FMtree: A fast locating algorithm of FM-indexes for genomic data

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Abstract

Motivation: As a fundamental task in bioinformatics, searching for massive short patterns over a long text has been accelerated by various compressed full-text indexes. These indexes are able to provide similar searching functionalities to classical indexes, e.g., suffix trees and suffix arrays, while requiring less space. For genomic data, a well-known family of compressed full-text index, called FM-indexes, presents unmatched performance in practice. One major drawback of FM-indexes is that their locating operations, which report all occurrence positions of patterns in a given text, are particularly slow, especially for the patterns with many occurrences.

Results: In this paper, we introduce a novel locating algorithm, FMtree, to fast retrieve all occurrence positions of any pattern via FM-indexes. When searching for a pattern over a given text, FMtree organizes the search space of the locating operation into a conceptual quadtree. As a result, multiple occurrence positions of this pattern can be retrieved simultaneously by traversing the quadtree. Compared with the existing locating algorithms, our tree-based algorithm reduces large numbers of redundant operations and presents better data locality. Experimental results show that FMtree is one order of magnitude faster than the state-of-the-art algorithms, and still memory-efficient.

Availability: FMtree is freely available at https://github.com/chhylp123/FMtree.

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Supplementary information: Supplementary data are available online.

1 Introduction

The string matching problem is to identify the occurrence positions of a short string \( P \) (called pattern) in a given long string \( T \) (called text). For genomic data, both the pattern \( P \) and the text \( T \) are the sequences over a small alphabet \( \Sigma = \{a,c,g,t\} \). In order to speed up the string matching process, a well-known approach is indexed matching. It first builds an index data structure for the text in advance, and then searches for the pattern via the index. If the text is static, this approach is usually much faster than online matching approach, which directly searches for the pattern over the text. Many bioinformatics applications have adopted the indexed string matching approach, such as read mapping (Langmead and Salzberg, 2012; Li, 2013), genome assembly (Li, 2012; Simpson and Durbin, 2012) and read error correction (Schulz et al., 2014).

A number of full-text indexes have been proposed for several decades. Classical indexes like suffix arrays (Manber and Myers, 1993), efficiently support two basic functions: count and locate. Given a pattern \( P \) and a text \( T \), the count function is to report the number of occurrences of \( P \) in \( T \), while the locate function is to retrieve all occurrence positions of \( P \) in \( T \). A serious problem of these classical indexes is that their space usage is relatively large, especially for a very long text. To address this problem, various compressed full-text indexes have been developed in recent years (Ferragina et al., 2009). Generally, most of them are able to be classified into three families: FM-indexes (Ferragina and Manzini, 2000; Grabowski et al., 2004), compressed suffix arrays (CSAs) (Grossi and Vitter, 2005; Sadakane, 2003) and Lempel-Ziv compression based indexes.
(LZ-indexes) (Arroyuelo, 2006; Arroyuelo et al., 2012). These indexes are designed to provide similar count and locate functionalities to classical indexes, while requiring less space. For genomic data, the most efficient family of compressed full-text indexes is FM-indexes (Gog et al., 2017; Vyverman et al., 2012), especially when searching for short patterns (Hon et al., 2004). Given a human genome with about 3.15 billion characters, FM-indexes usually require less than 3GB RAM, while classical suffix arrays require about 12GB RAM. In addition, thanks to the small alphabet size of genomic data, the counting time of FM-indexes is comparable to that of classical indexes (Deonovicz and Grabowski, 2013; Gog and Petri, 2014). Thus, FM-indexes have become the essential data structure in many bioinformatics algorithms (Langmead and Salzberg, 2012; Li, 2013; Marco-Sola et al., 2012).

The major bottleneck of FM-indexes is that their locating operation is several orders of magnitude slower than that of classical indexes (Ferragina et al., 2009). To reduce space usage, FM-indexes only save a small fraction of text positions, called sampled positions, rather than all of them. When locating a pattern via FM-indexes, the sampled positions of the pattern can be directly retrieved, while the non-sampled positions have to be calculated one-by-one exploiting the expensive LF-mapping operations (see details in Section 2.2). For short patterns with many occurrence positions, FM-indexes need to perform large numbers of LF-mapping operations until all non-sampled positions have been obtained. Unfortunately, searching for short patterns in a long text is an important task in bioinformatics (Langmead and Salzberg, 2012; Ahmadi et al., 2012; Cheng et al., 2015; Hach et al., 2010; Liu et al., 2015), and these short patterns are very frequent in practice (Xin et al., 2016). In this case, the cost of locating operations dominates the overall string matching time.

Unfortunately, although there are various studies about compressed full-text indexes, only a small fraction of them focus on accelerating the locating operations. González et al. propose locally compressed suffix array (LCSA) (González and Navarro, 2007; González et al., 2015) to improve the data locality of the locating operations. For popular compressed full-text indexes such as FM-indexes and CSAs, a serious problem is that locating patterns via them results in many random memory accesses. To solve this problem, LCSA directly compresses suffix array exploiting the repetitions of suffix array. Since all occurrence positions of a pattern are saved consecutively in suffix array, LCSA can obtain these positions by decompressing consecutive elements of suffix array. In this case, its memory accesses are highly local. However, compared with other compressed full-text indexes, LCSA requires much more space when indexing genomic data.

Besides, Ferragina et al. develop a distribution-aware algorithm (Ferragina et al., 2013), which adjusts FM-indexes or CSAs according to the distribution of the occurrence positions of query patterns. This algorithm assumes that the distribution of the patterns’ occurrence positions has been known in advance, so that it inclines to sample the text positions which have high probability to be located. However, in most cases, it is impossible to know this distribution during the index building phase. Besides, the distribution-aware algorithm cannot achieve good performance unless the distribution of the patterns’ occurrence positions is very skewed. This requirement also limits the usage of this algorithm.

In theory, LZ-indexes are more efficient than FM-indexes and CSAs when performing locating operations (Ferragina et al., 2009). But for genomic data, it is difficult to develop a highly optimized LZ-index like the existing sophisticated implementations of FM-indexes in many bioinformatics algorithms (Langmead and Salzberg, 2012; Li, 2013; Marco-Sola et al., 2012). Moreover, there does not exist a practical implementation of LZ-indexes which is able to process large texts with billions of characters.

Here we introduce a novel locating algorithm, FMtree, to significantly accelerate the locating operations of FM-indexes for genomic data. When locating a pattern via FM-indexes, the search space of locating operation is organized into a quadtree. By utilizing this quadtree, FMtree is able to calculate the non-sampled positions block-by-block, while current algorithms have to calculate these positions one-by-one. Thus, our tree-based locating algorithm is cache-friendly and avoids many unnecessary operations. Another advantage of FMtree is that it can be applied to any implementation of FM-indexes without modification. Overall experimental results show that FMtree significantly outperforms previous algorithms for genomic data.

2 Background

2.1 Definitions and notation

A string $S$ is a sequence of characters over the alphabet $Σ$, and the size of $Σ$ is $|Σ|$. We let $|S|$ denote the length of $S$, $S[i]$ denote the $i$-th character of $S$ ($0 \leq i \leq |S| − 1$), and $S[i,j]$ denote the substring that starts at $S[i]$ and ends at $S[j]$. Besides, consider a character $s$ and a string $S$, $sS$ denotes the concatenation of $s$ and $S$. We also let $s^n$ denote a string of length $n$ such that $s^0$ is an empty string, $s^1 = s$ and $s^{n+1} = s^n s$.

To solve the string matching problem, existing compressed full-text indexes need to support the following two basic operations:

- $count(P,T)$: Return the number of occurrences of pattern $P$ in text $T$.
- $locate(P,T)$: Return all occurrence positions of pattern $P$ in text $T$.

For the convenience of further discussion, we assume that a special character $\#$ is at the end of text $T$, where $\#$ is lexicographically smaller than other characters in $Σ$. Since we focus on genomic data, all characters in text $T$ and pattern $P$ belong to $Σ = \{a, c, g, t\}$ except $T[|T| − 1] = \#$.

2.2 Overview of FM-indexes

As a family of compressed full-text indexes, FM-indexes are first proposed to emulate classical suffix arrays (Ferragina and Manzini, 2000). Given a text $T$, its suffix array $SA$ (Manber and Myers, 1993) saves the positions of all suffixes of $T$ in lexicographic order. For a pattern $P$, it is obvious that the positions of all suffixes prefixed by $P$ are saved consecutively in an interval of $SA$, called $SA[\text{first}[P], \text{last}[P]]$. In fact, $SA[\text{first}[P], \text{last}[P]]$ consists of all occurrence positions of $P$ in $T$.

Compared with suffix arrays, FM-indexes provide similar searching functionalities, while requiring less space. The critical data structure of a FM-index is Burrows Wheeler Transform (Burrows and Wheeler, 1994) of $T$, called $BWT(T)$, which permutes the characters of $T$ reversibly. Conceptually, $BWT(T)$ can be constructed in the following two steps:

- Building a conceptual matrix $M(T)$ including all cyclic rotations of $T$ in lexicographic order. Each row in $M(T)$ is a cyclic rotation of $T$.
- Let $BWT(T)$ be the last column of $M(T)$.

| Fig. 1. An example of Burrows Wheeler Transform $BWT(T)$ and suffix array $SA$ for string $T = \text{"agttacacg"}$. |
An example is presented in Fig. 1. For FM-indexes, there are two important properties of \(M(T)\) and \(BWT(T)\):

- Let \(F\) be the first column of \(M(T)\), \(BWT(T)[i]\) precedes \(F[i]\) in text \(T\). It is obvious that the \(i\)-th row of \(M(T)\) corresponds to \(SA[i]\). Specifically, \(BWT(T)[i] = T[SA[i]]\) if \(SA[i] \neq 0\), and \(BWT(T)[i] = \#\) if \(SA[i] = 0\).
- For any character \(s \in \Sigma\), the \(i\)-th \(s\) in \(F\) and the \(i\)-th \(s\) in \(BWT(T)\) correspond to the same \(s\) in \(T\). For example in Fig. 1, \(F[5]\) and \(BWT(T)[1]\) are the first \(c\) in \(F\) and \(BWT(T)\), respectively. In fact, both of them correspond to \(T[7]\).

Based on the above properties, a core operation \(LF\) (Last-to-First mapping) of FM-indexes is defined as:

\[
LF(i) = C[BWT(T)[i]] + rank_{BWT(T)}(i)(BWT(T), l) \tag{1}
\]

where \(C[BWT(T)[i]]\) denotes the number of characters in \(T\) which are smaller than \(BWT(T)[i]\), and \(rank_{BWT(T)}(i)(BWT(T), l)\) is a rank operation that returns the number of \(BWT(T)[i]\) in \(BWT(T)[0, l-1]\). Essentially, \(LF\) operation scans text \(T\) backward, namely, \(F[i] = T[SA[i]]\), \(F[0] = l\), \(L[i][0] = BWT(T)[i] = T[SA[i]] - 1\) and \(SA[i] = \#\). For instance, in Fig. 1, \(SA[9] = 9, L[0] = 1, L[9] = 0\). Specifically, in \(F\), \(SA[i] = \#\) where \(i \leq l}\).

Counting via FM-indexes. When counting a pattern \(P\) in text \(T\), it is obvious that all \(M(T)\)'s rows prefixed by \(P\) are saved consecutively in an interval \(M(T)[p, e]\). Thus, to answer count \((P, T)\), FM-indexes first perform the backward search algorithm to determine the range \([sp, ep]\). After that, \(count(P, T) = ep - sp + 1\). Algorithm 1 presents the procedure of the backward search algorithm. More precisely, this algorithm searches \(P[0, |P| - 1]\) backward in \(P\)'s steps. In \(i\)-th step \(i = |P| - 1, |P| - 2, \ldots, 0\), this algorithm updates \([sp, ep]\) such that all \(M(T)[p, e]\) includes \(i\)-th \(s\)'s rows prefixed by \(P[i]\). Note that in first step \(i = |P| - 1, \[sp, ep\] is the range of a single character \(P[|P| - 1]\), so that it can be directly obtained via array \(C\) (line 2 in Algorithm 1). For any character \(s \in \Sigma\), \(C[s]\) saves the number of characters which are lexicographically smaller than \(s\) in \(T\). Finally, when \(i = 0\), the range \([sp, ep]\) of \(P[0, |P| - 1]\) is obtained and \(count(P, T) = ep - sp + 1\). Since \(M(T)[i]\) corresponds to \(SA[i]\), \([sp, ep]\) acts as an occurrence positions of \(P\) in \(T\).

Locating via FM-indexes. As mentioned above, the backward search algorithm of FM-indexes determines the range \([sp, ep]\) such that \(SA[sp, ep]\) consists of all occurrence positions of \(P\) in \(T\).

**Algorithm 1: backward_search(\(P\))**

**Input:** \(P[0, |P| - 1]\)  
**Output:** the \(SA\) range \([sp, ep]\) of \(P\)  
1: \(s = |P| - 1, s = P[s], i = s - 1\)  
2: \(sp = C[s], ep = C[s] + 1\)  
3: while \(i \geq 0\) and \(s < sp\) do  
   4: \(s = P[i], i = i - 1\)  
   5: \(sp = C[s] + rank_{BWT(T)}(sp)\)  
   6: \(ep = C[s] + rank_{BWT(T)}(sp) + 1\)  
7: end while  
8: if \(sp > ep\) then  
   9: return "not found"  
10: else  
   11: return \([sp, ep]\)  
12: end if

SA is saved, locate \((P, T)\) can be answered by retrieving \(SA[sp, ep]\) directly. However, for a long text, its \(SA\) is very space-consuming. Thus, FM-indexes only save a fraction of positions in \(SA\), called the sampled positions. This strategy reduces the space usage of FM-indexes, but of course comes at the expense of additional computational overhead.

Algorithm 2 presents the most practical locating algorithm of FM-indexes. To obtain position \(SA[i]\) \((sp \leq i \leq ep)\), this algorithm first scans text \(T\) backward by performing \(LF\) operation \(m\) times until a sampled position \(SA[i]\) is reached. After that, \(SA[i] = SA[j] + m\).

**Algorithm 2: locate(sp, ep)**

**Input:** the \(SA\) range \([sp, ep]\)  
**Output:** the position set \(R\) consists of all positions in \(SA[sp, ep]\)  
1: for \(i = sp\) to \(ep\) do  
2: \(j = i, m = 0\)  
3: while \(SA[j]\) is not sampled do  
4: \(j = LF(j), m = m + 1\)  
5: end while  
6: Add \(SA[j] + m\) to \(R\)  
7: end for  
8: return \(R\)

Implementation of FM-indexes. As we can see, both the counting operation and the locating operation of FM-indexes can be reduced to rank operations. To support rank operations, practical implementations of FM-index break \(BWT(T)\) into small blocks. For the beginning line of each block and each character \(s \in \Sigma\), the rank value is precomputed and saved. When calculating \(rank_{BWT}(T, l)\), these implementations first retrieve the precomputed rank value of the block which includes \(BWT(T)[i]\), and then add the number of \(s\) in this block before \(l\)-th line. Besides, the locating algorithm of FM-indexes requires a sampled suffix array \(SSA\), which saves all sampled positions in suffix array order. Several implementations of FM-indexes also need a bitmap \(B\), where \(B[i] = 1\) denotes that \(SA[i]\) is saved in \(SSA\). If \(B[i] = 1\), \(SA[i]\) can be found in \(SSA[rank_{BWT}(B, i)]\). We refer to the surveys (Ferragina et al., 2009; Navarro and Mäkinen, 2007) for more information about the implementations of FM-indexes.

**3 Methods**

**3.1 Analysis of Existing Locating Algorithm**

The first performance bottleneck is that existing locating algorithm needs to perform a large number of \(LF\) operations. As mentioned in Section 2.2, FM-indexes sample the positions in \(SA\) to reduce the space usage. A popular sampling strategy is to sample every \(SA[i]\) if \(SA[i] \mod D = 0\), where \(D\) is the regular sampling distance. Here we refer to this strategy as value sampling strategy. This strategy guarantees that any occurrence position of a pattern can be obtained in at most \(D - 1\) steps of \(LF\) operation. Thus, to locate a pattern with \(occ\) occurrence positions, the number of \(LF\) operations is \((D - 1) \times occ\) in worst case. Unfortunately, short and frequent patterns with large value of \(occ\) are widely used in practice, which results in massive \(LF\) operations. Apart from value sampling strategy, many FM-index-based bioinformatics algorithms adopt another sampling strategy, called subscript sampling strategy. This strategy samples every \(SA[i]\) if \(i \mod D = 0\), where \(D\) is the regular sampling distance. Compared with value sampling strategy, subscript sampling strategy leads to even worse locating performance. The reason is that for any position, value sampling strategy can guarantee to obtain it in at most \(D - 1\) steps of \(LF\) operation, while subscript sampling strategy cannot.
Besides, the poor data locality is another bottleneck of existing locating algorithm. To locate a position \(SA[i]\), existing locating algorithm needs to perform \(m\) steps of LF operation until a sampled position \(SA[i_m]\) is reached. Essentially, this procedure scans text \(T\) backward from \(SA[i_0]\) to \(SA[i_m]\), so that \(SA[i_m] = SA[i_n] = m\). In \(t\)-th step (\(t = 1, 2, \ldots, m\)), the aim of existing locating algorithm is to calculate \(i_t\) such that \(SA[i_t] = SA[i_0] - t = SA[i_1] - 1\). As shown in Algorithm 2, \(i_t\) is obtained by calculating \(LF(SA[i_{t-1}])\), which needs to access \(BWT(T)[i_{t-1}]\). In addition, if a FM-index is sampled by value sampling strategy, in \(t\)-th step, we need to access \(B[i_{t-1}]\) to check if \(SA[i_{t-1}]\) is a sampled position. Thus, the memory access addresses to \(BWT(T)\) and \(B\) in \(t\)-th step are determined by \(i_{t-1}\). Similarly, in \(l + 1\)-th step, the memory access addresses are determined by \(i_l\). If the suffix \(T[SA[i_l], |T| - 1]\) is not lexicographically similar to the suffix \(T[SA[i_{l-1}], |T| - 1]\), \(i_{t-1}\) and \(i_l\) would be very different. In this case, the memory accesses of these two steps are non-contiguous. For example, consider a non-sampled position \(SA[1003]\) of pattern \(P = \text{“agcag”}\) and \(BWT(T)[2136] = c\). To obtain \(SA[1003]\), existing locating algorithm checks \(BWT[1000]\) and calculates \(LF(1003)\) in first step. Since \(BWT(T)[2136] = T[S[SA[1003] - 1] = c\) and \(SA[LF(1003)] = SA[1003] - 1\), \(SA[LF(1003)]\) is actually an occurrence position of \(P = \text{“agcag”}\). Obviously, “agcag” is significantly lexicographically larger than “agcag”, so that \(LF(1003)\) is very different to \(1003\). In second step, existing locating algorithm of FM-indexes needs to check \(B[LF(1003)]\) and calculate \(LF(LF(1003))\). Therefore, the memory access addresses in first step and second step to \(BWT(T)\) and \(B\) are non-contiguous.

### 3.2 Our Proposed Algorithm: FMtree

The key idea of FMtree is to organize the search space of the locating operation into a conceptual quadtree, so that multiple locations can be located simultaneously by traversing the quadtree. This idea is based on the observation that, different occurrence positions of a pattern \(P\) may be obtained by performing similar LF operations. For example, consider two non-sampled positions \(SA[2136]\) and \(SA[2137]\) of pattern \(P = \text{“agcag”}\) and \(BWT(T)[2136] = BWT(T)[2137] = t\). In first step, existing locating algorithm calculates \(LF(2136)\) for \(SA[2136]\), and calculates \(LF(2137)\) for \(SA[2137]\). Since \(BWT(T)[2136] = BWT(T)[2137]\), \(LF(2136) = LF(2137)\), \(t\), both \(SA[LF(2136)]\) and \(SA[LF(2137)]\) are the occurrence positions of \(P = \text{“agcag”}\). As a result, \(LF(2136)\) and \(LF(2137)\) are very similar. In second step, for \(SA[2136]\) and \(SA[2137]\), existing locating algorithm calculates \(LF(LF(2136))\) and \(LF(LF(2137))\). Thus, if we locate \(SA[2136]\) and \(SA[2137]\) jointly, namely, we calculate \(LF(2136)\) and \(LF(2137)\) together in first step, and calculate \(LF(LF(2136))\) and \(LF(LF(2137))\) together in second step, the memory accesses in each step to \(BWT(T)\) and \(B\) would be contiguous.

More precisely, given two positions \(SA[i]\) and \(SA[j]\) with \(BWT(T)[i] = BWT(T)[j] = s\), if there does not exist \(s\) in \(BWT(T)[i+1, \ldots, j-1]\), it is obvious that \(LF(s) = LF(j) = 1\). Thus, for the positions in \(SA[sp, ep]\) with same character \(s\) in \(BWT(T)\), the results of one step of LF operation belong to the range \([LF(sp), LF(ep)]\), where \(SA[sp, ep]\) is the first position and last position in \(SA[sp, ep]\) with character \(s\) in \(BWT(T)\). If \(SA[sp, ep]\) consists of all occurrence positions of \(P\), \(SA[LF(sp), LF(ep)]\) actually includes occurrence positions of \(P\). Therefore, \(LF(sp), LF(ep)\) = backward_search(\(sp\)) = \(\text{backward_search}(\text{“agcag”}) = \{C[0] + \text{rank}_{C}(BWT(T), sp), C[1] + \text{rank}_{C}(BWT(T), ep) + 1\}\), as shown in Algorithm 1. In other words, to obtain all positions in \(SA[sp, ep]\), large numbers of LF operations for all positions can be reduced to a few rank operations only for \(sp\) and \(ep\).

Formally, this is based on the following theorem:

**Theorem 1.** Given a test \(T\) over alphabet \(\Sigma\) and its FM-index which is sampled by value sampling strategy with sampling distance \(D\). Let \(FM(P,T)\) be the sampled position including all sampled occurrence positions of \(P\) in \(FM\)-index, and \(L(P,T)\) be the position set including all occurrence positions of \(P\) in \(T\). Then \(L(P,T)\) can be calculated as follows:

\[
L(P,T) = \bigcup_{i=0}^{D-1} \{x|x = y + i, y \in FM(s^\ast P,T)\}
\]

where \(\ast\) is a wildcard of \(\Sigma\).

**Proof.** Generally, all positions in \(T\) are classified into \(D\) sets: \(\{g_0, g_1, \ldots, g_{(D-1)}\}\). Each set \(g_i\) consists of every position \(SA[j]\) of \(T\), where \(SA[j] \mod D = i\). Let \(L_q(P,T)\) be the position set including all occurrence positions of \(P\) in \(g_i\). Note that \(FM(P,T) = L_q(P,T)\).

Therefore, \(L_q(P,T)\) can be obtained as:

\[
L_q(P,T) = \{x|x = y + i, y \in FM(s^\ast P,T)\}
\]

Since \(L(P,T)\) consists of all occurrence positions of \(P\) in \(D\) sets \(\{g_0, g_1, \ldots, g_{(D-1)}\}\), \(L(P,T)\) is:

\[
L(P,T) = \bigcup_{i=0}^{D-1} L_q(P,T)
\]

**Basic algorithm of FMtree.** According to Theorem 1, we propose the core algorithm of FMtree. To utilize FMtree, FM-indexes must be sampled by value sampling strategy with regular sampling distance \(D\). When locating a pattern \(P\) via FM-indexes, there are total \(D\) steps in FMtree. Specifically, in \(i\)-th step (\(i = 0, 1, \ldots, D - 1\)), this algorithm consists of the following three stages:

- **FMtree first searches \(s^\ast P\) via FM-indexes to obtain their corresponding \(SA\) ranges.** In total, there are \(D^2\) \(SA\) ranges in \(i\)-th step, since \(s^\ast P\) represents \(D^2\) different strings. For each string \(S[0, |S| - 1]\) in \(i\)-th step (\(i = 1, \ldots, D - 1\)), its \(SA\) range \([sp, ep]\) is updated from the \(SA\) range \([sp, ep]\) of string \(S[0, |S| - 1]\) in \((i - 1)\)-th step by two rank operations to \(BWT(T)\). More precisely, \(sp = C[S[0]] + \text{rank}_{C}(BWT(T), sp)\), and \(ep = C[S[0]] + \text{rank}_{C}(BWT(T), ep) + 1\), as shown in Algorithm 1. Note that the \(SA\) range of \(P\) in 0-th step has been calculated in advance exploiting the backward search algorithm.

- **Then FMtree needs to retrieve the sampled positions in these \(SA\) ranges.** As shown in Section 2.2.1, FM-index saves all sampled positions of \(SA\) in \(SA\) in suffix array order, and utilizes bitmap \(B\) such that \(B[i] = 1\) denotes that \(SA[i]\) is saved in \(SA\). Therefore, given a \(SA\) range \([sp, ep]\), all sampled positions in \(SA[sp, ep]\) are saved consecutively in \(SA[sp, ep]\), \(sp = \text{rank}_{B}(B, sp)\) and \(ep = \text{rank}_{B}(B, ep)\).

- **Finally, once all sampled positions of \(s^\ast P\) have been obtained, FMtree adds to \(i\) these positions to obtain the occurrence positions of \(P\).**

With the above three stages, in \(i\)-th step, FMtree is able to obtain all positions in \(L_q(P,T)\). Thus, \(L(P,T)\) can be obtained in total \(D\) steps of FMtree. For genomic data with alphabet size |\(\Sigma| = 4\), the search space of FMtree is actually a quadtree of height \(D\), as shown in Fig. 2. Indeed, the \(i\)-th step of FMtree corresponds to the \(i\)-th layer of this quadtree. We observe that FMtree locates all occurrence positions of \(P\) block-by-block, while existing locating algorithm has to locate these positions one-by-one.
Further optimizations of FMtree. The key problem of FMtree is that with the increasing value of sampling distance $D$, the number of rank operations increases exponentially. In $i$-th step, the number of rank operations to BWT is $2 \times |S_A[i]| = 2 \times 4^i$. In addition, an equal number of rank operations to $B$ are also required to determine the SSA ranges. As such, the total number of rank operations when $D$ is large.

To solve this problem, we first propose an optimization to FMtree, called early leaf nodes calculation. For the basic FMtree, we observe that the cost of calculating its leaf nodes (i.e., the $(D-1)$-th step of FMtree) dominates its overall locating time. The reason is that in $(D-1)$-th step, the number of rank operations to both BWT and $B$ is $2 \times 4^{D-1}$, which is larger than the total number of rank operations in the rest $D-1$ steps of FMtree. Early leaf nodes calculation is proposed to avoid the expensive $(D-1)$-th step of FMtree. It is based on the following theorem:

**Theorem 2.** Given a text $T[0, |T|-1]$ and a pattern $P[0, |P|-1]$, the position set $L(P, T)$, which includes all occurrence positions of $P$ in $T$, can be calculated as follows:

$$L(P, T) = \bigcup_{i=1}^{D} \{x| y = i, y \in FM(P[i], |P|-1), T[y] = 1\}$$

(5)

$P[0, i-1] = T[y - i, y - 1]$

Proof. Since $FM(P[i], |P|-1), T = L_{log_i}P[i], |P|-1, T$, for each position $SA[j]$ in $FM(P[i], |P|-1), T$, $(SA[j] - i$ mod $D = D - i$. Then $L_{log_i}(D-1)P[0, |P|-1], T$ can be obtained as:

$$L_{log_i}(D-1)P[0, |P|-1], T = \{x| x = y - i, y \in FM(P[1], |P|-1), T[y - i, y - 1]\}$$

(6)

Therefore, $L(P, T)$ is:

$$L(P, T) = \bigcup_{i=1}^{D} L_{log_i}(D-1)P, T$$

(7)

Actually, the aim of the $(D-1)$-th step in basic FMtree is to obtain $L_{log_i}(D-1)P, T$. According to Theorem 2, this position set can be obtained using early leaf nodes calculation in following three stages:

- Early leaf nodes calculation first searches $P[1, |P|-1]$ via FM-indexes to obtain its corresponding SSA range $[sp_i, ep_i]$.
- Then for every $SA[j] (sp_j \leq j \leq ep_j)$ if $B[j] = 1$ and $T[SA[j] - 1] \neq P[0, i], early leaf nodes calculation adds it to a position set $R$. Note that since $T[SA[j] - 1] = BWT(T[j], early leaf nodes calculation actually checks all elements in $B[sp_i, ep_i]$ and $BWT(T[j], ep_i]$. Thus, the memory accesses in this stage are highly local. In contrast, the $(D-1)$-th step of basic FMtree results in many random memory accesses. A more practical and efficient implementation about this stage can be found in Supplementary Section S1.

```
Algorithm 3: FMtree($P, sp, ep, sp_i, ep_i, D$)
Input: the pattern $P[0, |P|-1]$; the SSA range $[sp, ep]$ of $P[0, |P|-1]$; the SSA range $[sp_i, ep_i]$ of $P[1, |P|-1]$; the sampling distance $D$

Output: the position set $R$ consists of all positions in $SA[sp, ep]$

1: total_num $= ep - sp + 1$, num $= 0$
2: perform early leaf nodes calculation exploiting $[sp, ep]$ and $P[0, i]$; add the obtained m positions to $R$; num $= num + m$
3: tree_height $= D - 1$
4: node.sp $= sp$, node.ep $= ep$, node.layer $= 0$
5: Queue, EnQueue(node)
6: while Queue is not empty && num $< total_num$ do
7: Queue, DeQueue(node)
8: sp $= node.sp$, ep $= node.ep$, layer $= node.layer$
9: if $ep - sp + 1 < threshold$ then
10: calculate positions in $SA[sp, ep]$ one-by-one in at most tree_height $- layer$ $- 1$ steps of LF operation; add the obtained m positions to $R$; num $= num + m$
11: else
12: $sp_{ occ} = rank_k(B, sp)$, $ep_{ occ} = rank_k(B, ep)$
13: num $= num + sep - sp_{ occ} + 1$
14: for $k = sp_{ occ}$ to sep do
15: Add $SSA[sa] + layer$ to $R$
16: end for
17: if layer $+ 1 < tree_height$ then
18: spchild $= C[sp] + rank_k(BWT(T), sp)$
19: epchild $= C[ep] + rank_k(BWT(T), ep)$
20: spchild $= C[sp] + rank_k(BWT(T), sp)$
21: epchild $= C[ep] + rank_k(BWT(T), ep)$
22: spchild $= C[sp] + rank_k(BWT(T), sp)$
23: epchild $= C[ep] + rank_k(BWT(T), ep) - 1$
24: spchild $= C[sp] + rank_k(BWT(T), ep) - 1$
25: epchild $= C[ep] + rank_k(BWT(T), ep) - 1$
26: for $t = 0$ to $3$ do
27: node.sp $= spchild + t$, node.ep $= epchild + t$
28: node.layer $= layer + 1$
29: Queue, EnQueue(node)
30: end for
31: end if
32: end if
33: end while
34: return $R$
```

Finally, early leaf nodes calculation subtracts 1 from the positions in $R$ which has been obtained in second stage.

Apart from early leaf nodes calculation, two simple branch-cut strategies are proposed to further improve the performance of FMtree (from 0-th step to $(D-2)$-th step). First, for an interval $SA[sp_i, ep_i]$ in $i$-th step $0 \leq i \leq D - 2$, if $ep_{ sp_i} - sp_{ ep_i} + 1$ is smaller than a predefined threshold, FMtree calculates all positions in $SA[sp, ep]$, one-by-one in at most $D - i - 2$ steps of LF operation. Thus, the number of LF operations for $SA[sp_i, ep_i]$ in following $D - i - 2$ steps is $(ep_{ sp_i} - sp_{ ep_i} + 1) \times (D - i - 2)$ in worst case. Note that the rank operation to BWT is the dominant cost of LF operation. When $D$ is large, if FMtree does not adopt this branch-cut strategy, the number of rank operations to BWT in following $D - i - 2$ steps is $2 \times (4^i + 4^{i+1} + \ldots + 4^{D-i-2}) = 8 \times (4^{D-i-2} - 1)/3$, which is much larger than $(ep_{ sp_i} - sp_{ ep_i} + 1) \times (D - i - 2)$. Similarly, the number of rank operations to B can also be reduced. Second, when locating a pattern with $occ$ occurrence positions, FMtree terminates once $occ$ occurrence positions have been obtained.
Full algorithm of FMtree. Algorithm 3 presents the full algorithm of FMtree. By utilizing a queue data structure Queue, the conceptual quadtree of FMtree is traversed in breadth-first order. In fact, the height of this quadtree is $D - 1$ instead of $D$ (line 3 in Algorithm 3). This is because early leaf nodes calculation (line 2 in Algorithm 3) is used to avoid the $(D - 1)$-th step in basic FMtree. For any node in quadtree, the $SA$ ranges of its four children are calculated jointly to improve the data locality (line 18-25 in Algorithm 3). A detailed analysis is presented in Supplementary Section S2.

4 Results

In our experiments, we used the following three datasets:

- DNA_200MB consists of 209.72 million characters from PizzackChili corpus (http://pizzachili.dec.uichile.cl/), which is the standard benchmark in compressed full-text indexes (Ferragina et al., 2009).
- For practical bioinformatics algorithms, their indexes must be able to process large texts with billions of characters. Thus, the human genome including 3.16 billion characters was used in our experiments.
- Another large text is the mouse genome. It consists of 2.73 billion characters.

These datasets were used as texts in our experiments. Like popular bioinformatics algorithms (Li, 2013; Li et al., 2009), character $n$ in these three datasets was converted to one of $a$, $c$, $g$ and $t$ randomly.

We first compare FMtree with two state-of-the-art methods, including locally compressed suffix array (LCMS) (González et al., 2015; González and Navarro, 2007) and LZ-index (Arroyuelo, 2006). LCMS is designed specifically to accelerate the locating operation of compressed full-text indexes, and LZ-index has been proven that it is very competitive in locating speed (Ferragina et al., 2009). Besides, we implemented two FM-index-based locating algorithms: Original_v and Original_s. The only difference between Original_v and Original_s is their sampling strategies.

Original_v locates patterns via the FM-index sampled by value sampling strategy, while Original_s locates patterns via the FM-index sampled by subscripts sampling strategy (see Section 3.1). For FMtree, Original_v and Original_s, we implemented a highly optimized FM-index for genomic data. Its main data structures ($C$ and $BWT(T)$) are similar to those in (Li et al., 2009), which is a well-established FM-index-based bioinformatics algorithm (see Supplementary Section S3). Note that FMtree, Original_v and Original_s are independent on any particular implementation of FM-indexes, so that we did not test these locating algorithms with other implementations of FM-indexes. Another family of compressed full-text indexes CSAs was not tested in our experiments. The reason is that for genomic data, previous studies (Ferragina et al., 2009; Gog and Petri, 2014) have shown that CSAs cannot outperform FM-indexes. LCSA and LZ-indexes for locating operation. For detailed description about the experimental setting, please see Supplementary Section S3.

4.1 Comparison on Small Text

In the first experiment, DNA_200MB was used as text to evaluate the performance of different methods. As previous studies about the locating operations (Ferragina et al., 2009; Gog and Petri, 2014), patterns were generated by randomly selecting 10 short substrings of length 5 from the text. By utilizing these short patterns with many occurrence positions, we could focus on the performance of locating operations and ignore the influence of counting operations. The reason is that compared with the locating time of different methods, their counting time was negligible in this experiment. For LZ-index, a parameter $c$ trades the locating time for space usage. With the increasing value of $c$, the space usage of LZ-index decreases, but its locating time increases. We set $c = \{1, 2, 3, 4\}$ in this experiment. For LCSA, its default parameters were directly used. For FM-indexes used in FMtree, Original_v and Original_s, we set the sampling distance $D = \{2, 3, 4, 5, 6, 7, 8\}$, to make the space usage of FM-indexes similar to that of LZ-index and LCSA.

As shown in Fig. 3, with similar space usage, FMtree is one or two order of magnitude faster than other methods. Apart from FMtree, LCSA outperforms other methods in locating speed. However, it requires much more space than the others. We also observe that the space usage of Original_s is slightly less than that of FMtree and Original_v. Unlike Original_s which uses subscript sampling strategy, FMtree and Original_v adopt value sampling strategy. Thus, FMtree and Original_v need an extra bitmap $B$ to mark all sampled positions in $SA$. In exchange, Original_s is about 1.5 times slower than Original_v, and at least 40 times slower than FMtree.

4.2 Comparison on Large and Practical Texts

In the second experiment, we studied the performance of different methods on two large texts: human genome and mouse genome. To generate patterns, we randomly extracted short substrings from both human genome and mouse genome. For each text, we generated four datasets including 100k patterns of length 12, 16, 20 and 25, respectively. In fact, short patterns of length 10 to 25 are widely used in existing bioinformatics

Fig. 3. Time/space tradeoffs of different methods for DNA_200MB.

Fig. 4. Time/space tradeoffs of different methods for human genome. For subgraph (a), (b), (c) and (d), the length of pattern is 12, 16, 20 and 25, respectively.
In this paper we propose a novel algorithm, FMtree, to accelerate the locating operations of FM-indexes for genomic data. When searching for a pattern via FM-indexes, FMtree builds a conceptual quadtree, so that multiple occurrence positions of the pattern can be obtained simultaneously by traversing this quadtree. In contrast, existing locating algorithms have to calculate all occurrence positions one-by-one. Therefore, FMtree reduces massive unnecessary operations and presents better data locality. We also introduce several strategies to further speed up FMtree.

We also introduce several strategies to further speed up FMtree. FMtree reduces massive unnecessary operations and presents better data locality. In the future, it would be interesting to optimize FMtree for the applications with large alphabet size.

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