed using read coordinates (e.g. base differences respective to the reference sequence). The read feature records start with the number of read features followed by the read features themselves. Finally the single mapping quality and per-base quality scores are stored.

Data series type	Data series name	Field	Description
int	FN	number of read features	the number of read features
int	FP	in-read-position[a]	position of the read feature
byte	FC	read feature code[a]	See feature codes below
*	*	read feature data[a]	See feature codes below
int	MQ	mapping qualities	mapping quality score
byte[read length]	QS	quality scores	the base qualities, if preserved

[a] Repeated FN times, once for each read feature.

Read feature codes

Each feature code has its own associated data series containing further information specific to that feature. The following codes are used to distinguish variations in read coordinates:

Feature code	Id	Data series type	Data series name	Description
Bases	b (0x62)	byte[ ]	BB	a stretch of bases
Scores	q (0x71)	byte[ ]	QQ	a stretch of scores
Read base	B (0x42)	byte,byte	BA,QS	A base and associated quality score
Substitution	X (0x58)	byte	BS	base substitution codes, SAM operators X, M and =
Insertion	I (0x49)	byte[ ]	IN	inserted bases, SAM operator I
Deletion	D (0x44)	int	DL	number of deleted bases, SAM operator D
Insert base	i (0x69)	byte	BA	single inserted base, SAM operator I
Quality score	Q (0x51)	byte	QS	single quality score
Reference skip	N (0x4E)	int	RS	number of skipped bases, SAM operator N
Soft clip	S (0x53)	byte[ ]	SC	soft clipped bases, SAM operator S
Padding	P (0x50)	int	PD	number of padded bases, SAM operator P
Hard clip	H (0x48)	int	HC	number of hard clipped bases, SAM operator H

Base substitution codes (BS data series)

A base substitution is defined as a change from one nucleotide base (reference base) to another (read base), including N as an unknown or missing base. There are 5 possible reference bases (ACGTN), with 4 possible substitutions for each base, and 20 substitutions in total. The codes for all possible substitutions are stored in a substitution matrix. To restore a base, one would use the reference base and the substitution code, resolving the base via lookup in the substitution matrix.

Substitution Matrix Format

Each of the 4 possible substitutions for a given reference base is assigned a 2-bit integer code (see below) with a value ranging from 0 to 3 inclusive. The 4 2-bit codes are packed into a single byte, high 2-bits first, for each base ACGTN (minus the reference base itself). The entire substitution matrix is written as 5 such bytes, one for each reference base, also in the order ACGTN.

Substitution Code Assignment

To assign the susbtitution code for a given reference base/read base, the substitutions for each reference base may optionally be sorted by their frequencies, in descending order, with same-frequency ties broken using the fixed order ACGTN. Although sorting by substitution frequency is not required by the CRAM format, assigning substitution codes based on frequency maximizes compression by ensuring that the most frequent substitutions use the shortest possible codes.

For example, let us assume the following substitution frequencies for base A:

AC: 15%

AG: 25%

AT: 55%

AN: 5%

Then the substitution codes are:

AC: 2

AG: 1

AT: 0

AN: 3

The first byte of the substitution matrix entry for reference base A is written as a single byte, with the codes in the order CGTN: 10 01 00 11 = 147 decimal, or 0x93 in this case. This will then be followed by 4 more bytes representing substitutions for reference bases C, G, T and N.

Decode mapped read pseudocode

```
1:  procedure DecodeMappedRead
2:      feature_number ← ReadItem(FN, Integer)
3:      for i ← 1 to feature_number do
4:          DecodeFeature
5:      end for
6:      mapping_quality ← ReadItem(MQ, Integer)
7:      if container_pmap.preserve_quality_scores then
8:          for i ← 1 to read_length do
9:              quality_score ← ReadItem(QS, Integer)
10:         end for
11:     end if
12: end procedure

13: procedure DecodeFeature
14:     feature_code     ← ReadItem(FC, Integer)
15:     feature_position ← ReadItem(FP, Integer)
16:     if feature_code ='B' then
17:         base                ← ReadItem(BA, Byte)
18:         quality_score       ← ReadItem(QS, Byte)
19:     else if feature_code ='X' then
20:         substitution_code   ← ReadItem(BS, Byte)
21:     else if feature_code ='I' then
22:         inserted_bases      ← ReadItem(IN, Byte[])
23:     else if feature_code ='S' then
24:         softclip_bases      ← ReadItem(SC, Byte[])
25:     else if feature_code ='H' then
26:         hardclip_length     ← ReadItem(HC, Integer)
27:     else if feature_code ='P' then
28:         pad_length          ← ReadItem(PD, Integer)
29:     else if feature_code ='D' then
30:         deletion_length     ← ReadItem(DL, Integer)
31:     else if feature_code ='N' then
32:         ref_skip_length     ← ReadItem(RS, Integer)
33:     else if feature_code ='i' then
34:         base                ← ReadItem(BA, Byte)
35:     else if feature_code ='b' then
36:         bases               ← ReadItem(BB, Byte[])
37:     else if feature_code ='q' then
38:         quality_scores      ← ReadItem(QQ, Byte[])
39:     else if feature_code ='Q' then
40:         quality_score       ← ReadItem(QS, Byte)
41:     end if
42: end procedure
```

10.7 Unmapped reads

The CRAM record structure for unmapped reads has the following additional fields:

Data series type	Data series name	Field	Description
byte[read length]	BA	bases	the read bases
byte[read length]	QS	quality scores	the base qualities, if preserved

```
1: procedure DecodeUnmappedRead
2:     for i ← 1 to read_length do
3:         base ← ReadItem(BA, Byte)
4:     end for
5:     if container_pmap.preserve_quality_scores then
6:         for i ← 1 to read_length do
7:             quality_score ← ReadItem(QS, Byte)
8:         end for
9:     end if
10: end procedure
```

11 Reference sequences

CRAM format is natively based upon usage of reference sequences even though in some cases they are not required. In contrast to BAM format CRAM format has strict rules about reference sequences.

1. M5 (sequence MD5 checksum) field of @SQ sequence record in the BAM header is required and UR (URI for the sequence fasta optionally gzipped file) field is strongly advised. The rule for calculating MD5 is to remove any non-base symbols (like \n, sequence name or length and spaces) and upper case the rest. Here are some examples:

   ```
   > samtools faidx human_g1k_v37.fasta 1 | grep -v '^>' | tr -d '\n' | tr a-z A-Z | md5sum
   -
   1b22b98cdeb4a9304cb5d48026a85128 -
   ```

   ```
   > samtools faidx human_g1k_v37.fasta 1:10-20 |grep -v '^>' |tr -d '\n' |tr a-z A-Z |md5sum
   -
   0f2a4865e3952676ffad2c3671f14057 -
   ```

   Please note that the latter calculates the checksum for 11 bases from position 10 (inclusive) to 20 (inclusive) and the bases are counted 1-based, so the first base position is 1.

2. All CRAM reader implementations are expected to check for reference MD5 checksums and report any missing or mismatching entries. Consequently, all writer implementations are expected to ensure that all checksums are injected or checked during compression time.

3. In some cases reads may be mapped beyond the reference sequence. All out of range reference bases are all assumed to be 'N'.

4. MD5 checksum bytes in slice header should be ignored for unmapped or multiref slices.

12 Indexing

General notes

Indexing is only valid on coordinate (reference ID and then leftmost position) sorted files.

Please note that CRAM indexing is external to the file format itself and may change independently of the file format specification in the future. For example, a new type of index file may appear.

Individual records are not indexed in CRAM files, slices should be used instead as a unit of random access. Another important difference between CRAM and BAM indexing is that CRAM container header and compression header block (first block in container) must always be read before decoding a slice. Therefore two read operations are required for random access in CRAM.

Indexing a CRAM file is deemed to be a lightweight operation because it usually does not require any CRAM records to be read. Indexing information can be obtained from container headers, namely sequence id, alignment start and span, container start byte offset and slice byte offset inside the container (landmarks). The exception to this is with multi-reference containers, where the "RI" data series must be read.

CRAM index

A CRAM index is a gzipped tab delimited file containing the following columns:

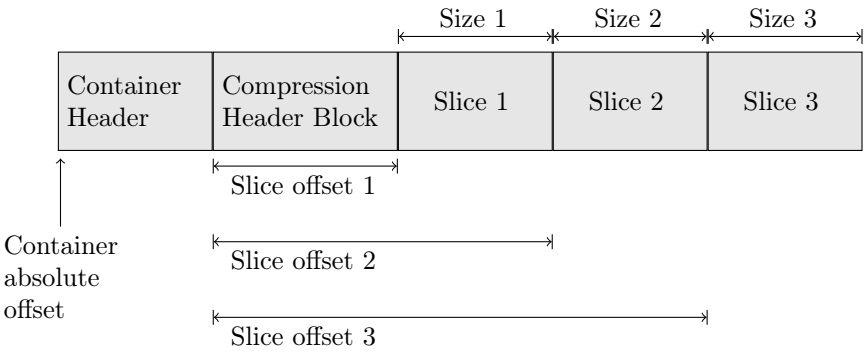
1. Reference sequence id
2. Alignment start (ignored on read for unmapped slices, set to 0 on write)
3. Alignment span (ignored on read for unmapped slices, set to 0 on write)
4. Absolute byte offset of Container header in the file.
5. Relative byte offset of the Slice header block, from the end of the container header. This is the same as the "landmark" field in the container header.
6. Slice size in bytes (including slice header and all blocks).

Each line represents a slice in the CRAM file. Please note that all slices must be listed in the index file.

Multi-reference slices may need to have multiple lines for the same slice; one for each reference contained within that slice. In this case the index reference sequence ID will be the actual reference ID (from the "RI" data series) and not -2.

Slices containing solely unmapped unplaced data (reference ID -1) still require values for all columns, although the alignment start and span will be ignored. It is recommended that they are both set to zero.

To illustrate this the absolute and relative offsets used in a three slice container are shown in the diagram below.



BAM index

BAM indexes are supported by using 4-byte integer pointers called landmarks that are stored in container header. BAM index pointer is a 64-bit value with 48 bits reserved for the BAM block start position and 16 bits reserved for the in-block offset. When used to index CRAM files, the first 48 bits are used to store the CRAM container start position and the last 16 bits are used to store the index of the landmark in the landmark array stored in container header. The landmark index can be used to access the appropriate slice.

The above indexing scheme treats CRAM slices as individual records in BAM file. This allows to apply BAM indexing to CRAM files, however it introduces some overhead in seeking specific alignment start because all preceding records in the slice must be read and discarded.

13 Encodings

13.1 Introduction

The basic idea for codings is to efficiently represent some values in binary format. This can be achieved in a number of ways that most frequently involve some knowledge about the nature of the values being encoded, for example, distribution statistics. The methods for choosing the best encoding and determining its parameters are very diverse and are not part of the CRAM format specification, which only describes how the information needed to decode the values should be stored.

Note two of the encodings (Golomb and Golomb-Rice) are listed as deprecated. These are still formally part of the CRAM specification, but have not been used by the primary implementations and may not be well supported. Therefore their use is permitted, but not recommended.

Offset

Many of the codings listed below encode positive integer numbers. An integer offset value is used to allow any integer numbers and not just positive ones to be encoded. It can also be used for monotonically decreasing distributions with the maximum not equal to zero. For example, given offset is 10 and the value to be encoded is 1, the actually encoded value would be offset+value=11. Then when decoding, the offset would be subtracted from the decoded value.

13.2 EXTERNAL: codec ID 1

Can encode types *Byte*, *Integer*.

The EXTERNAL coding is simply storage of data verbatim to an external block with a given ID. If the type is *Byte* the data is stored as-is, otherwise for *Integer* type the data is stored in ITF8.

Parameters

CRAM format defines the following parameters of EXTERNAL coding:

Data type	Name	Comment
itf8	external id	id of an external block containing the byte stream

13.3 Huffman coding: codec ID 3

Can encode types *Byte*, *Integer*.

Huffman coding replaces symbols (values to encode) by binary codewords, with common symbols having shorter codewords such that the total message of binary codewords is shorter than using uniform binary codeword lengths. The general process consists of the following steps.

- Obtain symbol code lengths.
  - If encoding:
    - Compute symbol frequencies.
    - Compute code lengths from frequencies.
  - If decoding:
    - Read code lengths from codec parameters.
- Compute canonical Huffman codewords from code lengths[5].
- Encode or decode bits as per the symbol to codeword table. Codewords have the "prefix property" that no codeword is a prefix of another codeword, enabling unambiguous decode bit by bit.

[5] `https://en.wikipedia.org/wiki/Canonical_Huffman_code`

The use of canonical Huffman codes means that we only need to store the code lengths and use the same algorithm in both encoder and decoder to generate the codewords. This is achieved by ensuring our symbol alphabet has a natural sort order and codewords are assigned in numerical order.

Important note: for alphabets with only one value, the codeword will be zero bits long. This makes the Huffman codec an efficient mechanism for specifying constant values.

Canonical code computation

1. Sort the alphabet ascending using bit-lengths and then using numerical order of the values.
2. The first symbol in the list gets assigned a codeword which is the same length as the symbol's original codeword but all zeros. This will often be a single zero ('0').
3. Each subsequent symbol is assigned the next binary number in sequence, ensuring that following codes are always higher in value.
4. When you reach a longer codeword, then after incrementing, append zeros until the length of the new codeword is equal to the length of the old codeword.

Examples

Symbol	Code length	Codeword
A	1	0
B	3	100
C	3	101
D	3	110
E	4	1110
F	4	1111

Parameters

Data type	Name	Comment
itf8[ ]	alphabet	list of all encoded symbols (values)
itf8[ ]	bit-lengths	array of bit-lengths for each symbol in the alphabet

13.4 Byte array coding

Often there is a need to encode an array of bytes where the length is not predetermined. For example the read identifiers differ per alignment record, possibly with different lengths, and this length must be stored somewhere. There are two choices available: storing the length explicitly (BYTE_ARRAY_LEN) or continuing to read bytes until a termination value is seen (BYTE_ARRAY_STOP).

Note in contrast to this, quality values are known to be the same length as the sequence which is an already known quantity, so this does not need to be encoded using the byte array codecs.

BYTE_ARRAY_LEN: codec ID 4

Can encode types *Byte[]*.

Byte arrays are captured length-first, meaning that the length of every array element is written using an additional encoding. For example this could be a HUFFMAN encoding or another EXTERNAL block. The length is decoded first followed by the data, followed by the next length and data, and so on.

This encoding can therefore be considered as a nested encoding, with each pair of nested encodings containing their own set of parameters. The byte stream for parameters of the BYTE_ARRAY_LEN encoding is therefore the concatenation of the length and value encoding parameters as described in section 2.3.

The parameter for BYTE_ARRAY_LEN are listed below:

Data type	Name	Comment
encoding<int>	lengths encoding	an encoding describing how the arrays lengths are captured
encoding<byte>	values encoding	an encoding describing how the values are captured

For example, the bytes specifying a BYTE_ARRAY_LEN encoding, including the codec and parameters, for a 16-bit X0 auxiliary tag ("X0C") may use HUFFMAN encoding to specify the length (always 2 bytes) and an EXTERNAL encoding to store the value to an external block with ID 200.

Bytes	Meaning
`0x04`	BYTE_ARRAY_LEN codec ID
`0x0a`	10 remaining bytes of BYTE_ARRAY_LEN parameters
`0x03`	HUFFMAN codec ID, for aux tag lengths
`0x04`	4 more bytes of HUFFMAN parameters
`0x01`	Alphabet array size = 1
`0x02`	alphabet symbol; (length = 2)
`0x01`	Codeword array size = 1
`0x00`	Code length = 0 (zero bits needed as alphabet is size 1)
`0x01`	EXTERNAL codec ID, for aux tag values
`0x02`	2 more bytes of EXTERNAL parameters
`0x80 0xc8`	ITF8 encoding for block ID 200

BYTE_ARRAY_STOP: codec ID 5

Can encode types *Byte[]*.

Byte arrays are captured as a sequence of bytes terminated by a special stop byte. The data returned does not include the stop byte itself. In contrast to BYTE_ARRAY_LEN the value is always encoded with EXTERNAL so the parameter is an external id instead of another encoding.

Data type	Name	Comment
byte	stop byte	a special byte treated as a delimiter
itf8	external id	id of an external block containing the byte stream

13.5 Beta coding: codec ID 6

Can encode types *Integer*.

Definition

Beta coding is a most common way to represent numbers in *binary notation* and is sometimes referred to as binary coding. The decoder reads the specified fixed number of bits (most significant first) and subtracts the offset value to get the decoded integer.

Parameters

CRAM format defines the following parameters of beta coding:

Data type	Name	Comment
itf8	offset	offset is subtracted from each value during decode
itf8	length	the number of bits used

Examples

If we have integer values in the range 10 to 15 inclusive, the largest value would traditionally need 4 bits, but with an offset of -10 we can hold values 0 to 5, using a fixed size of 3 bits. Using fixed Offset and Length coming

from the beta parameters, we decode these values as:

Offset	Length	**Bits**	**Value**
-10	3	000	10
-10	3	001	11
-10	3	010	12
-10	3	011	13
-10	3	100	14
-10	3	101	15

13.6 Subexponential coding: codec ID 7

Can encode types *Integer*.

Definition

Subexponential coding[6] is parametrized by a non-negative integer k. For values $n < 2^{k+1}$ subexponential coding produces codewords identical to Rice coding [7]. For larger values it grows logarithmically with n.

Encoding

1. Add *offset* to n.
2. Determine u and b values from n

$$b = \begin{cases} k & \text{if } n < 2^k \\ \lfloor log_2 n \rfloor & \text{if } n \geq 2^k \end{cases} \qquad u = \begin{cases} 0 & \text{if } n < 2^k \\ b - k + 1 & \text{if } n \geq 2^k \end{cases}$$

3. Write u in unary form; u 1 bits followed by a single 0 bit.
4. Write the bottom b-bits of n in binary form.

Decoding

1. Read u in unary form, counting the number of leading 1s (prefix) in the codeword (discard the trailing 0 bit).
2. Determine n via:
   (a) if $u = 0$ then read n as a k-bit binary number.
   (b) if $u \geq 1$ then read x as a $(u + k - 1)$-bit binary. Let $n = 2^{u+k-1} + x$.
3. Subtract *offset* from n.

[6] Fast progressive lossless image compression, Paul G. Howard and Jeffrey Scott Vitter, 1994. `http://www.ittc.ku.edu/~jsv/Papers/HoV94.progressive_FELICS.pdf`

[7] `https://en.wikipedia.org/wiki/Golomb_coding#Rice_coding`

Examples

Number	Codeword, k=0	Codeword, k=1	Codeword, k=2
0	0	00	000
1	10	01	001
2	1100	100	010
3	1101	101	011
4	111000	11000	1000
5	111001	11001	1001
6	111010	11010	1010
7	111011	11011	1011
8	11110000	1110000	110000
9	11110001	1110001	110001
10	11110010	1110010	110010

Parameters

Data type	Name	Comment
itf8	offset	offset is subtracted from each value during decode
itf8	k	the order of the subexponential coding

13.7 Gamma coding: codec ID 9

Can encode types *Integer*.

Definition

Elias gamma code is a prefix encoding of positive integers. This is a combination of unary coding and beta coding. The first is used to capture the number of bits required for beta coding to capture the value.

Encoding

1. Write it in binary.
2. Subtract 1 from the number of bits written in step 1 and prepend that many zeros.
3. An equivalent way to express the same process:
4. Separate the integer into the highest power of 2 it contains ($2N$) and the remaining N binary digits of the integer.
5. Encode N in unary; that is, as N zeroes followed by a one.
6. Append the remaining N binary digits to this representation of N.

Decoding

1. Read and count 0s from the stream until you reach the first 1. Call this count of zeroes N.
2. Considering the one that was reached to be the first digit of the integer, with a value of $2N$, read the remaining N digits of the integer.

Examples

Value	Codeword
1	1
2	010
3	011
4	00100

Parameters

Data type	Name	Comment
itf8	offset	offset to subtract from each value after decode

13.8 DEPRECATED: Golomb coding: codec ID 2

Can encode types *Integer*.

Note this codec has not been used in any known CRAM implementation since before CRAM v1.0. Nor is it implemented in some of the major software. Therefore its use is not recommended.

Definition

Golomb encoding is a prefix encoding optimal for representation of random positive numbers following geometric distribution.

Encoding

1. Fix the parameter M to an integer value.
2. For N, the number to be encoded, find
   (a) quotient $q = \lfloor N/M \rfloor$
   (b) remainder $r = N \bmod M$
3. Generate Codeword
   (a) The Code format : <Quotient Code><Remainder Code>, where
   (b) Quotient Code (in unary coding)
      i. Write a q-length string of 1 bits
      ii. Write a 0 bit
   (c) Remainder Code (in truncated binary encoding)
   Set $b = \lceil log_2(M) \rceil$
      i. If $r < 2^b - M$ code r as plain binary using $b - 1$ bits.
      ii. If $r \geq 2^b - M$ code the number $r + 2^b - M$ in plain binary representation using b bits.

Decoding

1. Read q via unary coding: count the number of 1 bits and consume the following 0 bits.
2. Set $b = \lceil log_2(M) \rceil$
3. Read r via $b - 1$ bits of binary coding
4. If $r \geq 2^b - M$
   (a) Read 1 single bit, x.
   (b) Set $r = r * 2 + x - (2^b - M)$
5. Value is $q * M + r - offset$

Examples

Number	Codeword, M=10, (thus b=4)
0	0000
4	0100
10	10000
26	1101100
42	11110010

Parameters

Golomb coding takes the following parameters:

Data type	Name	Comment
itf8	offset	offset is added to each value
itf8	M	the golomb parameter (number of bins)

13.9 DEPRECATED: Golomb-Rice coding: codec ID 8

Can encode types *Integer*.

Note this codec has not been used in any known CRAM implementation since before CRAM v1.0. Nor is it implemented in some of the major software. Therefore its use is not recommended.

Golomb-Rice coding is a special case of Golomb coding when the M parameter is a power of 2. The reason for this coding is that the division operations in Golomb coding can be replaced with bit shift operators as well as avoiding the extra $r < 2^b - M$ check.

14 External compression methods

External encoding operates on bytes only. Therefore any data series must be translated into bytes before sending data into an external block. The following agreements are defined.

Integer values are written as ITF8, which then can be translated into an array of bytes.

Strings, like read name, are translated into bytes according to UTF8 rules. In most cases these should coincide with ASCII, making the translation trivial.

14.1 Gzip

The Gzip specification is defined in RFC 1952. Gzip in turn is an encapsulation on the Deflate algorithm defined in RFC 1951.

14.2 Bzip2

Bzip2 is a compression method utilising the Burrows Wheeler Transform, Move To Front transform, Run Length Encoding and a Huffman entropy encoder. It is often superior to Gzip for textual data.

An informal format specification exists:
`https://github.com/dsnet/compress/blob/master/doc/bzip2-format.pdf`

14.3 LZMA

LZMA is the Lempel-Ziv Markov chain algorithm. CRAM uses the xz Stream format to encapsulate this algorithm, as defined in `https://tukaani.org/xz/xz-file-format.txt`.

14.4 rANS codec

rANS is the range-coder variant of the Asymmetric Numerical System[8].

The structure of the external rANS codec consists of several components: meta-data consisting of compression-order, and compressed and uncompressed sizes; normalised frequencies of the alphabet systems to be encoded, either in Order-0 or Order-1 context; and the rANS encoded byte stream itself.

Here "Order" refers to the number of bytes of context used in computing the frequencies. It will be 0 or 1. Ignoring punctuation and space, an Order-0 analysis of English text may observe that 'e' is the most common letter (12-13%), and that 'u' occurs only around 2.5% of the time. If instead we consider the frequency of a letter in the context of one previous letter (Order-1) then these statistics change considerably; we know that if the previous letter was 'q' then 'e' becomes a rare letter while 'u' is the most likely.

These observed frequencies are directly related to the amount of storage required to encode a symbol (e.g. an alphabet letter)[9].

14.4.1 rANS compressed data structure

A compressed data block consists of the following logical parts:

Value data type	Name	Description
byte	order	the order of the codec, either 0 or 1
int	compressed size	the size in bytes of frequency table and compressed blob
int	data size	raw or uncompressed data size in bytes
byte[]	frequency table	byte frequencies of input data written using RLE
byte[]	compressed blob	compressed data

14.4.2 Frequency table

The alphabet used here is simply byte values, so a maximum of 256 symbols as some values may not be present.

The symbol frequency table indicates which symbols are present and what their relative frequencies are. The total sum of symbol frequencies are normalised to add up to 4095.

Formally, this is an ordered alphabet $\mathbb{A}$ containing symbols s where s_i with the i-th symbol in $\mathbb{A}$, occurring with the frequency $freq_i$.

Order-0 encoding

The normalised symbol frequencies are then written out as {symbol, frequency} pairs in ascending order of symbol (0 to 255 inclusive). If a symbol has a frequency of 0 then it is omitted.

To avoid storing long consecutive runs of symbols if all are present (eg a-z in a long piece of English text) we use run-length-encoding on the alphabet symbols. If two consecutive symbols have non-zero frequencies then a counter of how many other non-zero frequency consecutive symbols is output directly after the second consecutive symbol, with that many symbols being subsequently omitted.

For example for non-zero frequency symbols 'a', 'b', 'c', 'd' and 'e' we would write out symbol 'a', 'b' and the value 3 (to indicate 'c', 'd' and 'e' are also present).

The frequency is output after every symbol (whether explicit or implicit) using ITF8 encoding. This means that frequencies 0-127 are encoded in 1 byte while frequencies 128-4095 are encoded in 2 bytes.

[8] J. Duda, *Asymmetric numeral systems: entropy coding combining speed of Huffman coding with compression rate of arithmetic coding*, `http://arxiv.org/abs/1311.2540`

[9] C.E. Shannon, *A Mathematical Theory of Communication*, Bell System Technical Journal, vol. 27, pp. 379-423, 623-656, July, October, 1948

Finally the symbol 0 is written out to indicate the end of the symbol-frequency table.

As an example, take the string `abracadabra`.

Symbol frequency:

Symbol	Frequency
a	5
b	2
c	1
d	1
r	2

Normalised to sum to 4095:

Symbol	Frequency
a	1863
b	744
c	372
d	372
r	744

Encoded as:

```
0x61      0x87 0x47      # 'a'           <1863>
0x62 0x02 0x82 0xe8      # 'b' <+2: c,d>  <744>
          0x81 0x74      # 'c' (implicit) <372>
          0x81 0x74      # 'd' (implicit) <372>
0x72      0x82 0xe8      # 'r'            <744>
0x00                     # <0>
```

Order-1 encoding

To encode Order-1 statistics typically requires a larger table as for an N sized alphabet we need to potentially store an NxN matrix. We store these as a series of Order-0 tables.

We start with the outer context byte, emitting the symbol if it is non-zero frequency. We perform the same run-length-encoding as we use for the Order-0 table and end the contexts with a nul byte. After each context byte we emit the Order-0 table relating to that context.

One last caveat is that we have no context for the first byte in the data stream (in fact for 4 equally spaced starting points, see "interleaving" below). We use the ASCII value ('\0') as the starting context and so need to consider this in our frequency table.

Consider `abracadabraabracadabraabracadabraabracadabra` as example input.

Observed Order-1 frequencies:

Context	Symbol	Frequency
\0	a	4
a	a	3
	b	8
	c	4
	d	4
b	r	8
c	a	4
d	a	4
r	a	8

Normalised (per Order-0 statistics):

Context	Symbol	Frequency
\0	a	4095
a	a	646
	b	1725
	c	862
	d	862
b	r	4095
c	a	4095
d	a	4095
r	a	4095

Encoded as:

```
0x00                # '\0' context
0x61      0x8f 0xff # a  <4095>
0x00                # end of Order-0 table

0x61                # 'a' context
0x61      0x82 0x86 # a            <646>
0x62 0x02 0x86 0xbd # b <+2: c,d> <1725>
          0x83 0x5e # c (implicit) <862>
          0x83 0x5e # d (implicit) <862>
0x00                # end of Order-0 table

0x62 0x02           # 'b' context, <+2: c, d>
```

```
0x72      0x8f 0xff  # r <4095>
0x00                 # end of Order-0 table

                     # 'c' context (implicit)
0x61      0x8f 0xff  # a <4095>
0x00                 # end of Order-0 table

                     # 'd' context (implicit)
0x61      0x8f 0xff  # a <4095>
0x00                 # end of Order-0 table

0x72                 # 'r' context
0x61      0x8f 0xff  # a <4095>
0x00                 # end of Order-0 table

0x00                 # end of contexts
```

14.4.3 rANS entropy encoding

The encoder takes a symbol s and a current state x (initially zero) to produce a new state x' with function C.

$$x' = C(s, x)$$

The decoding function D is the inverse of C such that $C(D(x)) = x$.

$$D(x') = (s, x)$$

The entire encoded message can be viewed as a series of nested C operations, with decoding yielding the symbols in reverse order, much like popping items off a stack. This is where the asymmetric part of ANS comes from.

As we encode into x the value will grow, so for efficiency we ensure that it always fits within known bounds. This is governed by

$$L \leq x < bL - 1$$

where b is the base and L is the lower-bound.

We ensure this property is true before every use of C and after every use of D. Finally to end the stream we flush any remaining data out by storing the end state of x.

Implementation specifics

We use an unsigned 32-bit integer to hold x. In encoding it is initialised to zero. For decoding it is read little-endian from the input stream.

Recall $freq_i$ is the frequency of the i-th symbol s_i in alphabet $\mathbb{A}$. We define $cfreq_i$ to be cumulative frequency of all symbols up to but not including s_i:

$$cfreq_i = \begin{cases} 0 & \text{if } i < 1 \\ cfreq_{i-1} + freq_{i-1} & \text{if } i \geq 1 \end{cases}$$

We have a reverse lookup table $cfreq\_to\_sym_c$ from 0 to 4095 (0xfff) that maps a cumulative frequency c to a symbol s.

$$cfreq\_to\_sym_c = s_i \quad where \quad c: \ cfreq_i \leq c < cfreq_i + freq_i$$

The $x' = C(s, x)$ function used for the $i - thsymbol$s is:

$$x' = (x/freq_i) \times \texttt{0x1000} + cfreq_i + (x \bmod freq_i)$$

The $D(x') = (s, x)$ function used to produce the i-th symbol s and a new state x is:

$$c = x' \& \texttt{0xfff}$$
$$s_i = cfreq\_to\_sym_c$$
$$x = freq_i(x'/\texttt{0x1000}) + c - cfreq_i$$

Most of these operations can be implemented as bit-shifts and bit-AND, with the encoder modulus being implemented as a multiplication by the reciprocal, computed once only per alphabet symbol.

We use $L =$ `0x800000` and $b = 256$, permitting us to flush out one byte at a time (encoded and decoded in reverse order).

Before every encode $C(s, x)$ we renormalise x, shifting out the bottom 8 bits of x until $x < \texttt{0x80000} \times freq_i$. After finishing encoding we flush 4 more bytes (lowest 8-bits first) from x.

After every decoded $D(x')$ we renormalise x', shifting in the bottom 8 bits until $x \geq \texttt{0x800000}$.

Interleaving

For efficiency, we interleave 4 separate rANS codecs at the same time[10]. For the Order-0 codecs these simply encode or decode the 4 neighbouring bytes in cyclic fashion using interleaved codec 1, 2, 3 and 4, sharing the same output buffer (so the output bytes get interleaved).

For the Order-1 codec we cannot do this as we need to know the previous byte value as the context for the next byte. Therefore split the input data into 4 approximately equal sized fragments[11] starting at 0, $\lfloor len/4 \rfloor$, $\lfloor len/4 \rfloor \times 2$ and $\lfloor len/4 \rfloor \times 3$. Each Order-1 codec operates in a cyclic fashion as with Order-0, all starting with 0 as their state and sharing the same output buffer. Any remainder, when the input buffer is not divisible by 4, is processed at the end by the 4th rANS state.

We do not permit Order-1 encoding of data streams smaller than 4 bytes.

[10] F. Giesen, *Interleaved entropy coders*, `http://arxiv.org/abs/1402.3392`

[11] This was why the '\0' → 'a' context in the example above had a frequency of 4 instead of 1.

rANS decode pseudocode

A naïve implementation of a rANS decoder, follows. This pseudocode is for clarity only and is not expected to be performant and we would normally rewrite this to use lookup tables for maximum efficiency. The function ReadByte below is undefined, but is expected to fetch the next single unsigned byte from an unspecified input source. Similarly for ReadITF8 (variable size inetger) and ReadUint32 (32-bit unsigned integer in little endian format).

For brevity, we have also omitted error checking and array bounds checks.

The interpretation of some pseudocode syntax is listed below.

String	Meaning
$x << y$	logical shift left of x by y bits.
$x >> y$	logical shift right of x by y bits.
x & y	bit-wise AND of x and y.
V_i	Element i of vector V.
	The entire vector V may be passed into a function.
$W_{i,j}$	Element i, j of two-dimensional vector W.
	The entire vector W or a one dimensional slice W_i (of size j) may be passed into a function.

```
1:  procedure RansDecode(input, output)
2:      order  ← ReadByte                          ▷ Implicit read from input
3:      n_in   ← ReadUint32
4:      n_out  ← ReadUint32
5:
6:      if order = 0 then
7:          RansDecode0(output, n_out)
8:      else
9:          RansDecode1(output, n_out)
10:     end if
11: end procedure
```

rANS order-0

The Order-0 code is the simplest variant. Here we also define some of the functions for manipulating the rANS state, which are shared between Order-0 and Order-1 decoders.

```
    (Reads a table of Order-0 symbol frequencies F_i
    (and sets the cumulative frequency table C_{i+1} = C_i + F_i)
1:  procedure ReadFrequencies0(F, C)
2:      sym ← ReadByte                             ▷ Next alphabet symbol
3:      last_sym ← sym
4:      rle ← 0
5:      repeat
6:          f ← ReadITF8
7:          F_sym ← f
8:          if rle > 0 then
9:              rle   ← rle − 1
10:             sym   ← sym + 1
11:         else
12:             sym ← ReadByte
13:             if sym = last_sym + 1 then
14:                 rle ← ReadByte
15:             end if
16:         end if
17:         last_sym ← sym
18:     until sym = 0
        (Compute cumulative frequencies C_i from F_i)
```

```
    C_0 ← 0
    for i ← 0 to 255 do
        C_{i+1} ← C_i + F_i
    end for
end procedure

(Bottom 12 bits of our rANS state R are our frequency)
function RansGetCumulativeFreq(R)
    return R & 0xfff
end function

(Convert frequency to a symbol. Find s such that C_s ≤ f < C_{s+1})
(We would normally implement this via a lookup table)
function RansGetSymbolFromFreq(C, f)
    s ← 0
    while f >= C_{s+1} do
        s ← s + 1
    end while
    return s
end function

(Compute the next rANS state R given frequency f and cumulative freq c)
function RansAdvanceStep(R, c, f)
    return f × (R >> 12) + (R & 0xfff) − c
end function

(If too small, feed in more bytes to the rANS state R)
function RansRenorm(R)
    while R < (1 << 23) do
        R ← (R << 8)+ ReadByte
    end while
    return R
end function

procedure RansDecode0(output, nbytes)
    ReadFrequencies0(F, C)                          ▷ Creates F and C vectors
    for j ← 0 to 3 do
        R_j ← ReadUint32                            ▷ Unsigned 32-bit little endian
    end for
    i ← 0
    while i < nbytes do
        for j ← 0 to 3 do
            if i + j ≥ nbytes then return
            end if
            f ← RansGetCumulativeFreq(R_j)
            s ← RansGetSymbolFromFreq(C, f)
            output_{i+j} ← s
            R_j ← RansAdvanceStep(R_j, C_s, F_s)
            R_j ← RansRenorm(R_j)
        end for
        i ← i + 4
    end while
end procedure
```

rANS order-1

As described above, the decode logic is very similar to rANS Order-0 except we have a two dimensional array of frequencies to read and the decode uses the last character as the context for decoding the next one. In the

pseudocode we demonstrate this by using two dimensional vectors $C_{i,j}$ and $F_{i,j}$. For simplicity, we reuse the Order-0 code by referring to C_i and F_i of the 2D vectors to get a single dimensional vector that operates in the same manner as the Order-0 code. This is not necessarily the most efficient implementation.

Note the code for dealing with the remaining bytes when an output buffer is not an exact multiple of 4 is less elegant in the Order-1 code. This is correct, but it is unfortunately a design oversight.

```
    (Reads a table of Order-1 symbol frequencies F_{i,j}
    (and sets the cumulative frequency table C_{i,j+1} = C_{i,j} + F_{i,j})
 1: procedure ReadFrequencies1(F, C)
 2:     sym ← ReadByte                                   ▷ Next alphabet symbol
 3:     last_sym ← sym
 4:     rle ← 0
 5:     repeat
 6:         ReadFrequencies0(F_sym, C_sym)
 7:         if rle > 0 then
 8:             rle  ← rle − 1
 9:             sym ← sym + 1
10:         else
11:             sym ← ReadByte
12:             if sym = last_sym + 1 then
13:                 rle ← ReadByte
14:             end if
15:         end if
16:         last_sym ← sym
17:     until sym = 0
18: end procedure

19: procedure RansDecode1(output, nbytes)
20:     ReadFrequencies1(F, C)                           ▷ Creates 2D F and C vectors
21:     for j ← 0 to 3 do
22:         R_j ← ReadUint32                             ▷ Unsigned 32-bit little endian
23:         L_j ← 0
24:     end for
25:     i ← 0
26:     while i < ⌊nbytes/4⌋ do
27:         for j ← 0 to 3 do
28:             f ← RansGetCumulativeFreq(R_j)
29:             s ← RansGetSymbolFromFreq(C_{L_j}, f)
30:             output_{i+j×⌊nbytes/4⌋} ← s
31:             R_j ← RansAdvanceStep(R_j, C_{L_j,s}, F_{L_j,s})
32:             R_j ← RansRenorm(R_j)
33:             L_j ← s
34:         end for
35:         i ← i + 1
36:     end while
        (Now deal with the remainder if buffer size is not a multiple of 4,)
        (using rANS state 3 exclusively.)
37:     i ← 4 × i
38:     while i < nbytes do
39:         f ← RansGetCumulativeFreq(R_3)
40:         s ← RansGetSymbolFromFreq(C_{L_3}, f)
41:         output_{i+3×⌊nbytes/4⌋} ← s
42:         R_3 ← RansAdvanceStep(R_3, C_{L_3,s}, F_{L_3,s})
43:         R_3 ← RansRenorm(R_3)
44:         L_3 ← s
45:         i ← i + 1
46:     end while
47: end procedure
```

15 Appendix

15.1 Choosing the container size

CRAM format does not constrain the size of the containers. However, the following should be considered when deciding the container size:

- Data can be compressed better by using larger containers
- Random access performance is better for smaller containers
- Streaming is more convenient for small containers
- Applications typically buffer containers into memory

We recommend 1 megabyte containers. They are small enough to provide good random access and streaming performance while being large enough to provide good compression. 1 MB containers are also small enough to fit into the L2 cache of most modern CPUs.

Some simplified examples are provided below to fit data into 1 MB containers.

Unmapped short reads with bases, read names, recalibrated and original quality scores

We have 10,000 unmapped short reads (100bp) with read names, recalibrated and original quality scores. We estimate 0.4 bits/base (read names) + 0.4 bits/base (bases) + 3 bits/base (recalibrated quality scores) + 3 bits/base (original quality scores) $\approx$ 7 bits/base. Space estimate is $10\,000 \times 100 \times 7$ bits ≈ 0.9 MB. Data could be stored in a single container.

Unmapped long reads with bases, read names and quality scores

We have 10,000 unmapped long reads (10kb) with read names and quality scores. We estimate: 0.4 bits/base (bases) + 3 bits/base (original quality scores) $\approx$ 3.5 bits/base. Space estimate is $10\,000 \times 10\,000 \times 3.5$ bits $\approx$ 42 MB. Data could be stored in 42×1 MB containers.

Mapped short reads with bases, pairing and mapping information

We have 250,000 mapped short reads (100bp) with bases, pairing and mapping information. We estimate the compression to be 0.2 bits/base. Space estimate is $250\,000 \times 100 \times 0.2$ bits ≈ 0.6 MB. Data could be stored in a single container.

Embedded reference sequences

We have a reference sequence (10Mb). We estimate the compression to be 2 bits/base. Space estimate is $10\,000\,000 \times 2$ bits ≈ 2.4 MB. Data could be written into three containers: 1 MB + 1 MB + 0.4 MB.