Finding tandem repeats in genomic data

Projects in Bioinformatics, 10 ECTS
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Tandem repeat: $ATCTG \; ATCTG$.

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- Find all TRs in string x of length n.

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Tandem repeat: $ATCTG\ \ ATCTG$.

- Find all TRs in string x of length n.
- Suffix tree- vs. suffix array algorithm.
- Both time $O(n \log n + z)$.

Tandem repeats and branching tandem repeats

- Non-branching vs. branching TRs.

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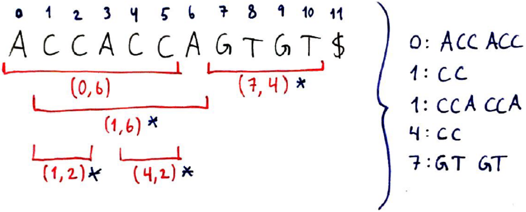
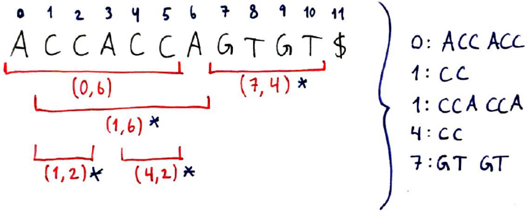


Tandem repeats and branching tandem repeats

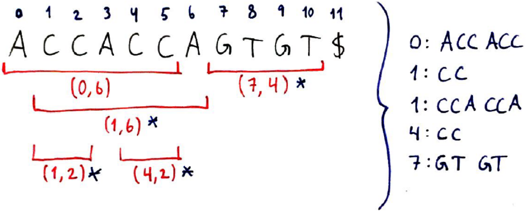
- Non-branching vs. branching TRs.



- Every *non-branching* TR is a *left-rotation* of another TR that starts one place to its right.

Tandem repeats and branching tandem repeats

- Non-branching vs. branching TRs.



- Every *non-branching* TR is a *left-rotation* of another TR that starts one place to its right.
- Find all TRs from branching ones in time $O(z)$.

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Suffix tree

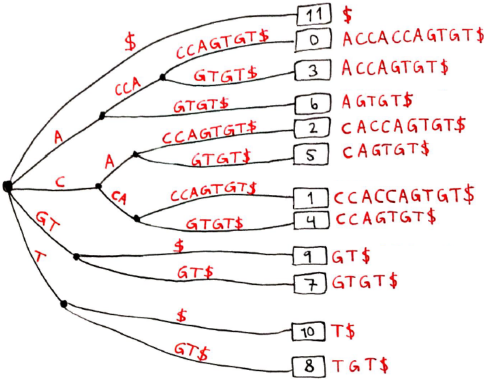
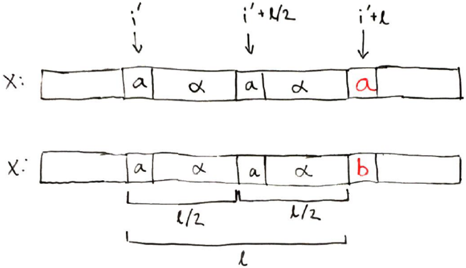
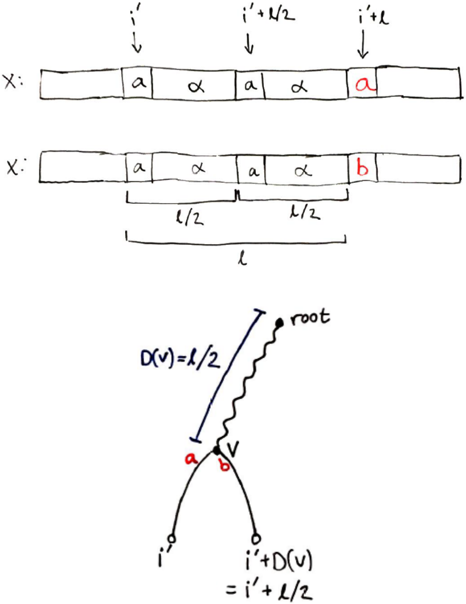


Figure: Suffix tree for string $x = ACCACCAGTGT\$$.

Finding branching TRs



Finding branching TRs



Finding branching TRs

Algorithm BRANCHING-REPEATS(T)

```
for each inner node, v, in T do
    for each leaf, i', in sub-tree of v do
        if leaf i' + D(v) is also in sub-tree of v and x[i'] ≠ x[i' + 2D(v)] then
            report (i', 2D(v))
        end if
    end for
end for
```

Finding branching TRs

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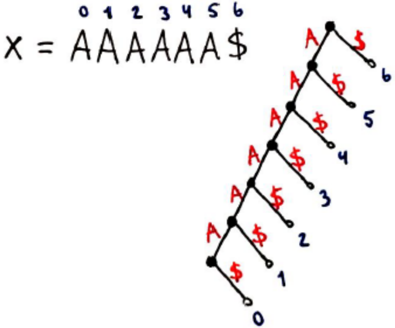
```

How to determine if leaf is in sub-tree of node v?

- DFS numbering $\Rightarrow$ constant query time.

Running time



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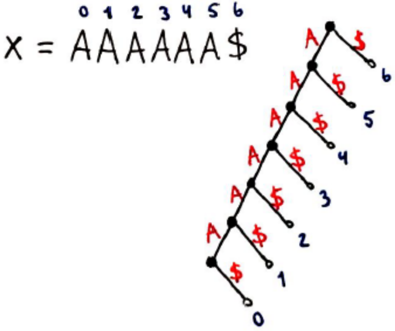

Worst case: $\Theta(n^2)$.

The smaller half trick

Algorithm BRANCHING-REPEATS-SMALLER-HALF(T)

for each inner node, v, in T **do**
    for each leaf, i', in "sub-tree of v except widest(v)" **do**
        if leaf $i' + D(v)$ is also in sub-tree of v **and** $x[i'] \neq x[i' + 2D(v)]$ **then**
            report $(i', 2D(v))$
        end if
        $j' \leftarrow i' - D(v)$
        if leaf j' is in sub-tree of *widest*(v) **and** $x[j'] \neq x[j' + 2D(v)]$ **then**
            report $(j', 2D(v))$
        end if
    end for
end for

The smaller half trick

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            report (i', 2D(v))
        end if
        j' ← i' − D(v)
        if leaf j' is in sub-tree of widest(v) and x[j'] ≠ x[j' + 2D(v)] then
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        end if
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```

Smaller half trick: $O(n \log n)$.

The smaller half trick

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end for

Smaller half trick: $O(n \log n)$.
Total time: $O(n \log n + z)$.

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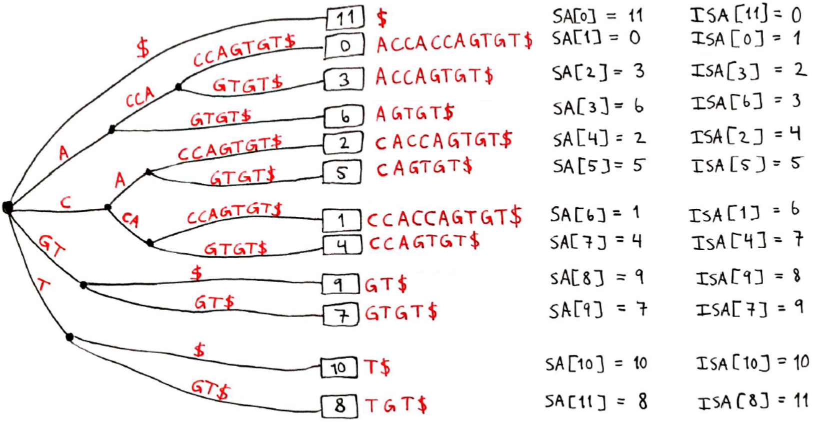
Suffix array



ℓ-intervals

SA:	LCP:
$	0
ACCACCAGTGT$	0
ACCAGTGT$	4
AGTGT$	1
CACCAGTGT$	0
CAGTGT$	2
CCACCAGTGT$	1
CCAGTGT$	3
GT$	0
GTGT$	2
T$	0
TGT$	1

ℓ-intervals

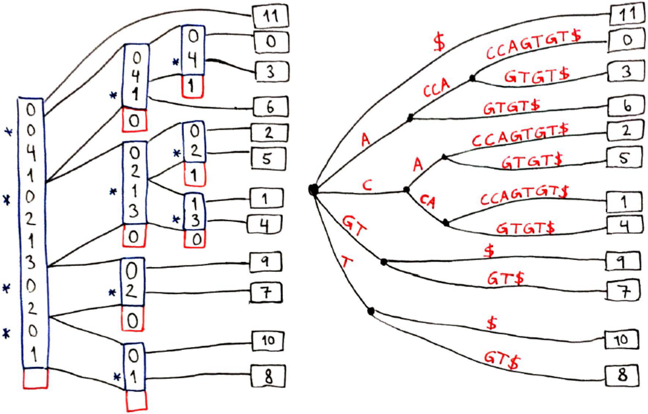
SA:	LCP:
$	0
ACCACCAGTGT$	0
ACCAGTGT$	$\boxed{4}$
AGTGT$	1
CACCAGTGT$	0
CAGTGT$	2
CCACCAGTGT$	1
CCAGTGT$	3
GT$	0
GTGT$	2
T$	0
TGT$	1

$\ell = min_{k \in (i,j)} LCP[k]$ and either

$i = 0$ or $LCP[i] < \ell$ and either

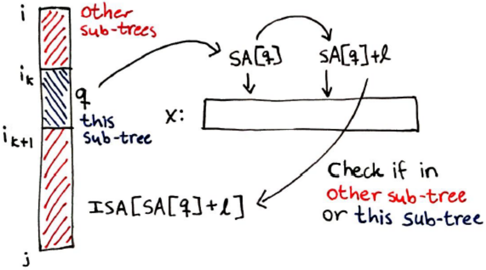
$j = n$ or $LCP[j] < \ell$

ℓ-intervals



- Use RMQ to find ℓ.

Find TRs using suffix array



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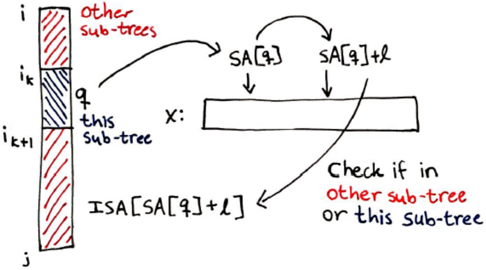
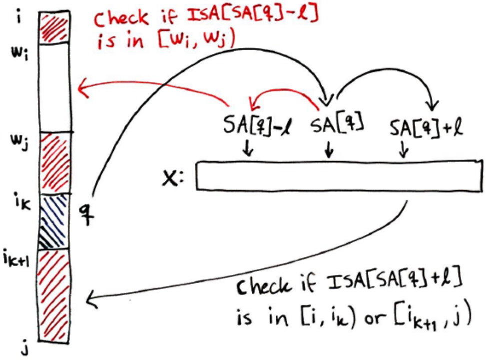
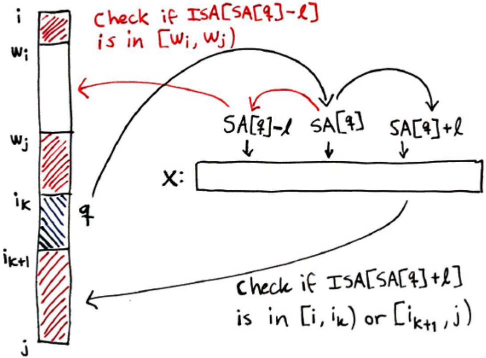


- Again time $\Theta(n^2) \Rightarrow$ use smaller half trick!

Find TRs using suffix array - smaller half trick

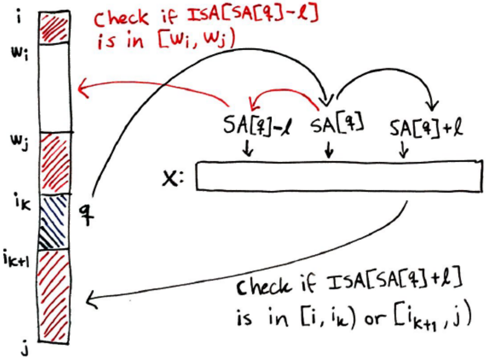


Find TRs using suffix array - smaller half trick



- Time $O(n \log n)$.

Find TRs using suffix array - smaller half trick



- Time $O(n \log n)$.
- Total time $O(n \log n + z)$.

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Implementation: Finding branching TRs

```
def branching_TR_smaller_half(x, sa, lcp):
    isa = construct_isa(sa)
    M = RMQ_preprocess(lcp)
    for (i, j) in get_inner_nodes(lcp, M, 0, len(x)):
        child_nodes = list(get_child_nodes(lcp, M, i, j))
        (w_i, w_j) = widest(child_nodes)
        (_, L) = RMQ(lcp, M, i + 1, j)
        for (ii, jj) in child_nodes:
            if (ii, jj) == (w_i, w_j):
                continue
            for q in valid_isa_index(sa, ii, jj, +L):
                r = isa[sa[q] + L]
                if (i <= r < j) and not (ii <= r < jj):
                    yield (sa[q], 2*L)
            for q in valid_isa_index(sa, ii, jj, -L):
                r = isa[sa[q] - L]
                if w_i <= r < w_j:
                    yield (sa[r], 2*L)
```

Implementation: Finding all TRs

```
def find_all_tandem_repeats(x, branching_TRs):
    for (i, L) in branching_TRs:
        yield (i, L)
        while can_rotate(x, i, L):
            yield (i-1, L)
            i -= 1

def can_rotate(x, i, L):
    return i > 0 and x[i - 1] == x[i + L - 1]
```

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Correctness

```
**********************
TANDEM REPEATS, (index, length), for string:
x: ACCACCAGTGT$
(0, 6): ACC ACC
(1, 2): C C
(1, 6): CCA CCA
(4, 2): C C
(7, 4): GT GT
**********************
```

```
**********************
TANDEM REPEATS, (index, length), for string:
x: aaaaaa$
(0, 2): a a
(0, 4): aa aa
(0, 6): aaa aaa
(1, 2): a a
(1, 4): aa aa
(2, 2): a a
(2, 4): aa aa
(3, 2): a a
(4, 2): a a
**********************
```

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TANDEM REPEATS, (index, length), for string:
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x: aaaaaa$
(0, 2): a a
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(1, 2): a a
(1, 4): aa aa
(2, 2): a a
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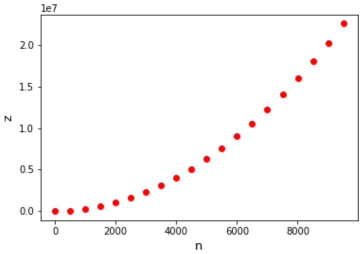
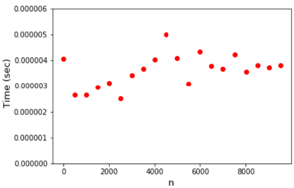
(3, 2): a a
(4, 2): a a
*********************
```

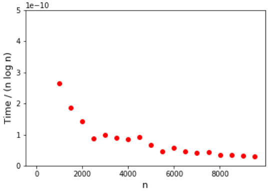
Number of found TRs for $A^n\$$:



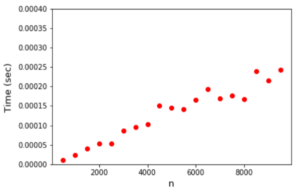
Running time: Worst case input

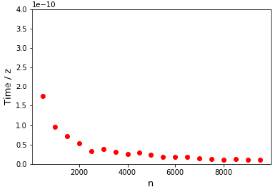
Finding branching tandem repeats:





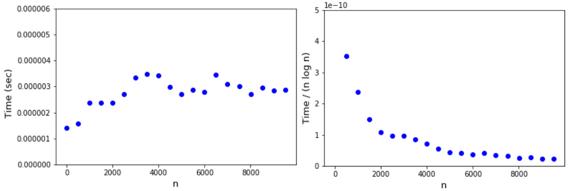
Finding all tandem repeats:





Running time: Random input

Finding branching tandem repeats:



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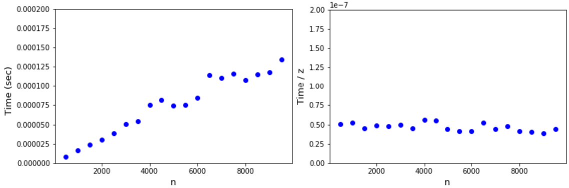

Discussion and conclusion

- TRs can be found using ST or SA.
- Same time complexity, $O(n \log n + z)$.
- ST better for visualising algorithm.
- SA more space efficient and simpler data structures.

Finding all TRs from the branching TRs

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- Non-branching $\Rightarrow x[i', i' + \ell] = a\beta a\beta a$.

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- (i', ℓ) is a left-rotation of $(i' + 1, \ell)$.

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- Non-branching $\Rightarrow x[i', i' + \ell] = a\beta a\beta a$.
- (i', ℓ) is a left-rotation of $(i' + 1, \ell)$.

We can find all the TRs by repeated left-rotations from the *branching* TRs! Time $O(z)$.