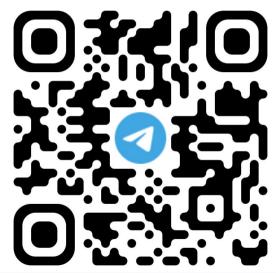
Anna Budkina

MIPT

16th October 2023

Telegram Chat



Glossary

- Alphabet $\{a_1, a_2, \ldots, a_A\}$
- String $S: s_1 s_2 \dots s_k$
- Substring S[i:j]: $s_i s_{i+1} \dots s_{j-1}$
- Prefix $S[:j]: s_1s_2 \dots s_j$
- Suffix S[j:] $s_j s_{j+1} \dots s_k$

Pattern Matching Task

Input:

- String $S: s_1 s_2 \dots s_n$
- String P (pattern): $p_1p_2 \dots p_m$, $m \leq n$

Output:

• Substring S[i:j]: S[i,j] = P.

index	suffix
6	\$
5	A\$
2	AABA\$
3	ABA\$
0	ABAABA\$
4	BA\$
1	BAABA\$



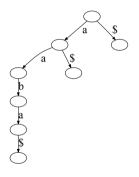
index	suffix
6	\$
5	A\$
2	AABA\$
3	ABA\$
0	ABAABA\$
4	BA\$
1	BAABA\$



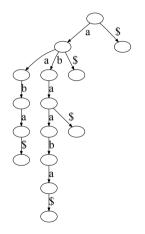
index	suffix
6	\$
5	A\$
2	AABA\$
3	ABA\$
0	ABAABA\$
4	BA\$
1	BAABA\$



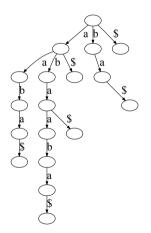
index	suffix
6	\$
5	A\$
2	AABA\$
3	ABA\$
0	ABAABA\$
4	BA\$
1	BAABA\$



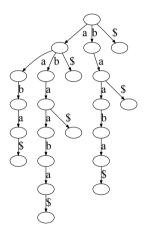
index	suffix
6	\$
5	A\$
2	AABA\$
3	ABA\$
0	ABAABA\$
4	BA\$
1	BAABA\$



index	suffix
6	\$
5	A\$
2	AABA\$
3	ABA\$
0	ABAABA\$
4	BA\$
1	BAABA\$

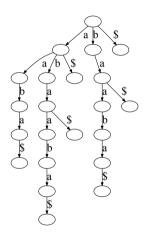


index	suffix
6	\$
5	A\$
2	AABA\$
3	ABA\$
0	ABAABA\$
4	BA\$
1	BAABA\$



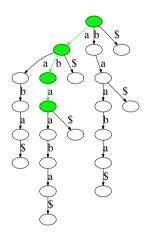
index	suffix
6	\$
5	A\$
2	AABA\$
3	ABA\$
0	ABAABA\$
4	BA\$
1	BAABA\$

Suffix Tree: finding pattern



$$P = ABA$$

Suffix Tree: finding pattern



$$P = ABA$$

S: ABAABA\$ (\$ - end of string)

\$ A B A A B A

```
$ A B A A B A
A $ A B A A B
B A $ A B A A
```

```
S: ABAABA$ ($ - end of string) Rotations
```

```
$ A B A A B A
A $ A B A A B
B A $ A B A A
A B A $ A B A
A B A $ A B
```

```
S: ABAABA$ ($ - end of string)

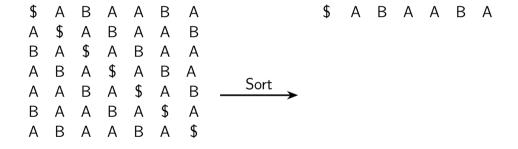
Rotations

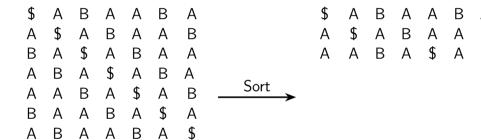
Rotations

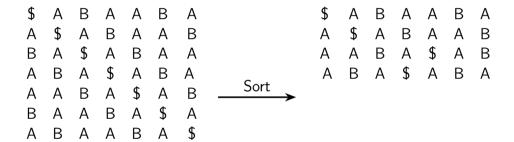
Rotations

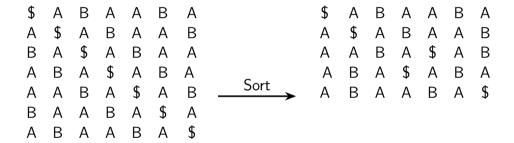
Rotations

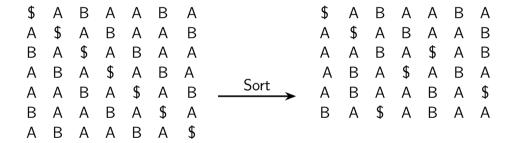
Rotations
```

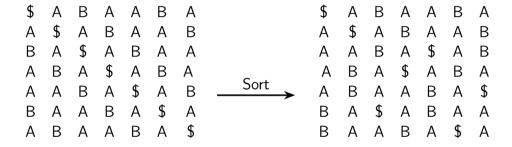


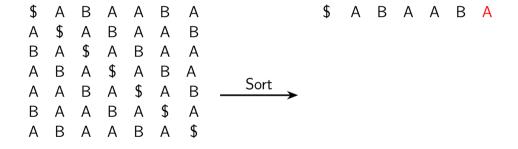


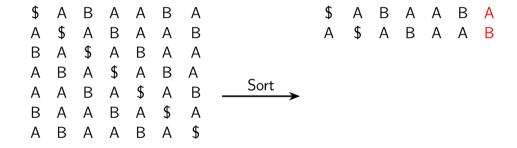


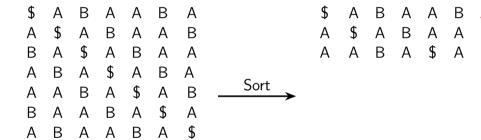


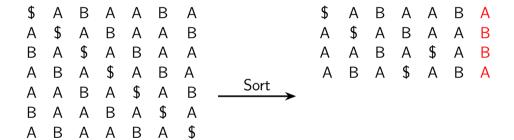


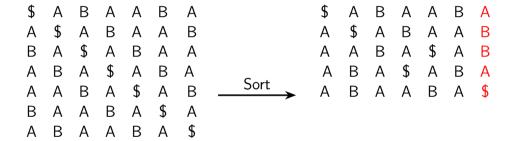


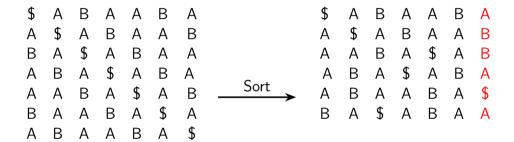


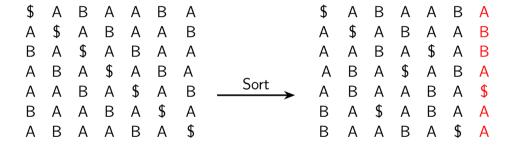












BWT compressing

$$S = ABAABA$$
\$
 $BWT(S) = ABBA$ \$AA

BWT compressing

$$S = ABAABA$$
\$
 $BWT(S) = ABBA$ \$AA
Let us code with RLE:

- 1 A
- 2 B
- 1 \$
- 2 A

BWT compressing

$$S = ABAABA$$
\$
 $BWT(S) = ABBA$ \$AA
Let us code with RLE:

- 1 A
- 2 B
- 1 \$
- 2 A

We will get string:

1*A*2*B*1\$2*A*

BWT: reversing: T ranking

Enumerate letters in the word S:

$$S = A_0 B_0 A_1 A_2 B_1 A_3$$
\$

BWT: LF mapping

$$S = A_0 B_0 A_1 A_2 B_1 A_3$$
\$

```
$ A B A A B A<sub>3</sub>
A<sub>3</sub> $ A B A A B<sub>1</sub>
A<sub>1</sub> A B A $ A B<sub>0</sub>
A<sub>2</sub> B A $ A B A<sub>1</sub>
A<sub>0</sub> B A A B A $
B<sub>1</sub> A $ A B A $
B<sub>1</sub> A $ A B A $
B<sub>0</sub> A A B A $ A<sub>0</sub>
```

BWT: LF mapping

$$S = A_0 B_0 A_1 A_2 B_1 A_3$$
\$

```
$ A B A A B A<sub>3</sub>
A<sub>3</sub> $ A B A A B<sub>1</sub>
A<sub>1</sub> A B A $ A B<sub>0</sub>
A<sub>2</sub> B A $ A B A<sub>1</sub>
A<sub>0</sub> B A A B A $
B<sub>1</sub> A $ A B A $
B<sub>1</sub> A $ A B A A<sub>2</sub>
B<sub>0</sub> A A B A $ A<sub>0</sub>
Last-First mapping
```

BWT: LF mapping: ordering

$$S = A_0 B_0 A_1 A_2 B_1 A_3$$
\$

```
$ A B A A B A<sub>3</sub>
A<sub>3</sub> $ A B A A B<sub>1</sub>
A<sub>1</sub> A B A $ A B<sub>0</sub>
A<sub>2</sub> B A $ A B A<sub>1</sub>
A<sub>0</sub> B A A B A $
B<sub>1</sub> A $ A B A $
B<sub>1</sub> A $ A B A $
B<sub>0</sub> A A B A $
```

BWT: LF mapping: ordering

$$S = A_0 B_0 A_1 A_2 B_1 A_3$$
\$

BWT: LF mapping: ordering

$$S = A_0 B_0 A_1 A_2 B_1 A_3$$
\$

BWT: LF mapping: B-ranking

$$S = A_0 B_0 A_1 A_2 B_1 A_3$$
\$

```
$ A B A A B A<sub>0</sub>
A<sub>0</sub> $ A B A A B<sub>0</sub>
A<sub>1</sub> A B A $ A B<sub>1</sub>
A<sub>2</sub> B A $ A B A<sub>1</sub>
A<sub>3</sub> B A A B A $
B<sub>0</sub> A $ A B A $
B<sub>1</sub>
A<sub>2</sub> B A $ A B A $
B<sub>1</sub>
A<sub>3</sub> B A A B A $
B<sub>1</sub>
A<sub>3</sub> B A A B A $
```

Sort letters by ascending order in First column.

Important remark!

We have built the FM index!

BWT: reversing from Fm index

$$S = A_0 B_0 A_1 A_2 B_1 A_3$$
\$

Idea

For each letter in F column we can get the previous letter in corresponding L column.

Question?

What is the last letter in S?

BWT: reversing

Starting from \$.

```
$ A<sub>0</sub>
```

 A_0 B_0

 A_1 B_1

 A_2 A_1

 A_3 :

 B_0 A_1

 B_1 A_1

Question

How to get string row with A_0 ?

BWT: reversing

Starting from \$.

```
$ A<sub>0</sub>
```

 A_0 B_0

 A_1 B_1

 A_2 A_1

43

 B_0 A_2

 B_1 A_3

Question

How to get string row with A_0 ?

Answer

Rows in F are sorted in lexicographical order.

$$Index(A_0) = 1 + 0$$

- 1 for \$
- 0 index of A_0

```
$A_0.
```

- A_0 B_0
- B_1
- A_1
- B_0 A_2

Question

How to get string row with B_0 ?

 A_0 .

 A_0

 A_0 B_0

 A_1 B_1

 A_2 A_1

 A_3

 B_0 A_2

 B_1 A_3

Question

How to get string row with B_0 ?

Answer

$$Index(B_0) = 1 + 4 + 0 = 5$$

- 1 for \$
- 4 number of A-s
- 0 index of B_0

```
A_0B_0.
```

\$ A₀

 A_0 B_0

 A_1 B_1

 A_2 A_1

 A_3 :

 B_0 A_2

 B_1 A_3

Question

How to get string row with A_2 ?

```
A_0B_0.
```

\$ A₀

 A_0 B_0

 A_1 B_1

 A_2 A_1

A₃ \$

 B_0 A_2

 B_1 A_3

Question

How to get string row with A_2 ?

Answer

$$Index(A_2) = 1 + 2 = 3$$

- 1 for \$
- 2 index of *A*₂

```
A_0B_0A_2.
```

\$ A₀

 A_0 B_0

 A_1 B_1

 A_2 A_1

 A_3

 B_0 A_2

 B_1 A_3

Question

How to get string row with A_1 ?

```
A_0B_0A_2.
```

\$ A₀

 A_0 B_0

 A_1 B_1

 A_2 A_1

 A_3 \$

 B_0 A_2

 B_1 A_3

Question

How to get string row with A_1 ?

Answer

$$Index(A_1) = 1 + 1 = 2$$

- 1 for \$
- 1 index of *A*₁

```
A_0B_0A_2A_1.
```

\$ A₀

 $\mathsf{A}_0 \quad \mathsf{B}_0$

 A_1 B_1

 A_2 A_1

 A_3

 B_0 A_2

 B_1 A_3

Question

How to get string row with B_1 ?

$$A_0B_0A_2A_1$$
.

- A_0
- A_0 B_0
- A_1 B_1
- A_2 A_1
- Δ_2
- B_0 A_2
- B_1 A_3

Question

How to get string row with B_1 ?

Answer

$$Index(A_1) = 1 + 4 + 1 = 6$$

- 1 for \$
- 4 number of A-s
- 1 index of B_1

```
A_0B_0A_2A_1B_1.
```

 A_0

 A_0 B_0

 A_1 B_1

 A_2 A_1

A₃ \$

 B_0 A_2

 B_1 A_3

Question

How to get string row with A_3 ?

$$A_0B_0A_2A_1B_1$$
.

 A_0

 A_0 B_0

 A_1 B_1

 A_2 A_1

A₃ \$

 B_0 A_2

 B_1 A_3

Question

How to get string row with A_3 ?

Answer

$$Index(A_1) = 1 + 3 = 4$$

- 1 for \$
- 3 index of A_3

```
A_0B_0A_2A_1B_1A_3.
```

 A_0

 A_0 B_0

 A_1 B_1

 A_2 A_1

 A_3

 B_0 A_2

 B_1 A_3

Question

Have we finished?

```
A_0B_0A_2A_1B_1A_3.
```

\$ A₀

 A_0 B_0

 A_1 B_1

 A_2 A_1

 A_3

 B_0 A_2

 B_1 A_3

Question

Have we finished?

Answer

Not yet!

We should reverse string:

 $A_3B_1A_1A_2B_0A_0$ \$

```
S = ABAABA

P = ABA

A_0

A_0

A_0

A_1

A_1

A_1

A_2

A_1

A_2

A_1

A_3

B_0

A_2
```

Question

How to go next?

```
S = ABAABA$
P = ABA
A_0
A_0
B_0
A_1
B_1
A_2
A_1
A_3
B_0
A_2
```

Question

How to go next?

Answer

Watch for the previous letter! B.

```
S = ABAABA$
P = ABA$
A_0
A_0
A_1
A_2
A_1
A_3
B_0
A_2
```

Question

Why B are stored sequentially?

```
S = ABAABA

P = ABA

A_0

A_0

A_0

A_1

A_1

A_1

A_2

A_1

A_3

B_0

A_2

B_1

A_2
```

Question

Why B are stored sequentially?

Answer

Because in row we find strings, started with BA!

BWT: pattern search with FM-indexing

```
S = ABAABA$
P = ABA
$ A<sub>0</sub>
A<sub>0</sub> B<sub>0</sub>
A<sub>1</sub> B<sub>1</sub>
A<sub>2</sub> A<sub>1</sub>
A<sub>3</sub> $
B<sub>0</sub> A<sub>2</sub>
```

Question

How to go next?

BWT: pattern search with FM-indexing

```
S = ABAABA

P = ABA

A_0

A_0

A_0

A_1

A_1

A_1

A_2

A_1

A_3

B_0

A_2

B_1

A_2
```

Question

How to go next?

Answer

Watch for the previous letter! A.

BWT: pattern search with FM-indexing

```
S = ABAABA$
P = ABA
A_0
A_0
B_0
A_1
B_1
A_2
A_1
A_3
B_0
A_2
B_1
A_3
```

• Scanning in last column L is slow

- Scanning in last column L is slow
 - Store prefix sums of As and Bs in L

We need space to store ranks

• Store "checkpoints"

```
F L N(A) N(B)
$ A<sub>0</sub> - -
A<sub>0</sub> B<sub>0</sub> 1 1
A<sub>1</sub> B<sub>1</sub> - -
A<sub>2</sub> A<sub>1</sub> - -
A<sub>3</sub> $ -
B<sub>0</sub> A<sub>2</sub> 3 2
B<sub>1</sub> A<sub>3</sub> - -
```

We need space to store ranks

• Store "checkpoints"

```
F L N(A) N(B)
$ A<sub>0</sub> - 1-1
A<sub>0</sub> B<sub>0</sub> 1 1
A<sub>1</sub> B<sub>1</sub> - -
A<sub>2</sub> A<sub>1</sub> - -
A<sub>3</sub> $ - 2-0
B<sub>0</sub> A<sub>2</sub> 3 2
B<sub>1</sub> A<sub>3</sub> - -
```

We want to get positions of P in T string

Naive solution: Add suffix array

```
SA F L
```

- 6 \$ A₀
- 5 A_0 B_0
- 2 A₁ B₁
- A_2 A_1
- 0 A₃ \$
- 4 B_0 A_2
- 1 B_1 A_3

We want to get positions of P in T string

- Naive solution: Add suffix array
- Build "partial suffix array": randomly select elements of suffix array to save

```
SA F L
```

- 6 A_0
- A_0 B_0
- A_1 B_1
- A_2 A_1
- 0 A_3 \$
- 4 B_0 A_2
- B₁ A₃

BWT: vs opponents

- Suffix Tree: >40 GB
- Suffix Array: >16 GB
- FM-index: <3GB

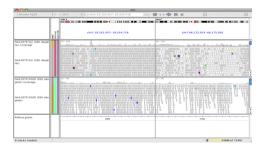
Burrows-Wheeler Transform

Aligning short-sequencing reads to genome.

- BWA-mem
- Bowtie, Bowtie2 (DNA-seq)
- Tophat, Tophat2, Hisat2 (RNA-seq)

Nucleotide Sequence Alignment





RNA-seq DNA-seq

Nucleotide Sequence Alignment

```
VN:1.0 SO:coordinate
      SN:chr20
                    LN:64444167
      ID: TopHat
                    VN:2.0.14
                                 CL:/srv/dna tools/tophat/tophat -N 3 --read-edit-dist 5 --read-rea
lign-edit-dist 2 -i 50 -I 5000 --max-coverage-intron 5000 -M -o out /data/user446/mapping tophat/index/chr
20 /data/user446/mapping tophat/L6 18 GTGAAA L007 R1 001.fastg
HWI-ST1145:74:C101DACXX:7:1102:4284:73714
                                                      190930 3
                                               chr20
     CCGTGTTTAAAGGTGGATGCGGTCACCTTCCCAGCTAGGCTTAGGGATTCTTAGTTGGCCTAGGAAATCCAGCTAGTCCTGTCTCTCAGTCCCCCTCT
    XM:i:3 X0:i:0 XG:i:0 MD:Z:55C20C13A9 NM:i:3 NH:i:2 CC:Z:= CP:i:55352714
HWI-ST1145:74:C101DACXX:7:1114:2759:41961
                                               chr20
                                                      193953 50
      TGCTGGATCATCTGGTTAGTGGCTTCTGACTCAGAGGACCTTCGTCCCCTGGGGCAGTGGACCTTCCAGTGATTCCCCTGACATAAGGGGCATGGACGA
   DCDDDDEDDDDDDDDDDDCCCDDDCDDDDDEEC>DFFFF13131TG33331HGRHHG3T33333T3333T3333TH33333HHHHHHFFFFFCCC
                 XM:i:3 XO:i:0 XG:i:0 MD:7:60G16T18T3 NM:i:3 NH:i:1
   AS:1:-16
HWT-ST1145:74:C101DACXX:7:1204:14760:4030
                                               chr20
                                                     270877 50
     DDDDDDDDDCCDDDDDDDDDEEEEEEEFFFEFEGHHHHFGDJJHJJJJJJJJJIIIGGFJJHIIIJJJJJJJGHHFAHGFHJHFGGHFFFDD@BB
                 XM:i:2 X0:i:0 XG:i:0 MD:Z:0A85G13
HWT-ST1145:74:C101DACXX:7:1210:11167:8699
                                               chr20
                                                     271218 50
                                                                    50M4700N50M
            GTGGCTCTTCCACAGGAATGTTGAGGATGACATCCATGTCTGGGGTGCACTTGGGTCTCCGAAGCACACATCCTCAAATATGACCTCTCG
accepted hits.sam
```

SAM Format