Context binning, model clustering and adaptivity for data compression of genetic data

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Abstract—Rapid growth of genetic databases means huge savings from improvements in their data compression, what requires better inexpensive statistical models. This article proposes automatized optimizations e.g. of Markov-like models, especially context binning and model clustering. While it is popular to just remove low bits of the context, proposed context binning automatically optimizes such reduction as tabled: state=bin[context] determining probability distribution, this way extracting nearly all useful information also from very large contexts, into a relatively small number of states. The second proposed approach: model clustering uses k-means clustering in space of general statistical models, allowing to optimize a few models (as cluster centroids) to be chosen e.g. separately for each read. There are also briefly discussed some adaptivity techniques to include data non-stationarity.

Keywords: data compression, genetic data, (hidden) Markov model, k-means clustering, adaptivity, non-stationarity

I. INTRODUCTION

We live in times of rapid growth of bioinformatics, e.g. for individual treatment of each patient based on sequencing in the precision medicine approach [1]. However, sequencing data for a single person can reach terabytes, requiring huge databases - which optimizations by improved data compression techniques can lead to significant savings.

Dependencies in this type of data are relatively weak. Beside Burrows-Wheeler transform [2], there are usually dominating simple techniques like entropy coding, RLE (run-length encoding: representing blocks of identical values), extending toward Markov models [3] - optimizations of which we are focused here, briefly presented in Fig. 1.

One optimization direction is toward higher order models and exploiting additional contexts like position, where the basic difficulty is exponential size growth with order. Proposed context binning allows for its practical approximations by automatically merging similar contexts, extracting nearly all useful information also from very large contexts, e.g. from $2^l$ previous values in $l$ table uses per symbol.

Second parallel optimization direction is varying models accordingly to local statistics. Briefly mentioned standard way is adaptation to include non-stationarity. Genetic data often has characteristic situation: of large number of reads treated as independent, what suggests using various models for different reads. While reads are too short for storing entire models in header, we can use clustering philosophy - finding a few optimized models (cluster centroids), and choosing one of them e.g. with a few bits written in header of read.

The proposed approaches are inexpensive from decoder and encoder side to directly apply. However, their optimization for actual data might be more costly - for example it could be done once e.g. for each sequencer model (like Illumina HiSeq 2000), and then used as default - e.g. 20 models for sequencer, compressor chooses 4 best of them for given file, then 2 bits per header choose one of 4 models.

Diagrams in this article contain analysis based on publicly available data - mainly first 1 million reads (all of 101 length) from FASTQ file ERR174310 (Whole Genome Sequencing of human, Illumina HiSeq 2000) downloaded from NCBI database[1]. Additionally, for long subsequent base sequence, nonstationarity analysis was made for human Chromosome 1 using FASTA file from ensembl.org webpage[2].

1https://www.ncbi.nlm.nih.gov/sra/ERR174310
2http://ftp.ensembl.org/pub/release-105fasta/homo_sapiens/dna/
II. CONTEXT BINNING

We would like to compress \( \{x_i\}_{i=1..N} \) sequence from size \( |A| = m \) alphabet \((x_i \in A)\), e.g. \( m = 4 \) for ATCG nucleotides, \( m \sim 40 \) quality scores, or some grouped symbols e.g. \( m \sim 4 \cdot 40 = 160 \) for (nucleotide, its quality score) grouped to include their statistical dependencies ((qscore<<2) | base).

Popular natural approach is encoding symbol-by-symbol, predicting conditional distribution of the next symbol based on the previous ones: \( \Pr(x_i|x_{i-1} \ldots x_1) \) and maybe some additional contexts like position. Assuming accurate entropy coding like Arithmetic Coding (AC) [4] or Asymmetric Numeral Systems (ANS) [5], symbol of probability \( p \) needs asymptotically \( \lg (1/p) \) bits (\( \lg \equiv \log_2 \)). While in prefix codes like Huffman we approximate this \( \lg (1/p) \) with a natural numbers of bits (\( p \) with natural powers of 1/2), AC/ANS asymptotically include also fractional bits.

Hence we can focus on conditional probability modelling with final evaluation as compression ratio given by:

\[
\frac{1}{N} \sum_{i=1}^{N} \lg (1/\Pr(x_i|x_{i-1} \ldots x_1)) \text{ bpv (bits/value)} \tag{1}
\]

In order \( l \) Markov model we restrict history to \( l \) previous values (with some special treatment of first \( l \) values): \( \Pr(x_i|x_{i-1} \ldots x_{i-l}) \) for \( x_i \in A, i > l \). The main difficulty is exponential growth of size of such models: requiring \( m^l \) of size \( m \) probability distributions. We can also add to context more looking relevant information, e.g. in FQZComp [3] there is also encoded position in read, number of changes of quality score.

Let us discuss here automatic merging of multiple such contexts into a smaller number of states providing nearly the same compression ratio at much smaller computational cost.

A. Direct context binning

Let \( C \) be a set of contexts, e.g. \( C = A^l \) for order \( l \) model, each defining a probability distribution \( P_c \) for \( c \in C, i > l \):

\[
\Pr(x_i|x_{i-1} \ldots x_{i-l}) = P_c(x_i) \text{ for } c = (x_{i-1}, \ldots , x_{i-l}) \tag{2}
\]

Taking all \( l+1 \) length windows:

\[
W = (x_i, x_{i-1}, \ldots , x_{i-l}) \in l+1..N
\]

denote \([0, 1] \ni P_c = |\{ w \in W : w_{2..l+1} = c \}|/|W|\)
as probability of context \( c \) (\( \sum_{c \in C} P_c = 1 \)),

\[
P_c(X) = \frac{1}{|W|} \{ w \in W : w_1 = x, w_{2..l+1} = c \}
\]
as probability distribution for new symbol after this context (\( \sum_{x \in A} P_c(x) = 1 \)). Empty contexts \( P_c = 0 \) can be handled e.g. by adding some tiny \( \epsilon > 0 \) to joint distribution on \( W \).

Now the optimized rate in bits/symbol can be written as

\[
R = \sum_{c \in C} P_c H(P_c) \text{ bpv (bits/value)} \tag{3}
\]

being Shannon entropy after context \( c \) of probability \( p_c \).

As context binning, we would like to merge similar contexts - replace \( C \) set of contexts with \( \bar{C} \) set of disjoint subsets of \( \bar{C} = \bigsqcup_{s \in C} s \).

Figure 2. Context binning for order 1 model for quality scores (top) and order 3 for bases (bottom). Distinguishing all previous 42 values (64 for bases) we need 2.44 bpv (1.97 for bases) - using presented conditional distributions. Completely neglecting this context we need 1.16 bpv more: 3.60 bpv (0.055, 1.92 for bases). The top plots and trees show optimized intermediate options: starting with singletons we merge subsets of contexts leading to the smallest bpv penalty constructing the tree, then merge leaves of its subtrees into smaller contexts. Presented context binning into 17 (5 for bases, marked with colors) states was chosen not to exceed 0.01 bpv from complete context models.
Having two disjoint subsets of contexts \( s, r \subseteq C \), \( s \cap r = \emptyset \), probability of their union and bits/value cost of their merging are:

\[
p_{s \cup r} = p_s + p_r
\]

\[
P_{s \cup r} = p_s P_s + p_r P_r
\]

\[
\Delta_{s,r} = (p_s + p_r)H(P_{s \cup r}) - p_s H(P_s) - p_r H(P_r) \tag{4}
\]

For optimization of such division, we can start with subsets as singletons \( s = \{c\} \) for \( c \in C \), with \( p_s = p_c \), \( P_s = P_c \). Then try to merge them in a way minimizing cost \( \Delta \) as increase of bits/symbol rate for not recognizing these two subsets of contexts - e.g. in greedy way as in used here Algorithm 1.

**Algorithm 1 Greedy search for context binning**

```plaintext
Algorithm 1
nodes = {{c}: c ∈ C} \quad \{\text{start with leaves as singletons}\}
available=true, ..., true \quad \{\text{not used yet}\}
initialize HEAP: insert with PUSH, POP retrieves lowest cost new node
for c ∈ C do
    PUSH((\Delta, \{c\}, \{c\})) using (4) cost of \{c\}, \{c\} → \{c, c\} merge
end for
for i = 1 to |C| - 1 do
    \{cur.left, right\} = POP \quad \{\text{retrieve lowest cost node candidate}\}
    while left or right not available do
        \{cur.left, right\} = POP \quad \{\text{skip already merged nodes}\}
    end while
    mark left and right as not available
    append True to available
    append cur to nodes, link left, right as its children in tree
    for all available node do
        PUSH((\Delta, cur, node)) using (4) to calculate merging cost \( \Delta \)
    end for
end for
```

This way we get tree of subsets of \( C \) as in example in Fig. 3. We can choose the actual context binning e.g. by starting with the root, and extending with the lowest cost neighboring nodes until reaching some threshold e.g. the number of binned contexts, total bpv distance from using entire context, bpv cost of adding new node, etc.

As there is freedom of bin enumeration, we can e.g. optimize it to be able to get denser and sparser binning from single table use: as bin[] and e.g. bin[] >> 3, this way merging 8 smaller bins into larger ones. To optimize it, we can start with finding larger number of bins. Then starting with these bins as contexts, optimize for smaller number of bins - finally grouping e.g. 8 small into 1 large.

**B. Nested context binning**

Above direct context binning allows e.g. to approximately represent 2 or a few previous values with a more reasonable number of states, also combine with other contexts like positions in Fig. 3. We can e.g. modify fast order 1 rANS implementation\(^3\) by adding single table use to get more valuable e.g. 1 byte context. E.g. for order 2 as state=bin12[|pval<<6]|val] for pval= \( x_{i-2} \), val= \( x_{i-1} \).

We can also combine multiple binnings e.g. to get approximated higher order models. Like in Fig. 4 for order 4 model: using \( \Pr(x_i|x_{i-1}, x_{i-2}, x_{i-3}, x_{i-4}) \) we can first perform binning of pairs of values using bin12[], then use second binning to group representations of both pair using bin24[]. This way we use two approximations reducing the original context size \( 4^2 = 16 \) into more reasonable e.g. 256 number of states (convenient 1 byte) determining probability distribution for \( x_i \).

This is the simplest, least expensive way (symmetric) to combine context binnings. In practice contributions of further contexts is usually weakening - suggesting to use smaller numbers of bins for them (asymmetric) or even depending on nearer bins (hierarchical), e.g. to allow for larger orders:

1) Symmetric: use identical context binning for all windows of given size (as discussed) e.g. 2 and 4 in Fig. 4 what is the least expensive (reusing previous binnings): e.g. \( 2^i \) order for \( i \) table uses per symbol.

2) Asymmetric: use separate context binnings for windows of various distance from current position - the further, the stronger reduction, e.g. bin12near[\( x_{i-1}, x_{i-2} \)] into 64 bins and bin12far[\( x_{i-3}, x_{i-4} \)] into 8 bins. To maintain the speed, the latter can be obtained by cutting bits from already calculated former e.g. bin12far[]=bin12near[] >> 3, what can be optimized by bin enumeration. For example we first find large binning for near values using \( \Pr(x_i|x_{i-1}, x_{i-2}) \) distribution, then on these bins perform second binning based on \( \Pr(x_i|x_{i-3}, x_{i-4}) \) evaluation, finally grouping

\(^3\)https://github.com/jkbonfield/rans-static
e.g. 8 small into 1 large.

3) Hierarchical: build tree of contexts - binning of further values depending on current nearer values, e.g. bin12far[] depending also on outcome of bin12near[] - what seems more appropriate from statistics perspective, but has much higher cost. To construct it, after building tree for near, restrict windows \( W \) to subsets corresponding to each bin, then build separate tree for each, and so on until e.g. some cost threshold.

C. Hidden state context models (HSCM)

Discussed higher order approaches might require multiple table uses per step, bringing a natural question of squeezing comparable behavior into a single optimized table.

For example by evolving, based on value \( \text{val} = x_i \), a hidden state acting as context - determining probability distribution for the next value \( \Pr(x_i|\text{val}) \approx \Pr(x_i|\text{state}) \):

\[
\text{state} = \text{transition}[\text{state}, \text{val}] \tag{5}
\]

This function could e.g. contain some counter, e.g. counting numbers of changes of quality scores like in FQZComp delta [3] - including long-range dependencies. To include some additional context like position, it can be put into \( \text{val} \) in [3], grouped or binned with the previous value. We can also use pair: (state, other context), e.g. grouped or binned, to determine probability distribution for the next value.

It is tempting to just use context binning to choose this transition function, however, it would require to find a fixed point of such operation (based on symbol sequence), what seems quite difficult. There is further mentioned machine learning-like approach for such optimization, let us first discuss inexpensive approach with state packing window of binned previous values.

1) Hierarchical context binning (HCB): The \( \text{fig 3} \) transition can be inexpensively optimized for state packing moving window of binned a few previous values, if this binning was made in hierarchical way as in bottom of Fig. [3] predicting \( x_t \), the previous value is used as \( \text{bin}[x_{t-1}] \) earlier as \( \text{bin12}[\text{bin}[x_{t-2}]] \), then \( \text{bin23}[\text{bin12}[\text{bin}[x_{t-3}]]] \), and so on - choosing further as binning from one position closer (can be trivial e.g. \( \text{bin23}[x] = x \)).

Choosing binning in such hierarchical way, we can easily shift this window into the next position, e.g.:

\[
(c_1, c_2, c_3) \rightarrow (\text{bin}[v], \text{bin12}[c_1], \text{bin23}[c_2])
\]

We can encode such binned context window into a single natural number e.g. using numeral systems:

\[
\text{state} = c_1 + \text{nc1} \ast (c_2 + \text{nc2} \ast (c_3 + \ldots))
\]

where \( c_1 \in \{0, \ldots, \text{nc1} - 1\} \), \( \text{nc} \) are numbers of bins for succeeding used positions. Then division by \( \text{nc} \) and taking modulo allows to uniquely decode \((c_1, c_2, c_3, \ldots)\). For convenient power-of-2 number of states, all \( \text{nc} \) would need to be power-of-2.

2) Continuous \( \rightarrow \) deterministic machine learning-like optimization: General HSCM could also allow to include long-range dependencies, e.g. counter like delta in FQZComp [3]. There might be considered some semi-automatic search/optimization, e.g. trying to include such counters or more complex types of behavior.

For automatic optimization it seems useful to first transform it into continuous optimization: of probability distributions of states after transition \( t \) (probabilistic instead of deterministic) - allowing to use gradient optimization methods like in machine learning approaches.
E.g. using softmax parametrisation \( t, d \) of distributions:

\[
(T_{x})_{rs} := \Pr(s_{i} = s|x_{i-1} = r, x_{i-1} = x) = \exp(t_{srx}) \\
\Pr(x_{i} = x|s_{i} = s) = \exp(\langle d_{x} \rangle_{s})
\]

satisfying: \( \forall_{rs} \sum_{s} \exp(t_{srx}) = 1 \), \( \forall_{s} \sum_{x} \exp(d_{sx}) = 1 \)

\[ P_{is} \equiv (P_{i})_{s} := \Pr(s_{i} = s) \]

For optimized evaluation function:

\[
\text{arg max}_{iid} F \quad \text{for} \quad F = \sum_{s} P_{is} \ln(\Pr(x_{i}|s_{i})) = \sum_{i} P_{i} \cdot d_{x}, \quad (6)
\]

being minus expected number of nits, e.g. also to be summed over DNA reads. Starting states can be chosen fixed being minus expected number of nits, e.g. also to be summed over DNA reads. Starting states can be chosen fixed

\[ P_{i+1} = P_{i} \cdot T_{x}, \]

\[ \text{For} \quad \text{optimized evaluation function:} \]

\[
\text{arg max}_{iid} F \quad \text{for} \quad F = \sum_{s} P_{is} \ln(\Pr(x_{i}|s_{i})) = \sum_{i} P_{i} \cdot d_{x}, \quad (6)
\]

The \( d \) can be removed estimating it from \( P_{is} \):

\[
\Pr(x|s) = \frac{\Pr(s|x) \Pr(x)}{\Pr(s)} = \frac{\sum_{t:x_{i}=x} P_{is}}{\sum_{s} P_{is}}
\]

To get deterministic transitions \( t_{srx} \in \{0,1\} \), we can try greedy approach: after optimizing \( M_{i} \), find maximal transition probability, then fix it to deterministic transition \( t_{srx} = 1, \forall s \neq t_{srx} = 0 \). And so on: interleaving continuous optimization \( (6) \) with already fixed transitions, and fixing the highest probability transition, until all \( t \) are deterministic.

To summarize, the choice of general HSCM is a promising direction with various optimization opportunities for both speed and compression ratio, which better understanding requires further research. Discussed model reduction should also help with overfitting, providing more universal, interchangeable models.

III. VARYING MODELS

The second discussed optimization direction is varying of models \( (M, \text{of various types}) \) - trying to better adapt to local statistics. Standard briefly mentioned here direction is adaptivity: using evolving models: \( M_{i} \) for position \( i \), with transition \( M_{i} \rightarrow x_{i} M_{i+1} \) based on processed symbol \( x_{i} \).

As in Fig. 3 and 6, here we will focus on proposed model clustering: optimizing some relatively small set of models \( \{M_{j}\}_{j=1..k} \) (as centroids of clusters) and switching between them, e.g. for each “read” - writing in its header which of \( k \) models to use (or maybe using some more complex switching mechanism).

A. Model clustering

Sequencing data usually contains large number of reads - of lengths from dozens to thousands of nucleotides (depending on technique). The reads are supposed to be finally aligned, what would e.g. allow to encode differences from such aligned consensus sequence - allowing for large compression ratio improvements (at least for bases).

Here let us assume we have just a set of reads as in standard FASTA/FASTQ file - treated independently. As there is usually freedom of read order, we could save \( \lg(\text{number of reads!}) \) bits e.g. by storing some information in their order. Each of these reads correspond to some local situation - might have different statistics.

The standard approach is using the same statistical model for each read, here it is proposed to group them into a few clusters of similar statistics and e.g. inform in each header which of these models to use. Encoder tests all and chooses the best one, decoder reads which should be used and decodes using it.

Algorithm 2 contains abstract pseudocode for standard k-means clustering algorithm \( 6 \) adopted for this application: loop interlacing assignment of all reads to the closest centroid (best model here), and optimizing centroid (model here) for all members of its current cluster, until some convergence condition.

**Algorithm 2 k-means clustering of models**

| Initialize: choose random \( k \) reads, calculate \( M_{j} \) model for \( j \)-th of them |
| while convergence condition e.g. change below some threshold do |
| for each read do |
| calculate cost in bits for using each of \( k \) models for this read |
| find minimal cost: \( j \)-th model, assign this read to \( R_{j} \subset R \) subset |
| end for |
| for each subset \( R_{j} \) do |
| calculate \( M_{j} = \text{model optimized for } R_{j} \) subset of reads |
| end for |
| end while |

It interleaves evaluation of models (assigning to the best ones), and optimizing models for subsets of assigned e.g. reads (preferably by some merging) - as being quite general, it can be applied also to very complex models.

For example we can fix set of distinguished contexts \( C \) e.g. as \( l \) previous values in order \( l \) model (order 1 in Fig. 5 [6]), or its reduced size binned version from the previous section. Then for each read calculate conditional (or joint) distributions \( (p_{c}, P_{c}) \), and for subsets of reads take their averages weighted with lengths.

CRAM FQZComp uses 2bit select in context as similar mechanism. Clustering e.g. k-means allows for its automatic optimization, also using 4 separate models should be faster as focusing on smaller tables than single 4x larger model.

B. Adaptivity for non-stationary sources

More standard approach for varying models is adaptivity. There are very general and powerful machine learning approaches like LSTM \( 7 \), but they are also extremely expensive - for practical data compression we should try to extract crucial behavior for inexpensive models. The basic approach is replacing averaging like \( v = \text{mean}(f(x_{i})) \), with “evolving averaging” - exponential moving average (EMA): \( v_{t+1} = \eta v_{t} + (1 - \eta) f(x_{i}) \rightarrow (1 - \eta) \sum_{d \geq 0} \eta^{d} f(x_{i-d}) \). (7)

There is a difficult question of choosing this \( 0 < \eta < 1 \) forgetting rate (usually \( > 0.9 \)), intuitively describing memory length of the system: \( \propto \eta^{d} \) contribution of \( d \) values before. We can translate it to half-life: contributions in distance
Figure 5. Model clustering of order 1 models for quality scores based on first 1 million reads of length 101 of ERR174310 - diagrams with context probabilities (blue bars), conditional distributions and bits/value histograms for 1,2,4,8 clusters found with k-means clustering, with numbers of reads for which given model leads to the smallest number of bits/value. We can observe split especially into low and high quality reads. We need to add which-model information in header of each read, which costs $\lg(k)$ if writing directly, or a bit more if using entropy coder, leading to $\approx 0.01 - 0.04$ additional bpv.

\[ \mu = -1/\lg(\eta) \] weakens twice: $\eta^{\mu} = 1/2$. Top of Fig. 7 shows behavior of such optimized half-lifes along human chromosome 1: it is usually $\approx 200$, but also with regions of shorter or longer memory.

EMA can be used in various ways, e.g. for evolution of covariance matrix in online-PCA \cite{8} and adaptive linear regression \cite{9}, or just of center and scale parameter for general exponential power distribution $\rho(x) \sim \exp(-|x|^\kappa)$ family \cite{10}.

For genetic data we rather focus on discrete probability distributions, requiring EMA for “evolving frequency count”. For this purpose it is convenient to work with cumulative distribution function (CDF): $CDF_i = \sum_{j<i} Pr(i)$. It for example allows for started in 2015 in LZNA compressor \cite{4} very fast SIMD implementations of adaptive rANS for up to size 16 alphabet:

\[ CDF_i = (\text{mixCDF} - CDF) \gg \text{rate} \]  \hspace{1cm} \text{(8)}

where rate corresponds to $-\lg(1-\eta)$, the mixCDF is CDF of recently processed block of symbols - such update literally shifts old distribution toward the new distribution.

In practice such update of entire probability distribution is usually used every symbol - what allows to be close to local (past) distribution, but is costly - it is worth to consider also sparser updates e.g. every 100 symbols, also allowing to practically update more complex models.

While the above is adaptive order 0 model, we can easily expand it into context adaptive models, e.g. higher order like

\[ \text{bases bits/value} \]

\begin{itemize}
  \item order 0: 3.502
  \item order 1: 2.441
  \item 2 clusters: 2.302
  \item $\approx 0.01$
  \item 4 clusters: 2.356
  \item $\approx 0.02$
  \item 8 clusters: 2.339
  \item $\approx 0.03$
  \item 16 clusters: 2.325
  \item $\approx 0.04$
  \item order 2 (1,2,4,8,16 clusters): 1.922, 1.898, 1.884, 1.868, 1.851 bpv (+0.0)
  \item order 3 (1,2,4,8,16 clusters): 1.918, 1.894, 1.876, 1.859, 1.834 bpv (+0.0)
\end{itemize}
in bottom of Fig. 7 For example maintaining separate CDF\(c\) for each considered context \(c \in C\) (e.g. \(l\)-previous, binned, hidden, etc.), for each processed symbol there is recognized context \(c \in C\). used CDF\(c\) probability distribution, which is later updated:

\[
CDF_c = (\text{mixCDF}_c - CDF_c) >> \text{rate} \quad (9)
\]

### IV. Conclusions and Further Work

There were proposed especially context binning and model clustering approaches - allowing for parallel inexpensive optimizations e.g. of context based models. Additional decoding cost is low (up to a few table uses per symbol). Encoding can also remain inexpensive, especially if restricting to some globally optimized models (e.g. for each model of DNA sequencer).

This is initial version of article to be expanded in the future (also applied in real compressors), for example:

- Bases and quality scores were treated here independently, while in practice they are slightly correlated.
- The reads were treated as independent, while in practice each base usually appears in multiple reads. To include their dependence we can e.g. first perform alignment to find consensus sequence (as looking most probable real sequence based on all the reads), then encode only differences from this consensus. Finally to encode this consensus, we can encode differences from the nearest reference sequence e.g. of humans.
- Mentioned Hidden State Context Model (HSCM) seems a promising development direction - allowing to include also far contexts in very inexpensive way (including advantages of RLE). However, it needs research for practical optimizations, approximations, maybe semi-manual.
- Discussed model clustering switches between a few models - it might be worth to develop mechanisms automatically switching between them based also on processed symbols, e.g. some adaptation with attraction to centroids.

Finally, we could prepare default e.g. 20 statistical models optimized based on a large dataset for a given model of sequencer. Then compressor tests on given file and chooses e.g. 4 best models - marked in file header. Then for each read writes 2 bits choosing one of these 4 models, allowing inexpensive parallel processing of reads.

Such models can be chosen by first identifying large potentially valuable context, like previous values, position in read, and then trying to squeeze it into inexpensive approximation e.g. using discussed context binning techniques.

### References

[1] E. A. Ashley, “Towards precision medicine,” Nature Reviews Genetics, vol. 17, no. 9, pp. 507–522, 2016.
[2] M. Burrows and D. Wheeler, “A block-sorting lossless data compression algorithm,” in Digital SRC Research Report. Citeseer, 1994.
[3] J. K. Bonfield, “Cram 3.1: Advances in the cram file format,” Bioinformatics, 2022. [Online]. Available: CRAM3.1 AdvancesinsingleCRAMFileFormat.
[4] J. Rissanen and G. G. Langdon, “Arithmetic coding,” IBM Journal of research and development, vol. 23, no. 2, pp. 149–162, 1979.
[5] J. Duda, K. Tahboub, N. J. Gadgil, and E. J. Delp, “The use of asymmetric numeral systems as an accurate replacement for huffman coding,” in 2015 Picture Coding Symposium (PCS). IEEE, 2015, pp. 65–69.
[6] J. MacQueen et al., “Some methods for classification and analysis of multivariate observations,” in Proceedings of the fifth Berkeley symposium on mathematical statistics and probability, vol. 1, no. 14. Oakland, CA, USA, 1967, pp. 281–297.
[7] F. A. Gers, N. N. Schraudolph, and J. Schmidhuber, “Learning precise timing with lstm recurrent networks,” Journal of machine learning research, vol. 3, no. Aug, pp. 115–143, 2002.
[8] M. K. Warmuth and D. Kuzmin, “Randomized online pca algorithms with regret bounds that are logarithmic in the dimension,” Journal of Machine Learning Research, vol. 9, no. Oct, pp. 2287–2320, 2008.
[9] J. Duda, “Parametric context adaptive laplace distribution for multimedia compression,” arXiv preprint arXiv:1906.03238, 2019.
[10] ——, “Adaptive exponential power distribution with moving estimator for nonstationary time series,” arXiv preprint arXiv:2003.02149, 2020.