Exercise sheet 10: Introduction to Mapping

Exercise 1

1a)

Extract the Burrows-Wheeler Transform B(S) of $S = TGGTGGTTGA\$$.

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Solution $B(S) = AGTTTGGT\$GG$

i	SA[i]	SA[i]-th suffix	Rotation	Last column
1	11	$	$TGGTGGTTGA	A
2	10	A$	A$TGGTGGTTG	G
3	9	GA$	GA$TGGTGGTT	T
4	2	GGTGGTTGA$	GGTGGTTGA$T	T
5	5	GGTTGA$	GGTTGA$TGGT	T
6	3	GTGGTTGA$	GTGGTTGA$TG	G
7	6	GTTGA$	GTTGA$TGGTG	G
8	8	TGA$	TGA$TGGTGGT	T
9	1	TGGTGGTTGA$	TGGTGGTTGA$	$
10	4	TGGTTGA$	TGGTTGA$TGG	G
11	7	TTGA$	TTGA$TGGTGG	G

1b)

Invert the Burrows-Wheeler-Transform $B(S) = TCAACT\$AA$ to obtain S.

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Hint 1 You can get the first column $F(S)$ of the Burrows Wheeler Matrix via counting and sorting the letters since it has a very predictably structure.

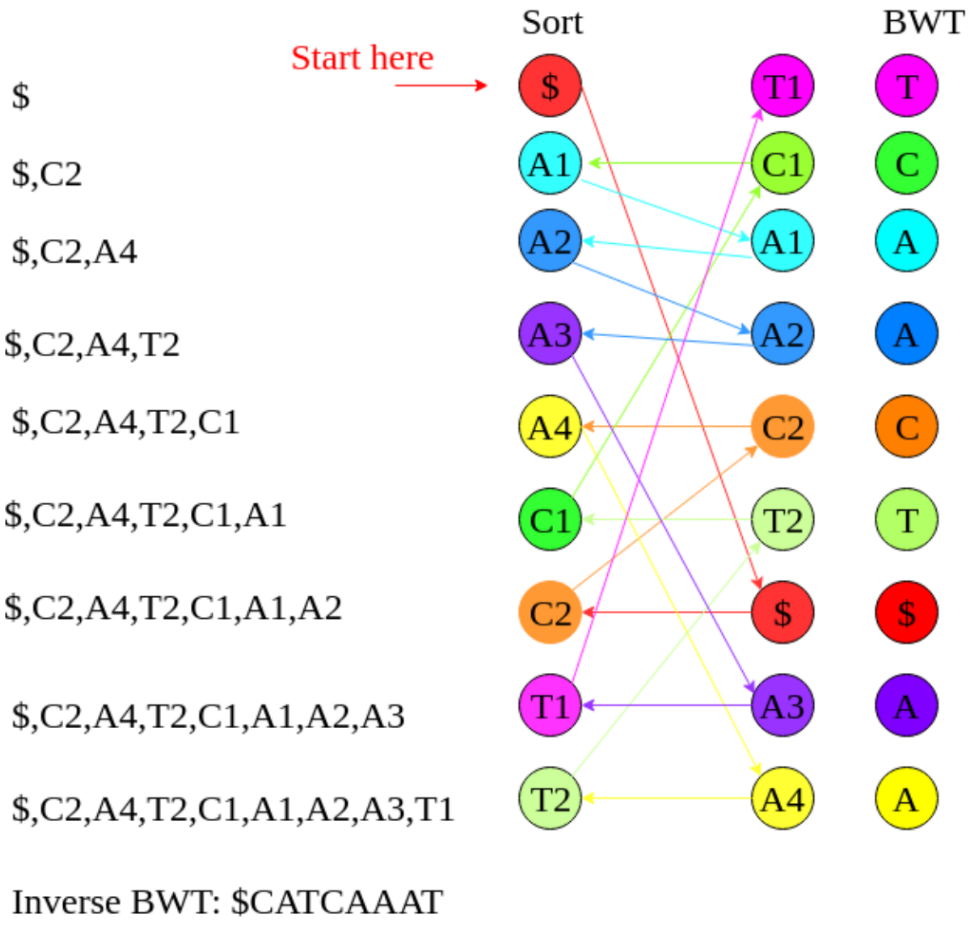
$F(S) = \$AAAACCTT$

Hint 2 Use the last-first mapping to assign indices to the corresponging letters in the first $F(S)$ and the last column $B(S)$

$F(S) = \$_1 A_1 A_2 A_3 A_4 C_1 C_2 T_3 T_4$

$B(S) = T_1 C_1 A_1 A_2 C_2 T_2 \$_1 A_3 A_4$

Solution 1



Solution 2 Step-by-step method:

Add
T
C
A
A
C
T
!
A
A

→

Sort
!
A
A
A
A
C
C
T
T

Add	
T	!
C	A
A	A
A	A
C	A
T	C
!	C
A	T
A	T

→

Sort	
!	C
A	A
A	A
A	T
A	T
C	A
C	A
T	!
T	C

Add		
T	!	C
C	A	A
A	A	A
A	A	T
C	A	T
T	C	A
!	C	A
A	T	!
A	T	C

→

Sort		
!	C	A
A	A	A
A	A	T
A	T	!
A	T	C
C	A	A
C	A	T
T	!	C
T	C	A

Add			
T	!	C	A
C	A	A	A
A	A	A	T
A	A	T	!
C	A	T	C
T	C	A	A
!	C	A	T
A	T	!	C
A	T	C	A

→

Sort			
!	C	A	T
A	A	A	T
A	A	T	!
A	T	!	C
A	T	C	A
C	A	A	A
C	A	T	C
T	!	C	A
T	C	A	A

Add				
T	!	C	A	T
C	A	A	A	T
A	A	A	T	!
A	A	T	!	C
C	A	T	C	A
T	C	A	A	A
!	C	A	T	C
A	T	!	C	A
A	T	C	A	A

→

Sort				
!	C	A	T	C
A	A	A	T	!
A	A	T	!	C
A	T	!	C	A
A	T	C	A	A
C	A	A	A	T
C	A	T	C	A
T	!	C	A	T
T	C	A	A	A

Add					
T	!	C	A	T	C
C	A	A	A	T	!
A	A	A	T	!	C
A	A	T	!	C	A
C	A	T	C	A	A
T	C	A	A	A	T
!	C	A	T	C	A
A	T	!	C	A	T
A	T	C	A	A	A

→

Sort					
!	C	A	T	C	A
A	A	A	T	!	C
A	A	T	!	C	A
A	T	!	C	A	T
A	T	C	A	A	A
C	A	A	A	T	!
C	A	T	C	A	A
T	!	C	A	T	C
T	C	A	A	A	T

Add						
T	!	C	A	T	C	A
C	A	A	A	T	!	C
A	A	A	T	!	C	A
A	A	T	!	C	A	T
C	A	T	C	A	A	A
T	C	A	A	A	T	!
!	C	A	T	C	A	A
A	T	!	C	A	T	C
A	T	C	A	A	A	T

→

Sort						
!	C	A	T	C	A	A
A	A	A	T	!	C	A
A	A	T	!	C	A	T
A	T	!	C	A	T	C
A	T	C	A	A	A	T
C	A	A	A	T	!	C
C	A	T	C	A	A	A
T	!	C	A	T	C	A
T	C	A	A	A	T	!

Add							
T	!	C	A	T	C	A	A
C	A	A	A	T	!	C	A
A	A	A	T	!	C	A	T
A	A	T	!	C	A	T	C
C	A	T	C	A	A	A	T
T	C	A	A	A	T	!	C
!	C	A	T	C	A	A	A
A	T	!	C	A	T	C	A
A	T	C	A	A	A	T	!

→

Sort							
!	C	A	T	C	A	A	A
A	A	A	T	!	C	A	T
A	A	T	!	C	A	T	C
A	T	!	C	A	T	C	A
A	T	C	A	A	A	T	!
C	A	A	A	T	!	C	A
C	A	T	C	A	A	A	T
T	!	C	A	T	C	A	A
T	C	A	A	A	T	!	C

Add								
T	!	C	A	T	C	A	A	A
C	A	A	A	T	!	C	A	T
A	A	A	T	!	C	A	T	C
A	A	T	!	C	A	T	C	A
C	A	T	C	A	A	A	T	!
T	C	A	A	A	T	!	C	A
!	C	A	T	C	A	A	A	T
A	T	!	C	A	T	C	A	A
A	T	C	A	A	A	T	!	C

→

Sort								
!	C	A	T	C	A	A	A	T
A	A	A	T	!	C	A	T	C
A	A	T	!	C	A	T	C	A
A	T	!	C	A	T	C	A	A
A	T	C	A	A	A	T	!	C
C	A	A	A	T	!	C	A	T
C	A	T	C	A	A	A	T	!
T	!	C	A	T	C	A	A	A
T	C	A	A	A	T	!	C	A

1c)

Search for CAT in $B(S) = TCAACT\$AA$.

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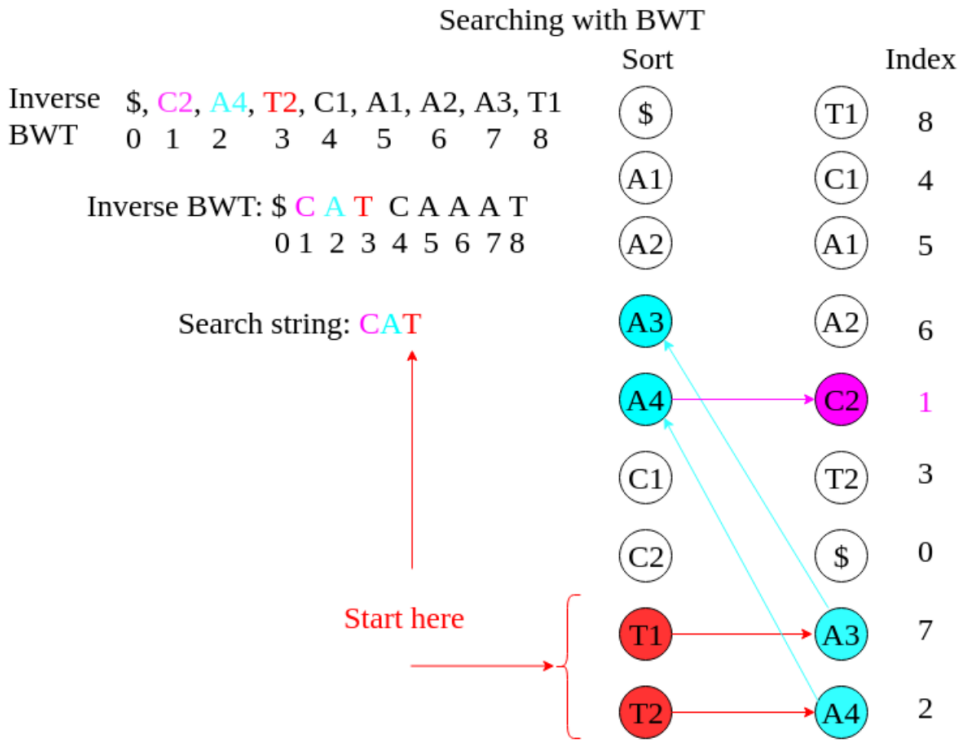
Solution



Exercise 2

Read the publication on the bwa-mem aligner at https://arxiv.org/abs/1303.3997 and pay particular attention to the re-seeding and chaining features of the algorithm. Now consider a read $R = CCCCGTTTT$ and a reference genome $T = ...CCCCATTTT...CCCCGA...AGTTTT...$ and explain step-by-step how re-seeding and chaining let bwa-mem let recover the correct best alignment of R to T.

2a)

What are the original SMEMs that get generated?

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Solution The original MEMs are CCCCG and GTTTT.

2b)

Would these SMEMs lead to discovery of the best possible alignment?

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Solution No, because it would not lead to a best possible match in the reference genome. The current seeds are too specific and we may miss the seeds that lead to the best mapping (CCC- CATTTT), therefore we need to reseed.

2c)

Which shortened new SMEMs are discovered with re-seeding (assume re-seeding gets perfor- med despite the below-threshold length of the SMEMs)?

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Solution Re-seeding around the central base of each MEM leads to discovery of CCCC and TTTT (both occur once more often than the originals).

2d)

What is the effect of chaining of colinear seeds?

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Solution The two new seeds are colinear on R and T , and can be merged into a chain, so only one local alignment has to be performed.

Exercise 3 - Programming assignment

For the programming tasks, please follow the instructions given in GitHub Classroom under the following link.

https://classroom.github.com/a/ABJ6qwOf
