Engineering Relative Compression of Genomes

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Abstract. Technology progress in DNA sequencing boosts the genomic database growth at faster and faster rate. Compression, accompanied with random access capabilities, is the key to maintain those huge amounts of data. In this paper we present an LZ77-style compression scheme for relative compression of multiple genomes of the same species. While the solution bears similarity to known algorithms, it offers significantly higher compression ratios at compression speed over a order of magnitude greater. One of the new successful ideas is augmenting the reference sequence with phrases from the other sequences, making more LZ-matches available.

Keywords: DNA compression, relative compression, genome databases.

1 Introduction

The old saying “Time is money” remains true in IT systems, where time savings are often accomplished by means of data compression techniques, especially if they are adopted to the characteristics of processed data and coupled with procedures for fast search or random access directly over the compressed representation. Data compression not only saves the storage but also reduces transmission times and can even let extracting particular pieces of information faster. The last phenomenon has long been observed in database communities, and can be attributed to the fact that more compact form reduces the number of memory accesses, particularly important in the hierarchical computer architectures (disks, RAM, caches of different levels, CPU registers), so common these days.

One of the main tasks of bioinformatics is to collect and analyze huge genomic data, typically obtained with sequencing methods. Rapid development in DNA sequencing technologies led to drastic growth of data publicly available in sequence databases, e.g., GenBank at NCBI or 1000 Genomes project, to name a few. To illustrate this progress, we note that the first draft sequence of the human genome was published in 2001, and now, a decade later, the cost of acquiring a single (individual) human genome is below $10,000 and is still expected

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to drop significantly in the next few years. Storing genetic sequences of many individuals of the same species promises new discoveries for the whole field of biology, and low cost of acquiring an individual human genome gives way to “personalized medicine”, making use of one’s individual genetic profile.

It should be stressed that DNA sequences within the same species are both large and highly repetitive. For example, only about 0.1% of the 3 GB human genome is specific; the rest is common to all humans. This poses interesting challenges to efficient storage and fast access to those data. Most classic data compression techniques fail to recognize this tremendous redundancy, simply because finding matches with e.g. an LZ77 variant with a sliding window would require a multi-gigabyte buffer, not counting the match-finding structures. Using a context-based statistical coding (e.g., PPM) may efficiently exploit the repetitions only if the considered context is long enough, otherwise the context statistics are polluted with “accidental” matches. This phenomenon is specific for genomic data, which are almost incompressible within a single individual, which also means that short subsequences, e.g., shorter than 10 symbols, are very likely to occur many times in seemingly random places. On the other hand, maintaining a high-order statistical model over a large collection of data may be prohibitive due to enormous memory requirements.

Interestingly, also most of the DNA-specialized compressors from the literature are not appropriate to handle modern genomic databases. There are a number of reasons for that: (i) most of them focus on compression ratio, not on compression and decompression speed or the memory use during the compression process; from those reasons those cannot be practically run on sequences larger than, say, several megabytes; (ii) considering the compression ratio, most effort has been put to succinctly represent a single genome (which is believed to be almost incompressible anyway, hence only tiny improvements were at the stake), not to be particularly efficient in detecting inter-genome redundancy; (iii) most of the algorithms do not support extracting a range of symbols from the middle of the compressed stream. Only since around 2009 we can observe a surge of interest in practical, multi-sequence oriented, DNA compressors, usually coupled with random access capabilities and sometimes also offering indexed search. We are going to take a close look at those solutions in the next section.

A different, even if related, problem is compression of large sets of sequence reads (usually obtained from Solid, Illumina or 454 sequencers). Those data contain three streams: Title lines, DNA symbols and quality scores, and in the main stream it is possible to look for LZ77 matches only over those DNA symbols for which the quality scores are high enough (i.e., in non-noisy areas) to improve compression ratio, compression speed and reduce memory requirements [7].

In this work, we propose an algorithm for effective compression of multiple genomic (DNA) sequences of the same species and show experimental results suggesting its supremacy over existing solutions. Although the general framework of relative LZ77-style compression is not new in this context, we add some new ideas to the existing algorithms.
2 Related work

The first DNA-specific compressor was BioCompress [10], presented in 1993 by Grumbach and Tahi. It was basically an LZ77 compression scheme, but also with support for reverse complement repeats. Since then, more than ten other compressors have been published, and the new ideas involved encoding approximate repeats, order-2 arithmetic encoding for literals, forming probability distributions for each symbol on the basis of approximate partial matches, combining predictions from a panel of experts, off-line substitution of repeated substrings, and more (the references can be found in the survey [9]). Unfortunately, most of the algorithms presented in the literature are computationally intensive and have been tested only on small datasets (on the order of a few MB’s or less)\footnote{\textit{In case of many papers on DNA compression, much longer sequences, to experiment with, were not yet available at their publication time.}}.

Probably the first DNA compressors running at acceptable speed were the variants proposed by Manzini and Rastero [18]. They resigned from searching for approximate repeats, as a major culprit in causing the slowness of many other solutions in this area. Instead, their algorithms are able to detect exact and reverse complement repeats and are (implicitly) efficient on approximate matches thanks to making use of frequent regularities in match locations of successive matches. Moreover, the stronger (and slower) variants, dna2 and dna3, apply order-2 or order-3 arithmetic encoding of some components in their sequence parsing.

In 2009, the first algorithms focused on compressing DNA sequences from the same species have appeared [4,1], followed soon by more mature proposals [17,5,14,15,11,12]. We present them in the following paragraphs.

Mäkinen et al. [17] added new functionalities to compressed DNA sequences: \textit{display} (which can also be called the random access functionality) returning the substring specified by its start and end position, \textit{count} telling the number of times the given pattern occurs in the text, and \textit{locate} listing the positions of the pattern in the text. Although those operations are not new in full-text indexes (possibly also compressed), the authors noticed that the existing general solutions, paying no attention to long repeats in the input (for the survey of compressed full-text indexes, see [19]), are not very effective here and they proposed novel self-indexes\textsuperscript{3} for the considered problem.

Claude et al. [5] pointed out that the full-text indexes from [17], albeit fast in counting, are relatively slow in extracting the locations of the matches, a feature shared by all compressed indexes based on the \textit{Burrows–Wheeler transform} [2,19]. They proposed two schemes. One is an inverted index on \textit{q}-grams, tailored to the repetitive nature of the input data by using a strong LZ77-style compressor (7-zip) on byte-encoded differential posting lists. The text itself, i.e., the concatenation of all individual sequences, is compressed with a popular grammar-based algorithm Re-Pair [16], capable of extracting arbitrary substrings fast. The other scheme is a purely grammar-based self-index. The inverted index offers excellent space-time tradeoffs (on real data, not in the worst case),
but can basically work with substrings of fixed length $q$ (we believe it is possible to heuristically adapt this scheme to any substring length, but this issue is not discussed in the cited work). The grammar-based self-index is more elegant and can work with any substring length, but uses significantly more space, is slower and needs a large amount of RAM in the index build phase.

Kuruppu et al. [14], in their earlier work, propose a surprisingly simple yet quite efficient compression scheme with random access (it is not an index though). They choose one of the sequences as the reference sequence and compress it with a self-index (in the experiments in the cited work, however, a general-purpose compressor, 7-zip, with no random access capabilities, was used). The other sequences are greedily parsed into LZ-factors of the reference sequence. Some extra data structure is added to provide random access.

The work [15] from the same team is a follow-up paper, presenting a stronger LZ77-style algorithm. In this work, however, the authors’ implementation is not augmented with extra data enabling random access. Still, it is mentioned how it can be (easily) added and we are convinced the extra penalty in space will be small. As their algorithm is a departure point of our proposal, we describe it more extensively in the next section.

Kreft and Navarro [11] presented an innovative LZ77 variant called LZ-End enabling extraction of arbitrary phrases in optimal time complexity. While this algorithm has many applications, one of the immediate ones is for compressing DNA sequences, combining quite good compression ratios with very fast access.

In a recent work from the same authors [12], a self-index based on the LZ-End idea is developed, with less than 3 times the space needed for the compressed sequence itself. The reported pattern finding rate is below 30 microseconds per occurrence, on a DNA collection and patterns of length 10. This is the first self-index based on an algorithm from the LZ77 family.

3 RLZ-opt in brief

Repetitive data are naturally well handled by compressors from the LZ77 [20] family. The feature common to all those algorithms is to parse the input data into a sequence of matches and literals, usually entropy-encoded, e.g. with Huffman coding. An LZ-match (also called a factor) is a reference to an earlier occurrence of the same subsequence, expressed as the distance (offset) to that earlier subsequence and its length. If, at the current position, there is no (satisfactory) match, a literal is emitted and the compressor moves forward by one symbol. We note that greedy parsing, i.e., always choosing the longest match, is usually a bad strategy. Parsing the input into matches and literals is a vital factor for the compression ratio and the problem of optimal parsing is solved only under a simplified assumption of known cost functions for encoding match offsets and match lengths [8].

RLZ-opt, the algorithm from Kuruppu et al. [15], follows the LZ77 route, but has some features not often met in that family of compressors. First, it is designed for genomic sequences, where random access to an individual sequence
(even better, only a small snippet of it) is a welcome feature. For this reason, one of the sequences in the input collection is chosen (and encoded) as the reference sequence, while all the other sequences are encoded with relation to the first one, but without any cross-references to one another. Second, matches are found thanks to a suffix array, which is unusual, since most LZ77 compressors make use of a hash array (or, more rarely, a search tree). Building a suffix array is relatively slow, but this structure facilitates effective non-greedy parsing.

The RLZ-opt algorithm is based on several principles. A lookahead buffer is used for each considered location in the text, which basically means that if the match at position $i + 1$ is longer than the match at position $i$, a literal may be emitted at position $i$ followed by a match. This idea is however extended, not to a fixed-size buffer, but to a buffer whose size changes dynamically, depending on the length of the currently longest match found (details can be found in the cited work). Another principle is refraining from LZ-encoding of short matches; they are encoded as a run of literals. This is an idea known in the DNA compression community, see e.g. [13]. Although the match length threshold is fixed (chosen arbitrarily), this solution gives a fair boost in compression ratio. As a last thing, they notice that long and short (i.e., those encoded as literals) matches tend to appear alternatively, and the offset of the long match can usually be predicted quite well from the offset of the previous long match. Those offsets (match positions) usually form long increasing sequences, hence an algorithm for solving the classic longest increasing subsequence (LISS) problem is used to detecting those matches (called LISS factors), whose offsets are then cheaply encoded. The LISS factors are often followed by single-symbol factors which represent single nucleotide polymorphisms (SNPs) in DNA. We note that prediction of the next factor position is another incarnation of the implicit approximate repeat detection idea, again known from [18].

The parsing products in RLZ-opt, e.g. the match lengths and run-of-literals lengths, are compacted with Golomb encoding.

4 Our algorithm

As said, our algorithm is essentially similar to RLZ-opt [15], and the main differences are:

1. in addition to the reference sequence we use extra reference phrases from the other sequences for which matches exist,
2. our LZ-parsing is different (details later),
3. our LZ match-finding procedure is based on hashing rather than a suffix array, with great benefits for compression speed and also adding some flexibility helping to reduce memory requirements during the compression,
4. Huffman coding rather than Golomb coding is used in representation of various statistics data,
5. compression is performed in blocks (with shared Huffman models), to facilitate random access.
Even without the main novelty of our scheme, adding extra reference phrases, the algorithm (without random access capabilities and segmentation to blocks, for a fair comparison) produces archives smaller than the Kuruppu et al. ones by from 23% to 28%. We attribute this to the chosen LZ-parsing, which in particular aggressively looks for a certain class of approximate matches, and Huffman encoding, not only more compact than Golomb, but also applied to more byproducts of the compression process. Incorporating the idea of extra reference phrases increases the reduction to 26% to 33%. First we present the algorithm in the basic form, without the extra reference phrases and then explain this enhancement.

4.1 Basic variant

For clarity of exposition we assume that the input data are not partitioned into blocks. One of the input sequences is chosen as the reference sequence and all the other sequences are encoded relative to it. Let us then assume that $T^1$ is the reference sequence, and $T^i$ for $2 \leq i \leq r$ are the following sequences that will be encoded relatively to $T^1$. The reference sequence cannot be compressed as effectively as the other ones and actually constitutes a substantial part of the final archive. We first divide the reference sequence into blocks of size 8192 symbols and store explicitly start positions of each block in the compressed (output) form of this sequence. It is possible that the start positions for $i$th and $(i - 1)$th block are equal, which means that the whole block contained only $N$ symbols (this phenomenon is quite frequent especially on the available human genomes). Using blocks also enables fast access to data (only local decompression of the reference sequence is needed). Then, within each block except for those $N$-only blocks, we divide the reference sequence into triplets over the alphabet of size 5 and pack into bytes. The resulting byte stream is Huffman-encoded, to prevent inefficiencies on middle-sized runs of $N$ symbols, which are not rare either (we note that a natural means to handle runs of the same symbols, the RLE technique, is not so convenient for random access). We also hash overlapping subsequences of the reference sequence (of length $M_1$), to enable further match searches.

In the next phase we process the sequences $T^i$, $2 \leq i \leq r$, one by one, scanning them from left to right and looking for matches in the reference sequence. Our parsing strategy is non-greedy but does not mimic the lookahead approach known from [15]. Instead, we adhere to two simple rules: a shorter match is chosen if its offset is significantly cheaper to encode, and it is worth to detect matches with (one or more) single-character gaps inside, which are frequent in genomes (a popular form of mutation). Note that the latter idea, although expressed in different terms, roughly corresponds to predicting the positions for LISS factors in [15]. Matches with gaps have a gap count limit $k = 2$. We denote the minimum match length of the first (contiguous) piece of a gapped match with $M_1$ and the minimum match extension, i.e., the length of each next piece of a gapped match, with $M_2$. 
LZ-matches are traditionally represented as a pair: reference offset and match length. We encode offsets as differences between the sequence position in the current genome and the matched-to sequence position in the reference genome. This tends to produce relatively small numbers (both negative and non-negative) but the extra step, differential encoding of those values makes the resulting stream even flatter.

As said, our parsing scheme may prefer a shorter match if its offset encoding is cheaper. The chosen heuristics allows for a match by up to 28 characters shorter than the currently most prospective match, if the absolute value of its offset in the presented differential form is less than 64 and this offset property also does not hold for the “currently best” match. The constant 64 is related to the byte coding used before further Huffman coding; in the former case the offset codeword has 1 byte while in the latter case 5 bytes. We illustrate it with an example. Let the longest found match be of length 60 and the absolute difference between the current position (in the current sequence) and the position in the referenced sequence (i.e., the beginning of the longest matched string) is 2000. Moreover, the respective absolute difference for the previously encoded match is 300. Apart from that match of length 60 we also have a shorter match, of length 40, and the absolute difference between the respective positions is only 345 for that shorter match. Now, since $1700 \geq 64$, $45 < 64$ and $60 - 40 \leq 28$, we prefer the shorter match of those two. A twin heuristic allows to accept a match with a more expensive offset if its length is over 28 greater than of the currently best match.

Handling long runs of N symbols deserves special care, since it is possible that the reference sequence does not contain them. To this end, we encode runs of N symbols of length at least $M_1$ as a pseudomatch (with the run’s actual length and an artificial unique offset).

There are four conceptual streams in our solution: match offsets, match lengths, literals (those symbols which do not belong to any match) and match / literal flags. The latter items are not binary since they also tell the number of gaps in a match. As we limit the number of gaps to 2, the flags are quaternary. In this way a gapped match is represented by a single offset (but the number of encoded match lengths is equal to the number of its pieces). Variable-length byte coding is used for match offsets and match lengths. The separate byte positions imply separate order-0 Huffman models which are responsible for the final compression stage. For example, the first byte in a match offset has 251 values for offset differences from $-125$ to $125$, one value telling the offset delta is less than $-125$ (followed by 4 extra bytes), one value telling the offset delta is greater than $125$ (followed by 4 extra bytes), one value denoting an N-run and one value for signaling a match to a string from the concatenated extra reference phrases (see later).

Literals are processed like the reference sequence (only without dividing them into blocks), with packing in triplets into bytes and applying Huffman. Finally, match / literal flags are also byte-packed and submitted to yet another Huffman model.
4.2 Extra reference phrases

We have noticed that good LZ-compressors are very efficient on our data if no restriction to match references is put. Still, unrestricted set of reference positions to LZ-matches prevents random access. Some compromise has to be found then. Our solution is to take long enough runs of successive literals in $T^i$, $2 \leq i \leq r$, and append them to the reference sequence. They act as a reservoir for extra matches. The offset of such a match, as mentioned earlier, has a unique 1-byte prefix, and what follows is the match position from the beginning of the area of extra reference phrases (no delta coding used here). The minimal length of a literal run is $M_3 = 32$. Note that we detect the literal runs on the fly and attach at the end of the extended reference sequence, hence this idea does not require an extra pass over data. In a single pass we cannot be sure, which extra phrases will give a match for some future sequence, so the value of $M_3$ is chosen quite arbitrarily, but it cannot be too small; we assume that the literal run should be longer than the minimal match length to increase the probability of finding a match to it. It is also possible in an extra pass over the compressed data to remove the unsuccessfully added extra phrases, but due to the additional time we decided not to implement this feature in the current version.

5 Experimental results

We have run experiments to evaluate the performance of our algorithm. The test machine was a 2.4 GHz Dual-Core AMD Opteron CPU with 16 GB RAM running Red Hat 4.1.2-46, a single core of the CPU was used. We have implemented our algorithm in C++, and compiled with g++ 4.1.2.

The test collections include the two yeast datasets and a dataset of four human genomes, all publicly available and used earlier in [15].

Note there exists a discrepancy in size of the human genomes (12066.06 MB in our tests, 11831.71 MB in the cited work). This is due to omitting the N symbols in the reference sequence in RLZ-opt.

In our experiments the (very rare, and occurring only in two of the four human genomes) symbols different to A, C, G, T, or N are converted to N (they denote some more specific kinds of uncertainty in labeling nucleotides in the sequencing process). We found out from the authors that the same methodology was used in [15].

We tested our algorithm in two variants, where the “advanced” one includes the idea of extra reference phrases. The other tested algorithms include Conrad 0.2 [13] and RLZ-opt. We have not tested the older DNA compressors, XM [3] and dna2 [15], because their available implementations handle only the 4-symbol alphabet. In spite of our attempts, we were unable to get a fully working version of the LZ-End compressor [11] from the authors; the program we had in our hands sends to the output only semi-compressed data (not interesting from the compression point) and thus also compression time and especially decompression

\footnote{S. Puglisi, private corr., Feb. 2011.}
Table 1. Compression results for two repetitive yeast collections.

| dataset       | S. cerevisiae | S. paradoxus |
|---------------|---------------|--------------|
|               | size (MB)     | ent. (bpb)   | comp. (s) | dec. (s) |
| original      | 485.87        | 2.18         | —         | —        |
| RLZ-opt       | 9.33          | 0.15         | 310       | 2.60     |
| conrad 0.2    | 16.50         | 0.27         | 707       | 41       |
| ours, basic   | 7.18          | 0.118        | 15.13     | 2.97     |
| ours, adv.    | 6.94          | 0.114        | 12.70     | 2.88     |

| dataset       | H. sapiens |
|---------------|------------|
|               | total size (MB) | rel. seq. size (MB) | add. seq. size (MB) | ent. (bpb) | comp. (MB) | dec. (s) |
| original      | 12066.06    | —               | —         | 2.183     | —         | —        |
| RLZ-opt       | 703.11      | 639.27         | 63.85     | 0.48      | 19575     | 117.73   |
| conrad 0.2    | 1033.88     | —               | —         | 0.69      | 32766     | 1157     |
| ours, basic   | 730.03      | 702.03         | 28.00     | 0.484     | 983.75    | 152.30   |
| ours, adv.    | 729.55      | 702.03         | 27.52     | 0.484     | 987.34    | 153.60   |

Table 2. Compression results for four humane genomes.

time cannot be honestly measured. From those reasons we gave up benchmarking it.

On the yeast collections our dominance over the main competitor, RLZ-opt, is very significant: more than an order of magnitude faster compression and the archives are smaller by 26% or 33%, respectively (using our stronger variant). In decompression, however, RLZ-opt is by about 10% faster. Our decompression timings on a machine with a slower CPU stand in contrast to those from [15] (which were about three times longer) and we can guess this is because our test platform is equipped with a 15 rpm hard disk. In fact, it is often reported that for fast LZ77 compressors the I/O is a key factor in speed.

On humane genomes the overall picture is seemingly different, but the extra columns in Table 2 help to explain it: our reference sequence is significantly larger after compression, since our scheme is simple and random access friendly, which is not so in the RLZ-opt where a general-purpose compressor, 7zip (switches: -mx9 -md512m), with no random access capabilities, was used for that. On the remaining sequences, i.e., in the task of relative compression, we are clearly better. Again, in compression speed our solution dominates (about 20 times faster) but RLZ-opt is faster in decompression.

Humane genome sequences are not only large but also much more similar to each other than the yeast datasets. An adverse side-effect of this phenomenon is that there are lots of collisions in hashing which make the compression slow. To mitigate this effect we took a couple of precautions. On the yeast datasets the minimum match parameters (described in the previous section) are set as
follows: $M_1 = 13$, $M_2 = 4$, while on the humane genomes they are set to: $M_1 = 20$, $M_2 = 4$. This, for example, means that the hashed sequences are
longer on the human genomes and collisions are not that frequent. Also, on the
human sequences we perform the matching on the chromosome level rather than
on whole sequences (this concerns all the tested algorithms). We believe this is
a sound approach from the biological point and also clearly beneficial for the
compression speed and memory use requirements.

The parameters $M_1, M_2, M_3$ were chosen experimentally but without severe
tuning. Still, it might be interesting to know how their selection affects the effi-
ciency of our algorithms. Recall that $M_3$ corresponds to the minimum length of a
literal run treated as an extra reference phrase, i.e., setting it to a very high value
practically turns our advanced variant into the basic variant (both in compres-
sion ratio and speed), which, we believe, is still very competitive. The parameter
$M_2$ is responsible for matches with (one-symbol) gaps. Setting $M_2$ to a much
too high value (instead of 4 in all our experiments) results in compression loss
across all datasets, from a few to about 10%. The compression speed may also
drop moderately. Finally, $M_1$ cannot be too small, since encoding short matches
and the triple (offset, length, flag) is costlier than encoding them as individual
DNA letters. It seems that the optimum is around $M_1 = 13$ for all datasets.
For human genomes, however, which are much more repetitive than other col-
lections of sequences, this threshold had to be raised, otherwise the compression
speed dropped several times. According to our preliminary experiments, also
for human sequences using $M_1 = 13$ gives (slightly) better compression but the
price is too high. We admit that manual setting of different values to $M_1$ in our
tests is a weakness of our algorithm, which can possibly be eliminated by some
rudimentary quick check on a collection to compress.

For the yeast datasets we chose as the references the sequences marked ap-
propriately in their home repository. It is an interesting problem to find a fast
and reliable heuristic to select the “best” reference sequence in the collection.
Our preliminary attempts were unsuccessful but we are going to take a closer
look at this issue in the future.

For the yeast datasets we chose as the references the sequences marked ap-
propriately in their home repository. It is an interesting problem to find a fast
and reliable heuristic to select the “best” reference sequence in the collection.
We found out that choosing the sequence that maximizes the number of (possi-
bly repeating) subsequences of length $M_1 = 13$ in it works correctly most of the
time, in our experiments failing only in case of one human chromosome. This
heuristics is rather fast, working at about 300 MB/s in memory, hence may be
a practical choice (however, as said, in our experiments for Tables 1 and 2 the
reference sequences were specified manually).

6 Conclusions

The volume of available genomic data grows at an accelerating rate and effi-
cient means to store, access and analyze them need to be developed, which is
addressed in the recent surge of interest in related problems. We have presented a new efficient data compression scheme for storing DNA sequences (genomes) from many individuals of the same species, hence sharing lots of similarities. Experimental comparison with the predecessor of our solution, the algorithm of Kuruppu et al. [15], shows that we are more than an order of magnitude faster in compression and the compression ratio is improved by about 30%. The key new ideas are augmenting the reference sequence with extra reference phrases taken from the other sequences (without compromising decompression speed much), specific LZ-parsing which implicitly detects some class of approximate repeats, and more compact encoding of the various byproducts of the scheme. Although not tested yet, we believe our algorithm has a promise also for archiving repetitive collections in software version control systems.

A number of issues requires further study. We need to add random access support, which is rather straightforward. Hash-based LZ-matching, although fast on relatively small data, slows down on large inputs, in particular, human genomes. Some steps to mitigate this problem have been taken in the current work but more effort should be put here. We are going to experiment with hash functions in our setting to minimize the number of collisions. Another aim is to improve the idea of extra reference phrases via eliminating those phrases which do not bring overall gain.

An alternative to the idea of extra reference phrases could be using two (or more) reference sequences. In this variant, it is crucial to encode the latter sequence(s) with reference to the first one, otherwise on the available datasets, with relatively few sequences, a compression loss would be inevitable. This, of course, poses a burning question about random access to data encoded in such a way. We believe fast random access is possible using the classic rank/select operations. To give a flavor of this idea, let us assume we have two reference sequences and the second, $T^2$, of length $n$, is LZ-encoded relative to the first one, and we also assume gapless matches for clarity. We create a (conceptual) bit-vector $B[1,n]$, with 1s exactly in the positions where LZ-matches start and just after they end. Now, $\text{rank}(B, k)$ is odd if position $k$ in $T^2$ is inside some match and then $k - \text{select}(B, \text{rank}(B, k))$ tells where exactly within this match $k$ is. We also need to perform select on the match offsets and lengths and have some extra structures to handle prefix sums. To reduce the overhead of $B$, in reality we use its compressed representation (see, e.g., [6]).

Finally, we note that our algorithm could be used in the inverted index from [5] for compressing the text part, as a more succinct, but probably slower, alternative to the Re-Pair component.

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