

Tractability Results for the Consecutive-Ones Property with Multiplicity

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The Consecutive-Ones Property

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Definition

- ▶ A **binary matrix M** has the **Consecutive Ones-Property (C1P)** if its columns can be ordered in such a way that in each row, **all 1's are contiguous (A C1P Ordering)**.
- ▶ Classical combinatorial object, used in graph theory (Booth and Lueker 1976), physical mapping (Goldberg et al. 1995), ...

A C1P matrix

a	b	c	d	e
1	1	0	1	0
1	0	1	0	0
0	1	0	1	1

A non-C1P matrix

f	g	h	i	j
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The Consecutive-Ones Property: Important Results

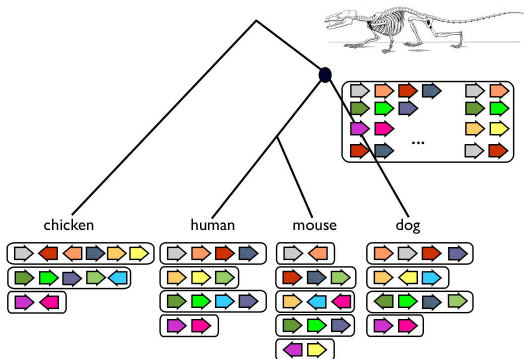
- ▶ Introduced by Fulkerson and Gross (1965), motivated by problems in genetics.
- ▶ Characterization of non-C1P matrices in terms of forbidden submatrices: Tucker (1972).
- ▶ Deciding if a binary matrix M is C1P can be done in polynomial time and all C1P column orderings can be represented in linear space with a PQ-tree: Booth and Lueker (1976).
- ▶ Decision algorithm based on partition refinement: Habib et al. (2000).
- ▶ Link with PQR-trees and partitive families: Meidanis et al. (1998, 2005), McConnell (2004).
- ▶ Algorithmical study of Tucker submatrices: Dom (2008), Blin et al. (2010).

Reconstructing Ancestral Gene Orders

Reconstructing Ancestral Gene Orders (AGOs)

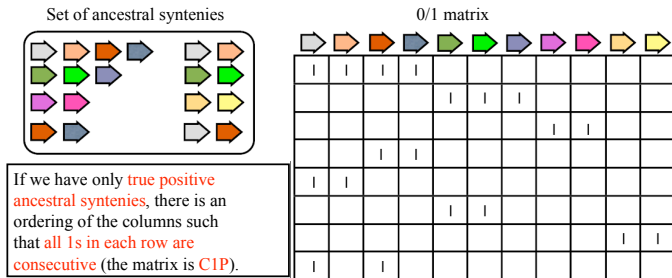
Given a **phylogenetic tree** on a set of **extant (i.e., sequenced)** species, we want to **infer possible gene orders** of an **(unknown) ancestor** in this tree. We have

1. a set of (orthologous) **genomic markers**, and
2. a set of **ancestral syntenies**: groups of markers that are believed to have been **contiguous** in this ancestral genome.



Reconstructing AGOs and the C1P

AGOs correspond to C1P orderings of the binary matrix M with **rows** (**columns**) corresponding to **genomic markers** (**ancestral syntenies**).



A possible C1P ordering, that represents a set of CARs.



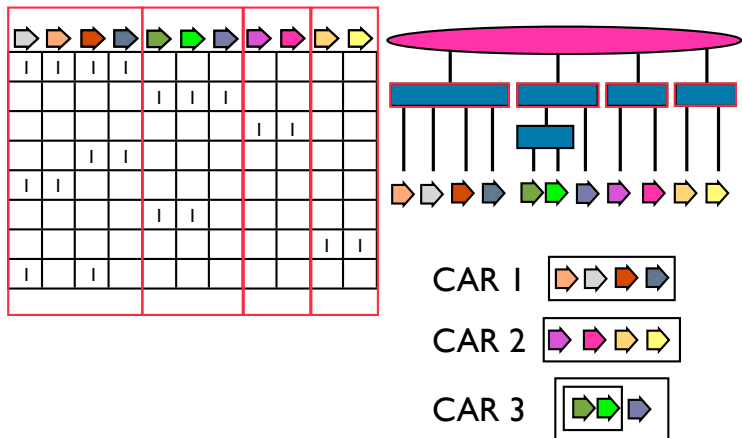
Another one, that represents **another possible ancestral architecture**.



Each C1P ordering describes a set of possible **Contiguous Ancestral Regions (CARs)**: Ma et al. (2006), Adam and Sankoff (2007), Chauve and Tannier (2008), ...

Reconstructing AGOs and the C1P

If binary matrix M is **C1P**, we can represent all C1P orderings, i.e., ancestral gene orders, with a **PQ-tree** (Booth and Lueker, 1976).

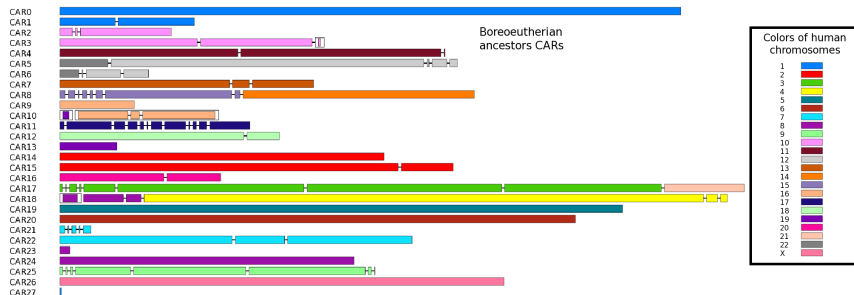


CARs are the children of the root of this PQ-tree

Reconstructing AGOs and the C1P: An Example

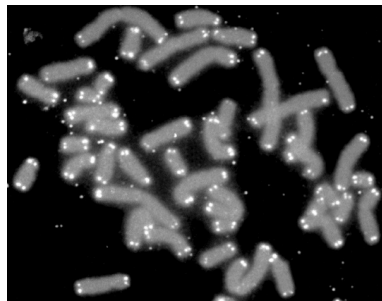
Placental mammals ancestor from 11 extant genomes (Chauve and Tannier, 2008)

- ▶ 689 markers (100kb resolution)
- ▶ 2326 ancestral syntenies
- ▶ well resolved ancestral genome with 28 CARs



Telomeres

A **telomere** is a region of the DNA sequence at the end of a chromosome, which protects the end of the chromosome from deterioration or from fusion with neighboring chromosomes



A Natural Question

In general, a CAR is an ancestral chromosomal segment, so which CARs are believed to

- (a) form a complete ancestral chromosome? or, more generally,
- (b) contain an extremity of a chromosome: an **ancestral telomere**?

The C1P with Multiplicity

- ▶ Allow each column c of the matrix to appear multiple ($\mathbf{m}(c) \geq 1$) times in any “ordering” S (a sequence) of columns of M
- ▶ The question is then to decide if there is an S that is “C1P” (contains each row somewhere as a subsequence) and that each column c satisfies its multiplicity constraint $\mathbf{m}(c)$
- ▶ We call such a sequence S an **mC1P ordering with multiplicity vector \mathbf{m}**

A non-C1P matrix

a	b	c	d	e
1	1	0	1	0
1	0	0	0	1
1	0	1	1	0

mC1P ordering: $\mathbf{m}(a) = 2$
 $(\mathbf{m}(b), \dots, \mathbf{m}(e) = 1)$

e	a	b	d	c	a
0	1	1	1	0	1
1	1	0	0	0	1
0	1	0	1	1	1

The C1P with Multiplicity

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In the literature:

- ▶ Even for matrices with 3 ones per row and $\mathbf{m}(c) \leq 2$ for all columns c , this decision problem is NP-hard: Wittler et al. (2009)

Reconstructing AGOs with Telomeres and the mC1P

We model telomeres with a column c' with multiplicity

- ▶ Let ancestral synteny $abcd$ contain a marker that is an extremity of an ancestral chromosome (i.e., the synteny is telomeric in two extant decendants of the ancestor)
- ▶ $abcd$ is represented in M as follows:

	a	b	c	d		c'
			\vdots			
...	1	1	1	1	...	1
...	1	1	1	1	...	0
			\vdots			

- ▶ This ensures that if M has the mC1P, then the occurrences of c' are located at the extremities of the CARs (o.w. M does not have the mC1P)

Matrices with Matched Multirows: A Polytime Solvable Class of mC1P Instances

M	1	2	3	4	5	a	b
r_1	1	1	0	0	0	1	1
\hat{r}_1	1	1	0	0	0	0	0
r_2	1	1	1	0	0	0	0
r_3	0	0	1	1	1	0	1
\hat{r}_3	0	0	1	1	1	0	0
r_4	0	0	0	1	1	0	1
\hat{r}_4	0	0	0	1	1	0	0
r_5	1	0	0	1	1	0	0

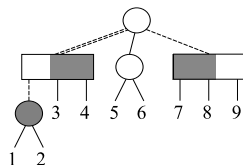
\hat{M}	1	2	3	4	5
r_1	1	1	0	0	0
r_2	1	1	1	0	0
r_3	0	0	1	1	1
r_4	0	0	0	1	1
r_5	1	0	0	1	1

Left: Binary matrix M , with matched multirows. Let $\mathbf{m}(1) = \dots = \mathbf{m}(5) = 1$ and $\mathbf{m}(a) = \mathbf{m}(b) = 2$: a and b are multicolumns and r_1 , r_3 and r_4 are multirows.

Right: The corresponding matrix \hat{M} . Since in \hat{M} , by definition $\hat{r}_i = r_i$ for all multirows r_i , the matched multirows are discarded.

Idea of the Approach

	1	2	3	4	5	6	7	8	9	c'
r_1	1	1	0	0	0	0	0	0	0	1
\hat{r}_1	1	1	0	0	0	0	0	0	0	0
r_2	1	1	1	0	0	0	0	0	0	0
r_3	0	0	1	1	0	0	0	0	0	1
\hat{r}_3	0	0	1	1	0	0	0	0	0	0
r_4	0	0	0	0	0	0	1	1	0	1
\hat{r}_4	0	0	0	0	0	0	1	1	0	0
r_5	0	0	0	0	0	0	0	1	1	0
r_6	0	0	0	0	1	1	0	0	0	0

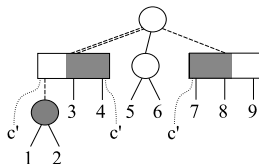


Left: Binary matrix M , with matched multirows. Let $\mathbf{m}(c') = 2$.

Right: PQ-tree for \hat{M} . P-nodes are represented by circular nodes and Q-nodes by rectangular nodes.

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r_3	0	0	1	1	0	0	0	0	0	1
\hat{r}_3	0	0	1	1	0	0	0	0	0	0
r_4	0	0	0	0	0	0	1	1	0	1
\hat{r}_4	0	0	0	0	0	0	1	1	0	0
r_5	0	0	0	0	0	0	0	1	1	0
r_6	0	0	0	0	1	1	0	0	0	0

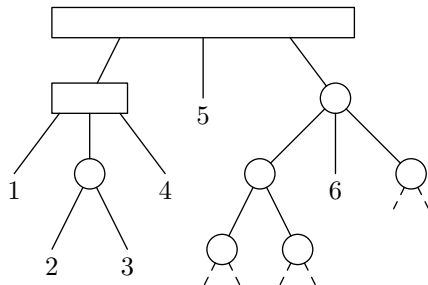


Left: Binary matrix M , with matched multirows. Let $\mathbf{m}(c') = 2$.

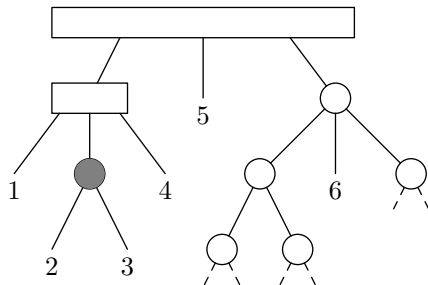
Right: PQ-tree for \hat{M} . P-nodes are represented by circular nodes and Q-nodes by rectangular nodes.

An example of a valid mC1P-ordering is $c' 1 2 3 4 c' 7 8 9 5 6$ which is obtained by inserting two copies of c' into the corresponding positions. Notice that inserting c' between 2 and 3 would **break** row r_2 .

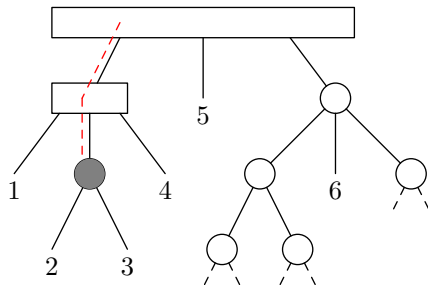
Consistency Check: The Four Cases



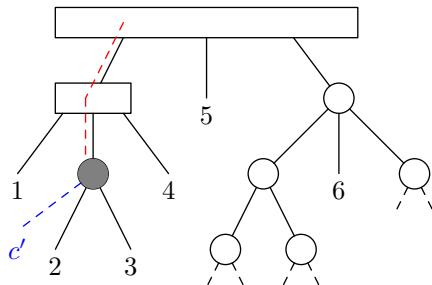
Consistency Check: Case 1



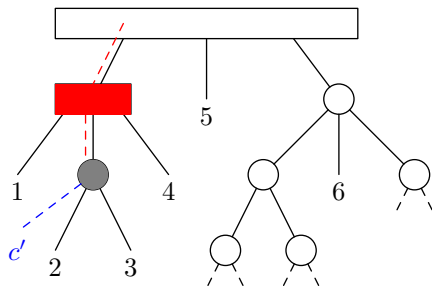
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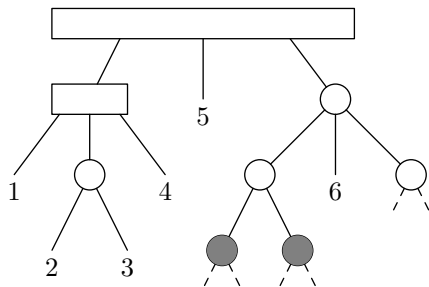


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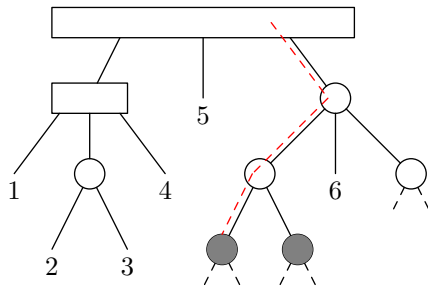


Here, insertion of c' would break either row 123 or row 234.

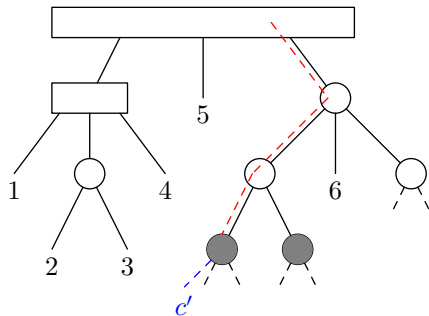
Consistency Check: Case 2



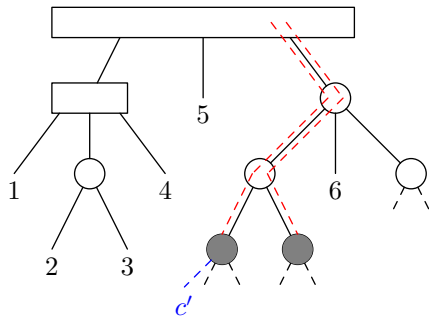
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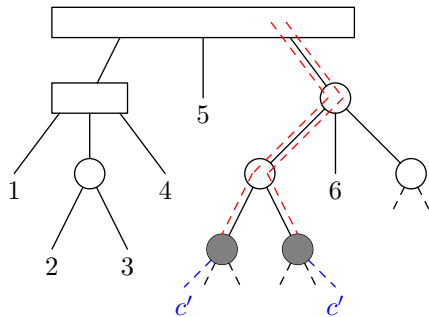
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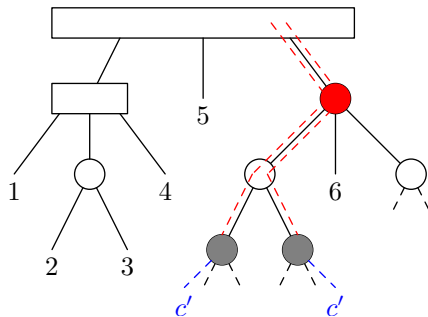
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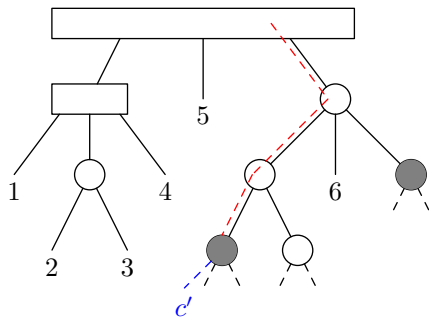


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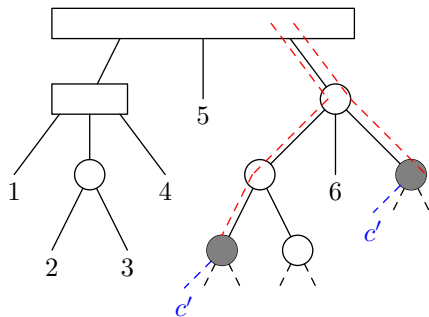


Here, insertion of c' would break one of the rows associated with this node.

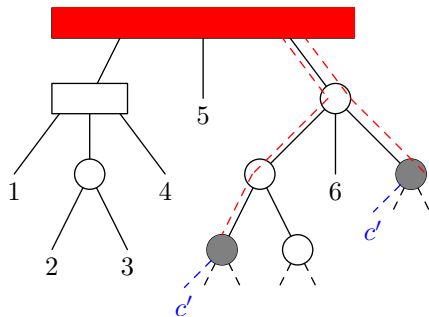
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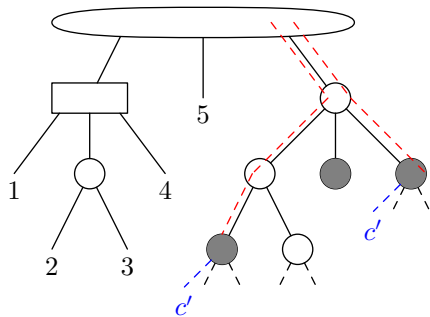


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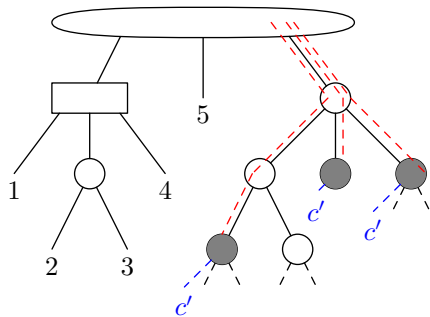


Here, insertion of c' would break one of the rows associated with the root node.

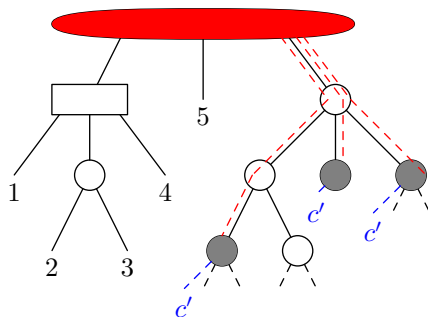
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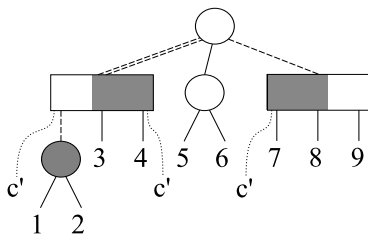
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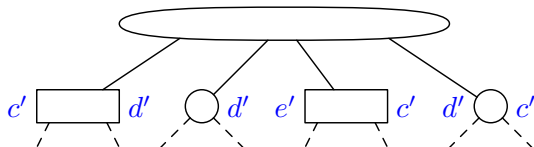
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Multiplicity Check

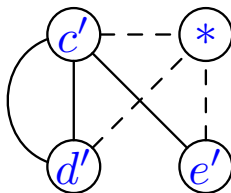
- ▶ If the consistency check succeeds for each row, we simply have to ensure that the PQ-tree satisfies the **multiplicity requirement**



Case with Several Multicolumnns



This corresponds to an **Eulerian cycle** in the following multigraph



Conclusion

Here we extend the domain of tractable instances of deciding the C1P with multiplicity. Several questions remain open:

- ▶ Is this the **largest class of tractable instances** of the mC1P?
- ▶ Is there structure analogous to the PQ-tree that could encode all mC1P-orderings of a matrix that satisfies this property? (Note that our data structure does not incorporate the multiplicity constraint)
- ▶ Our algorithm takes time $O(mn)$ where m (n) is the number of rows (columns). It is open whether there is an $O(m + n + \ell)$ -time algorithm where ℓ is the number of entries 1 in M

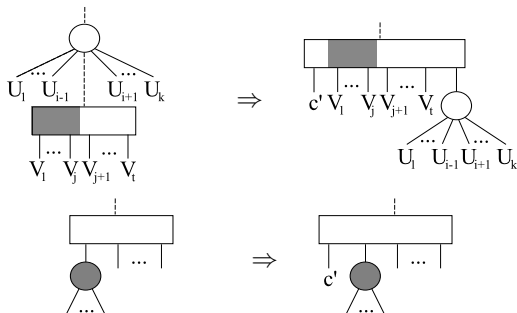
Acknowledgements

- ▶ Éric Tannier for suggesting the idea of using the mC1P to model telemers in this setting
- ▶ NSERC discovery grant

Thanks!

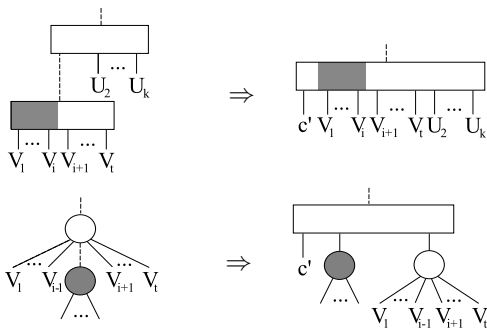
Any Questions or Comments?

Transformation Rules



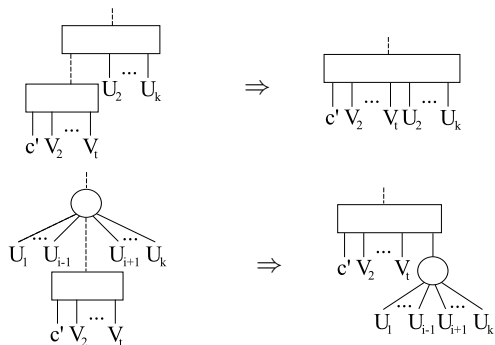
Transformation rules for the LCAs to construct an augmented PQ-tree. An LCA and its parent node are replaced by the nodes shown on the right. The LCA (or the segment of an LCA, respectively) are highlighted in gray.

Transformation Rules



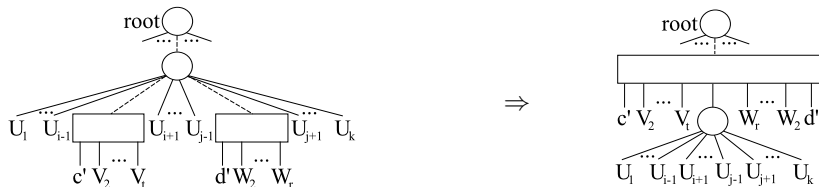
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Transformation Rules



Transformation rules for bottom-up iteration to construct an augmented PQ-tree. A newly created Q-node and its parent node are replaced by the nodes shown on the right.

Transformation Rules



Special transformation rules for bottom-up iteration to construct an augmented PQ-tree. A newly created Q-node two levels below the root node and its parent node are replaced by the nodes shown on the right.