Computational Biology

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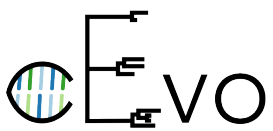
James Munday & Marcus Overwater

Computational Evolution
Department of Biosystems Science and Engineering

HS 2023



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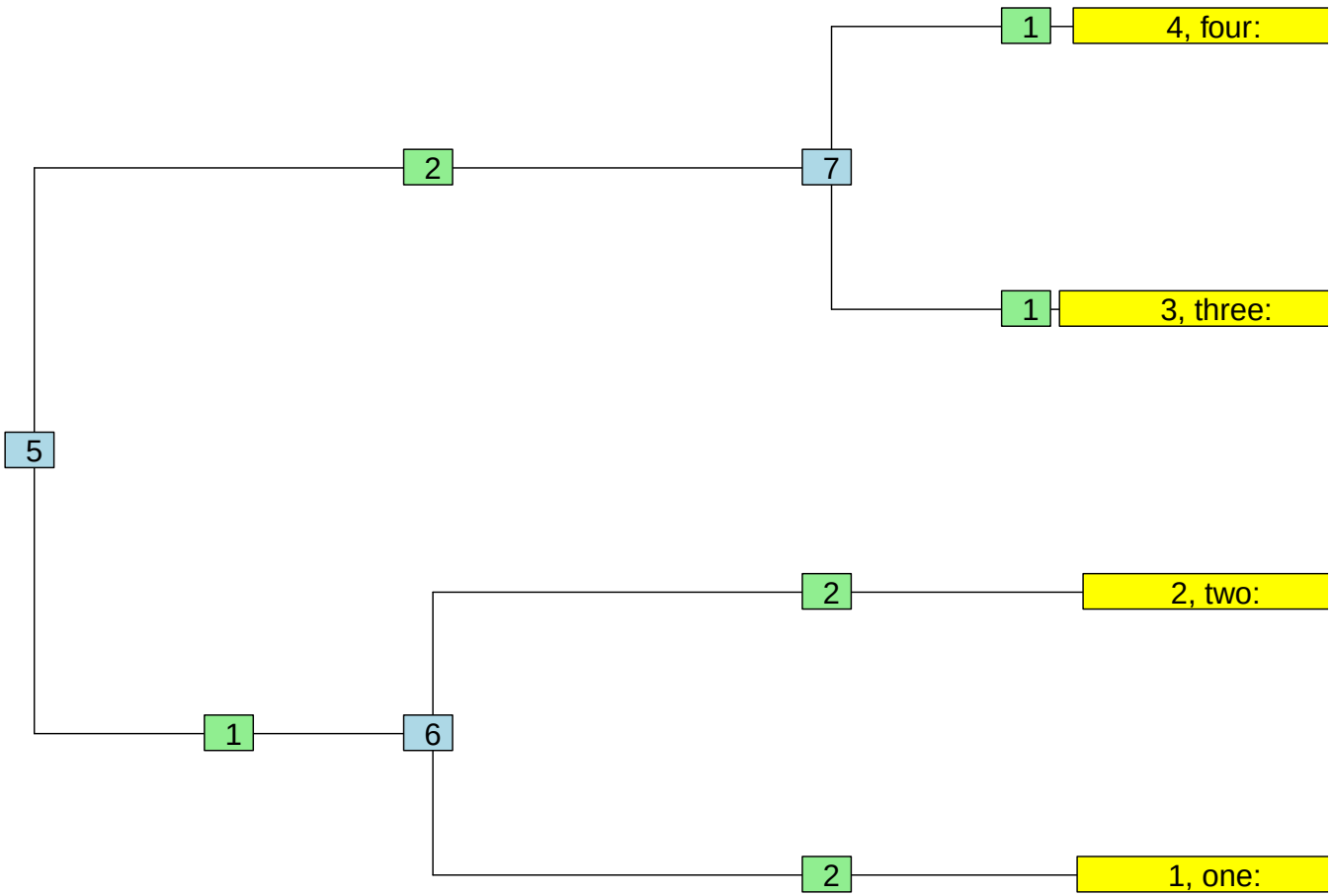
  - Felsenstein's tree pruning algorithm.

Tree traversal to simulate nucleotide evolution



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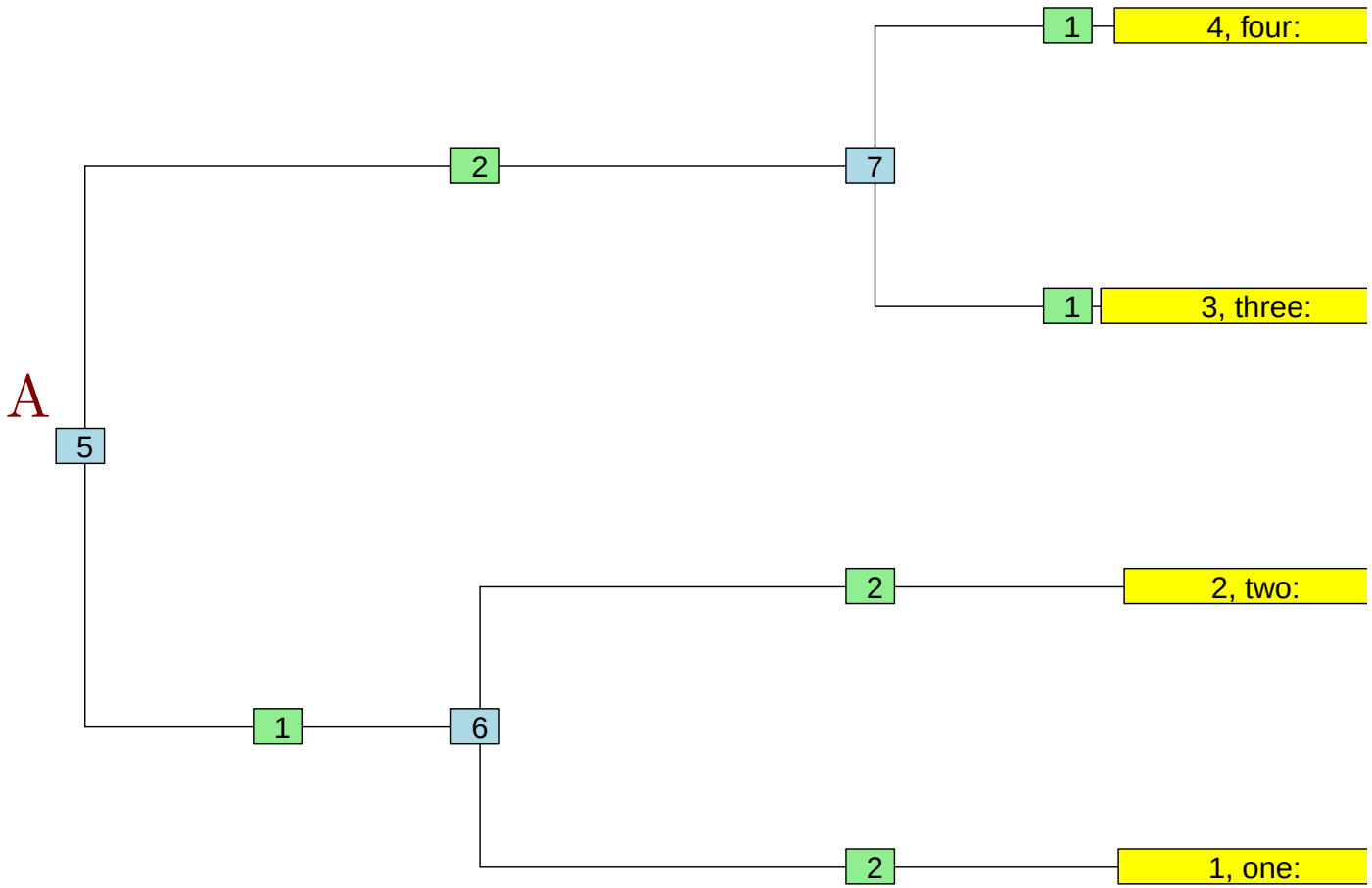

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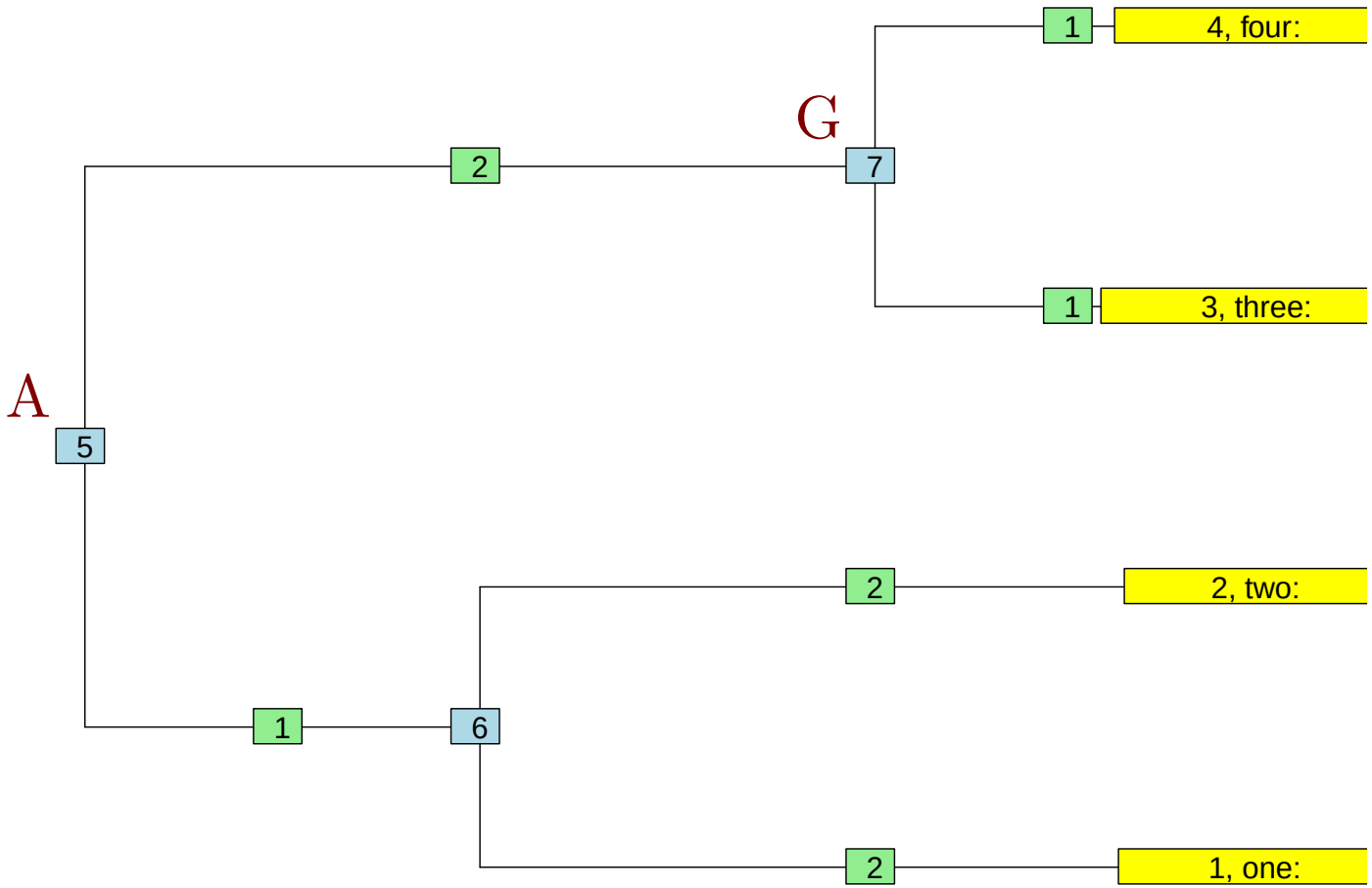
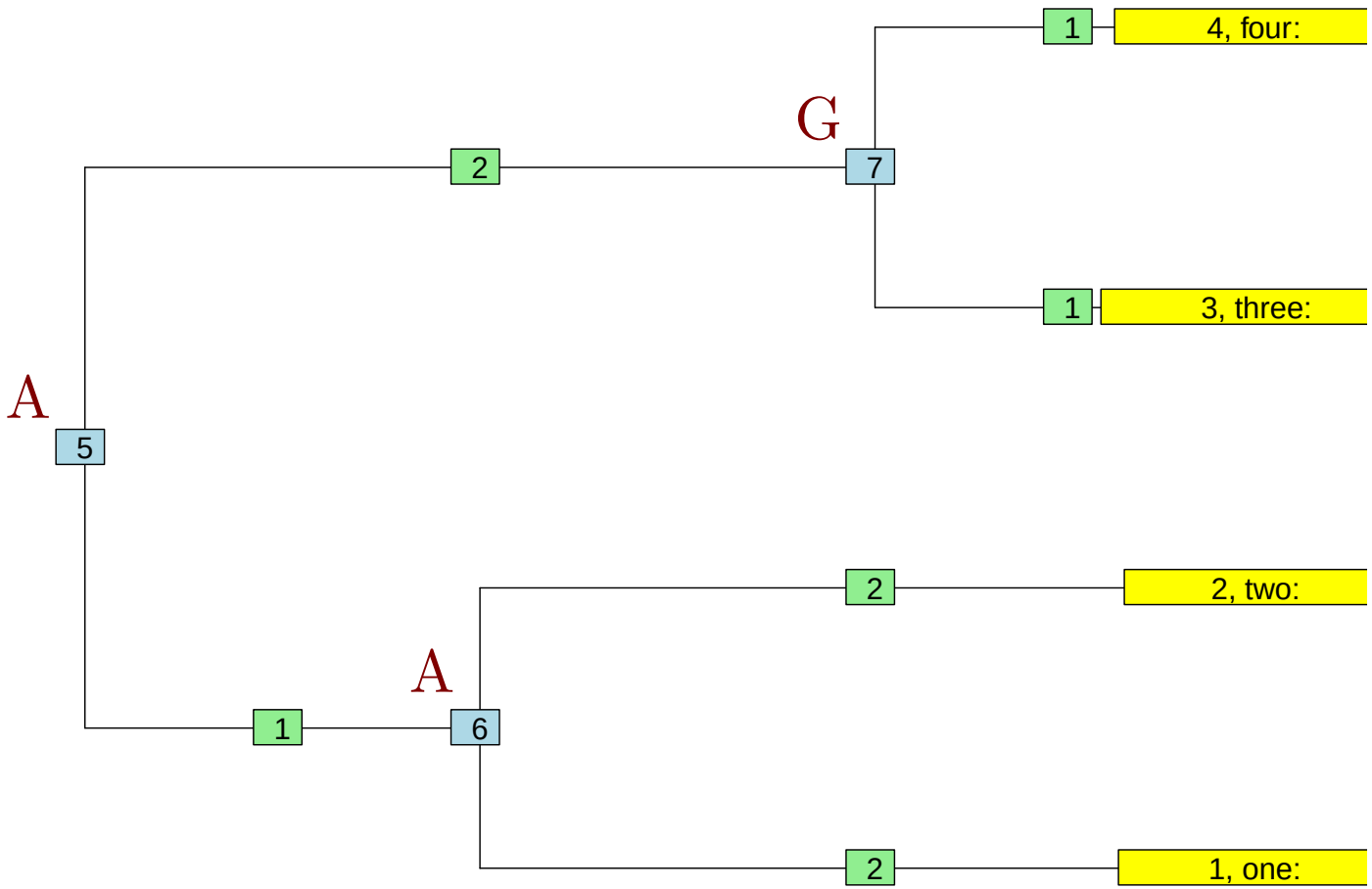


Tree traversal to simulate nucleotide evolution

Always visit the parent node before the two children



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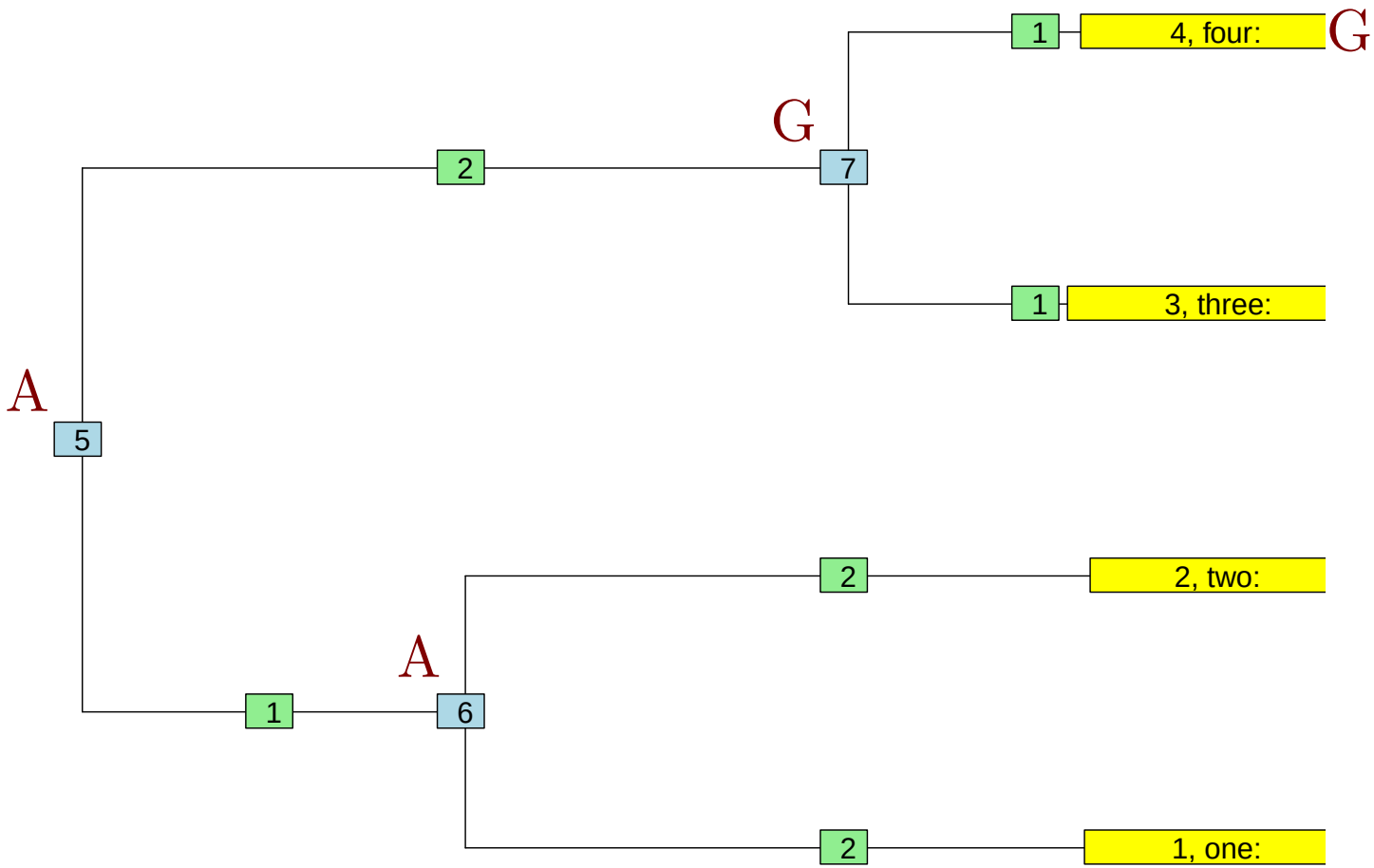

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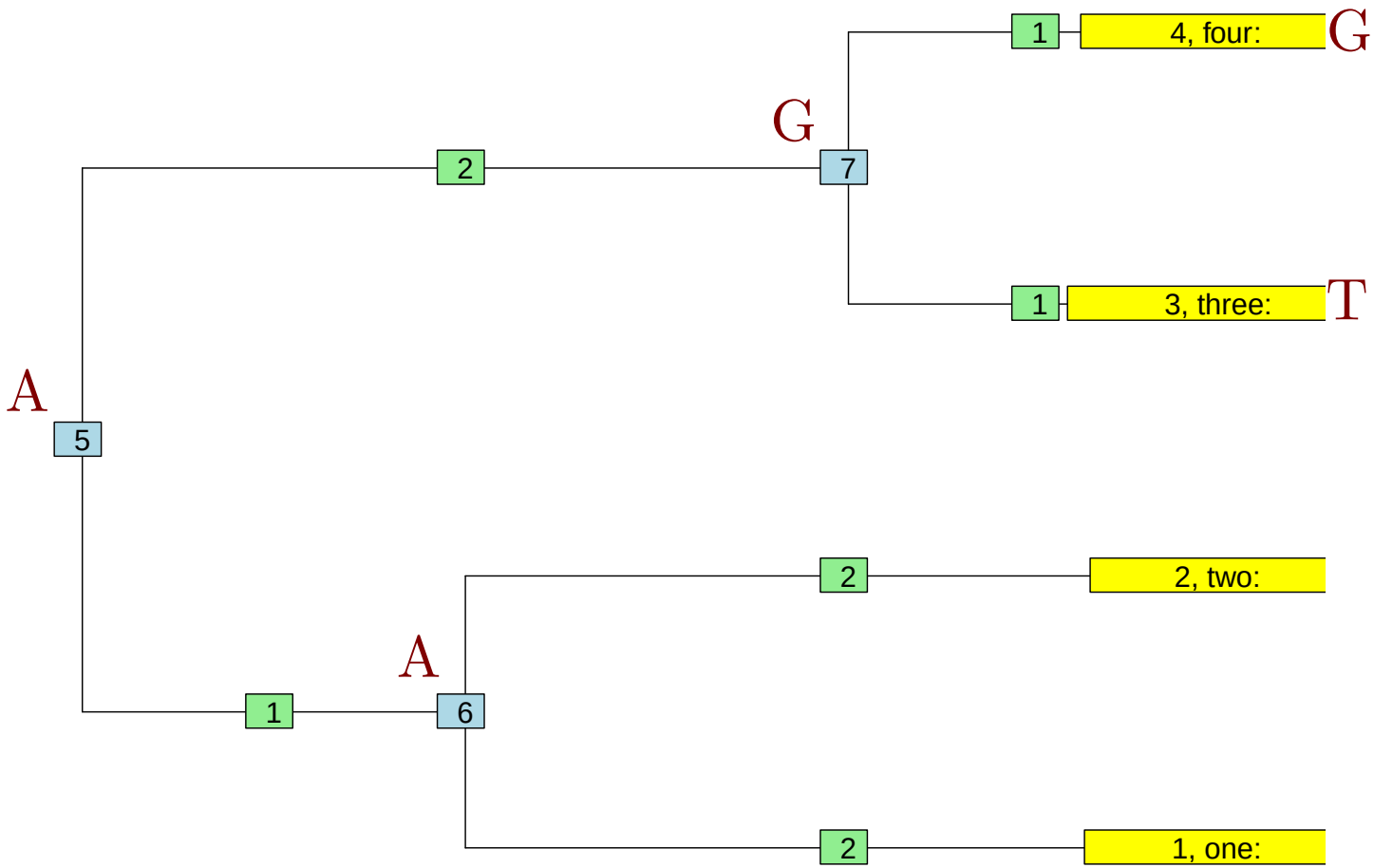

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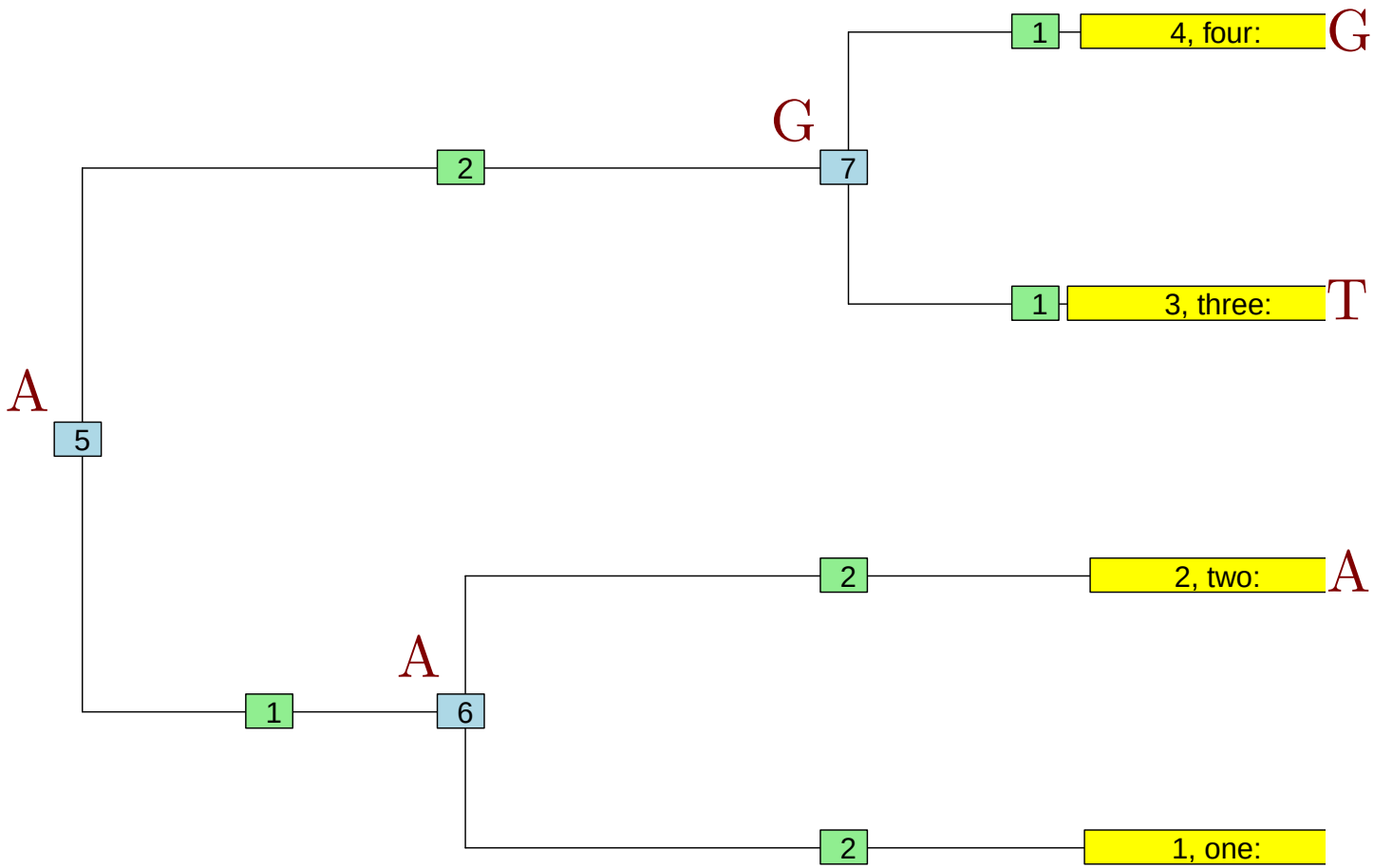

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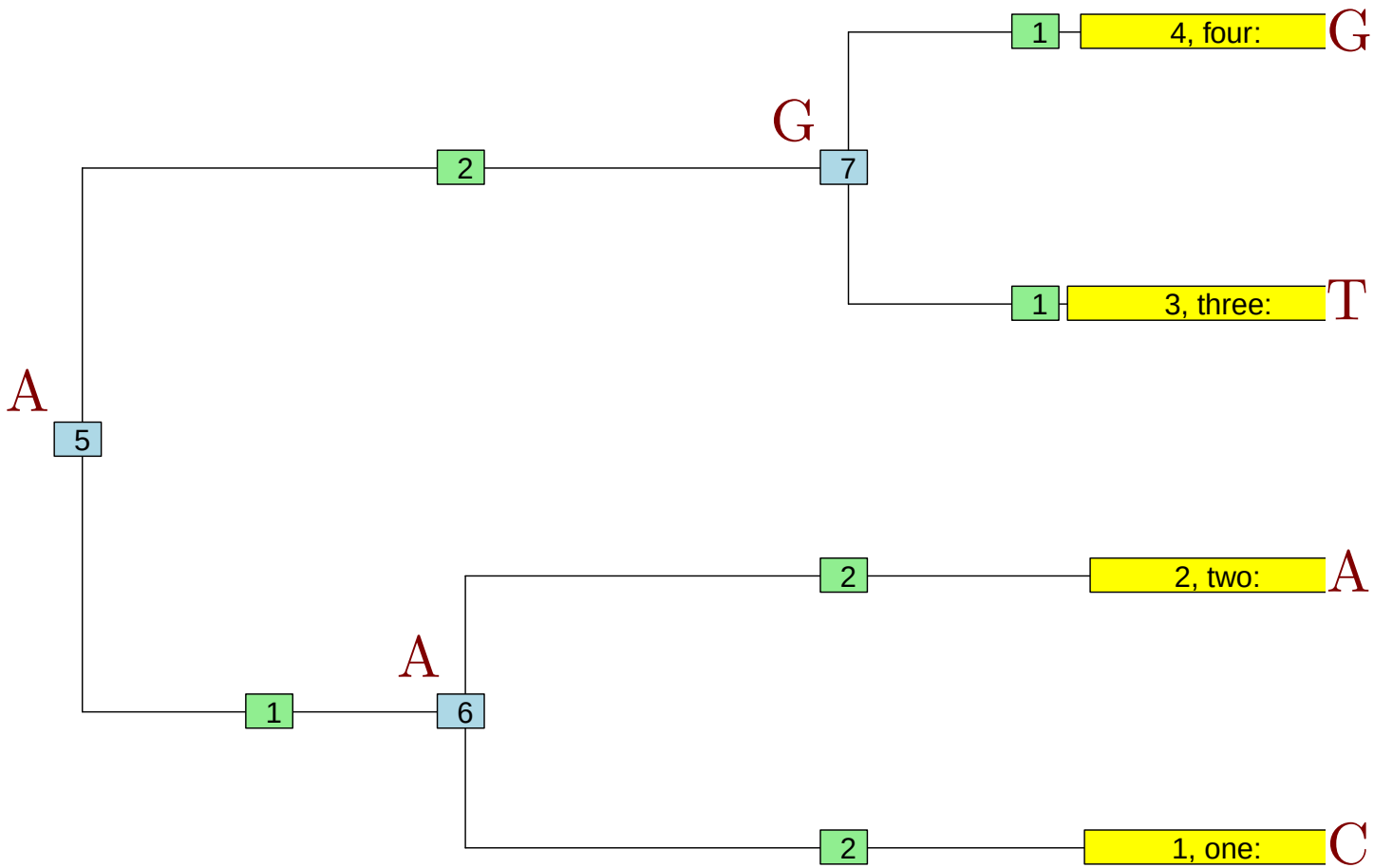
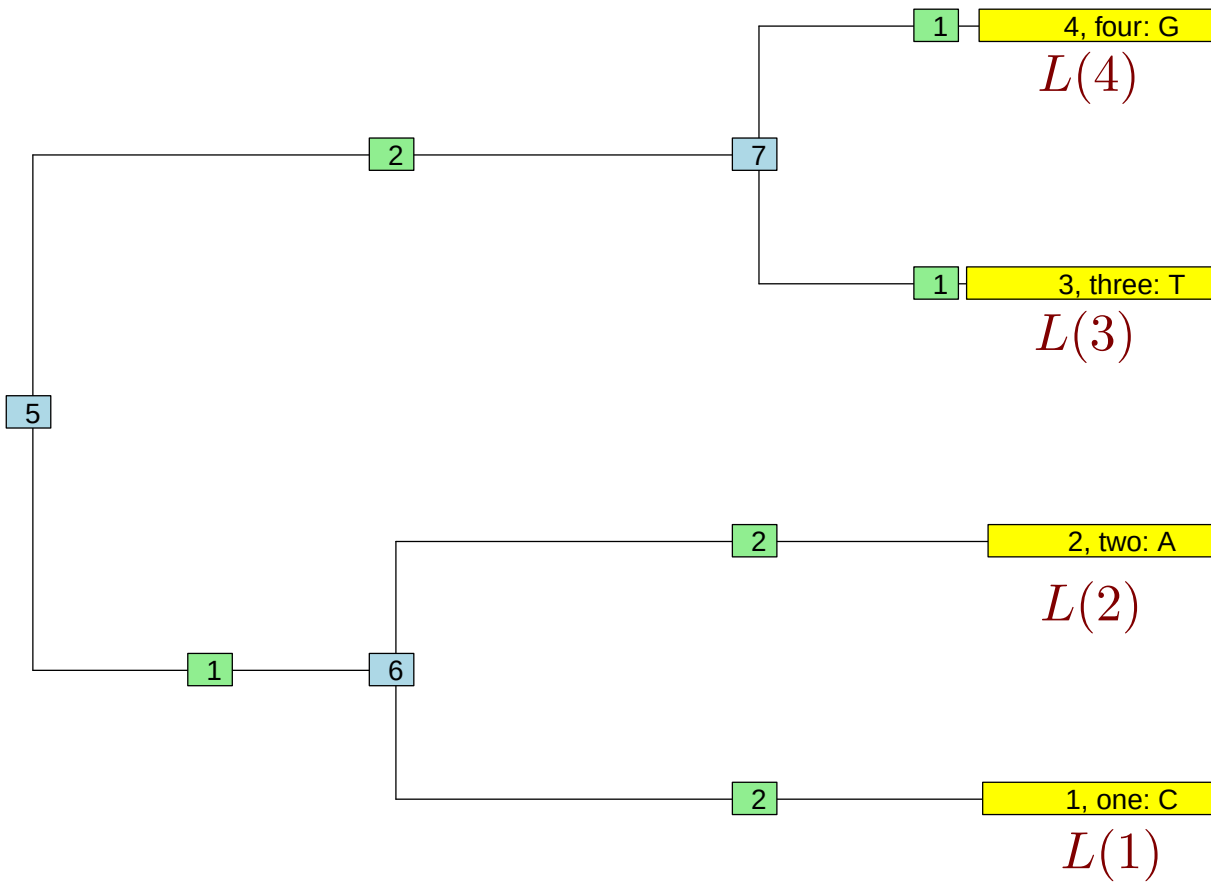


Tree traversal for likelihood computation

We look for the probability of the data below by each node, given its nucleotide state.



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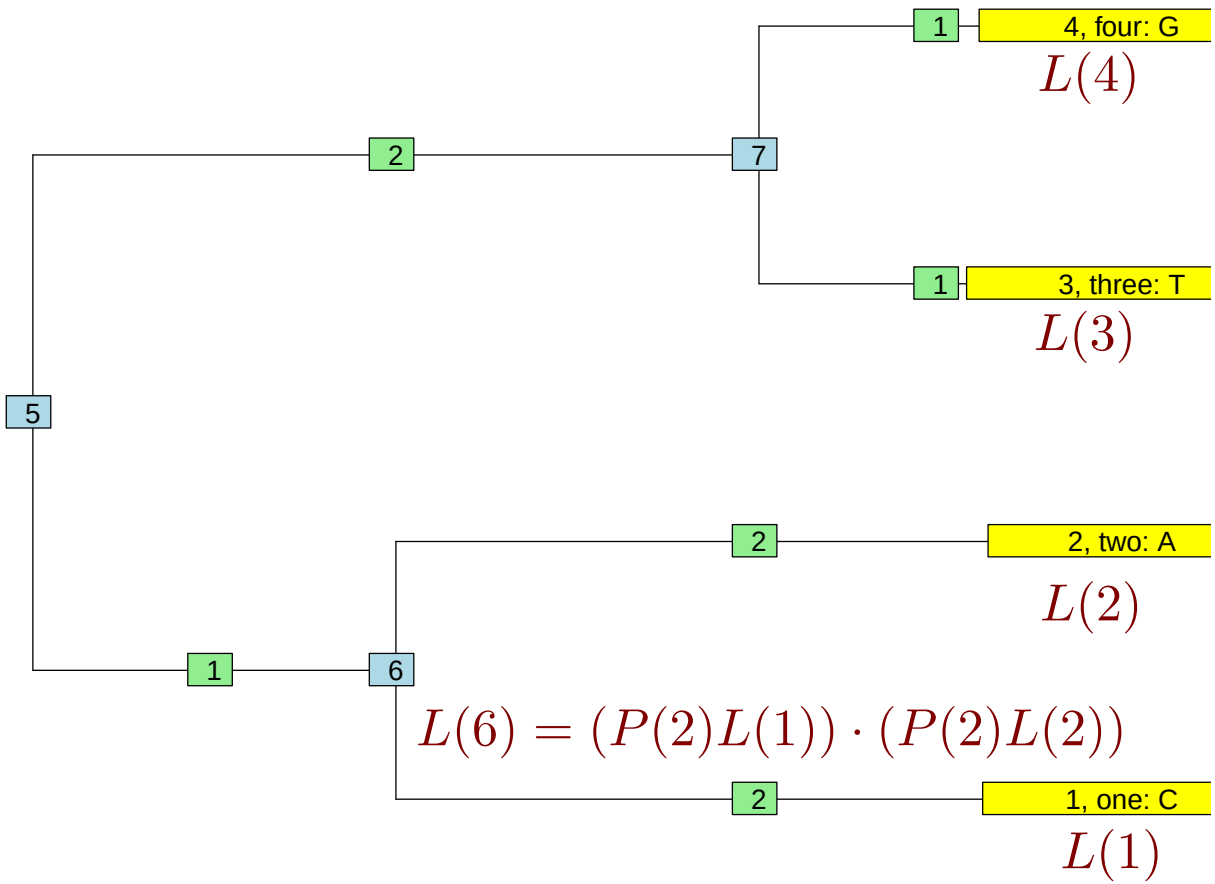

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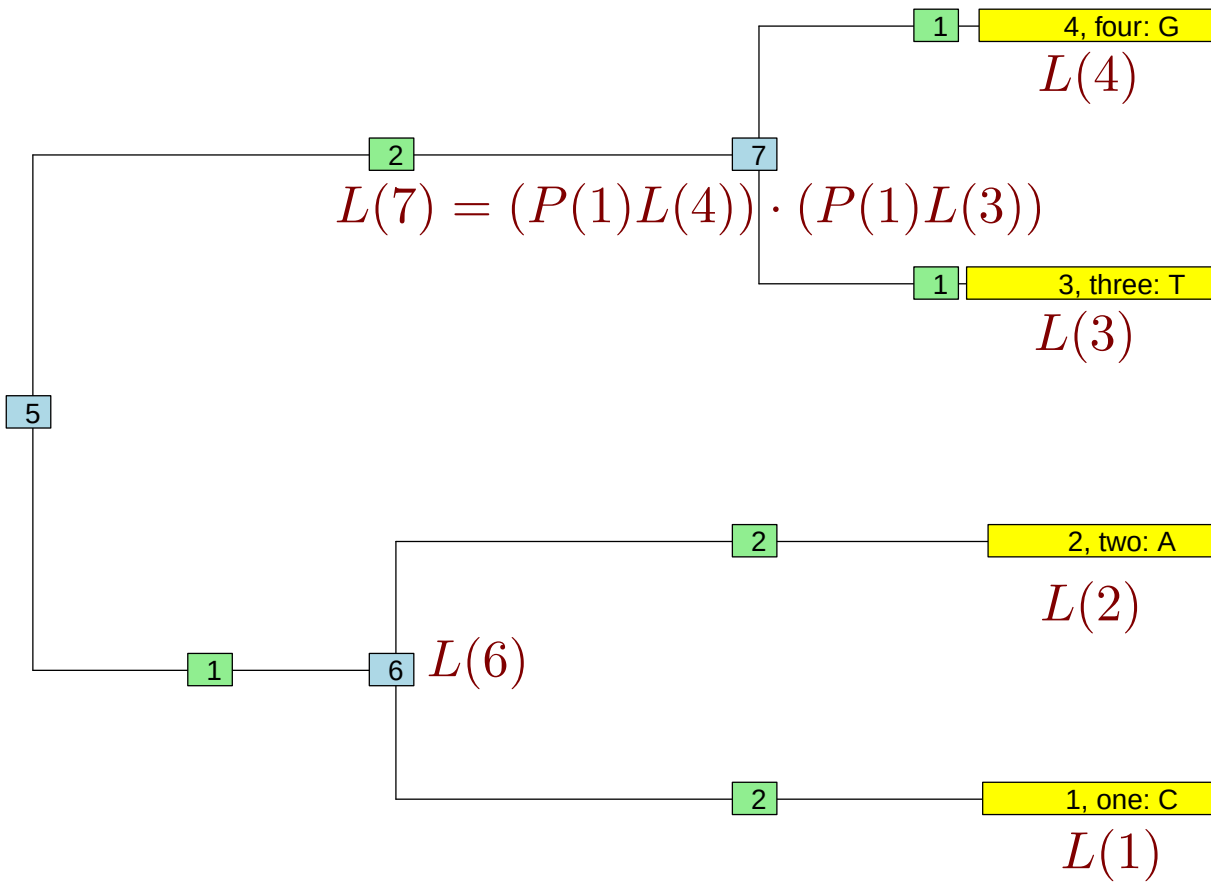

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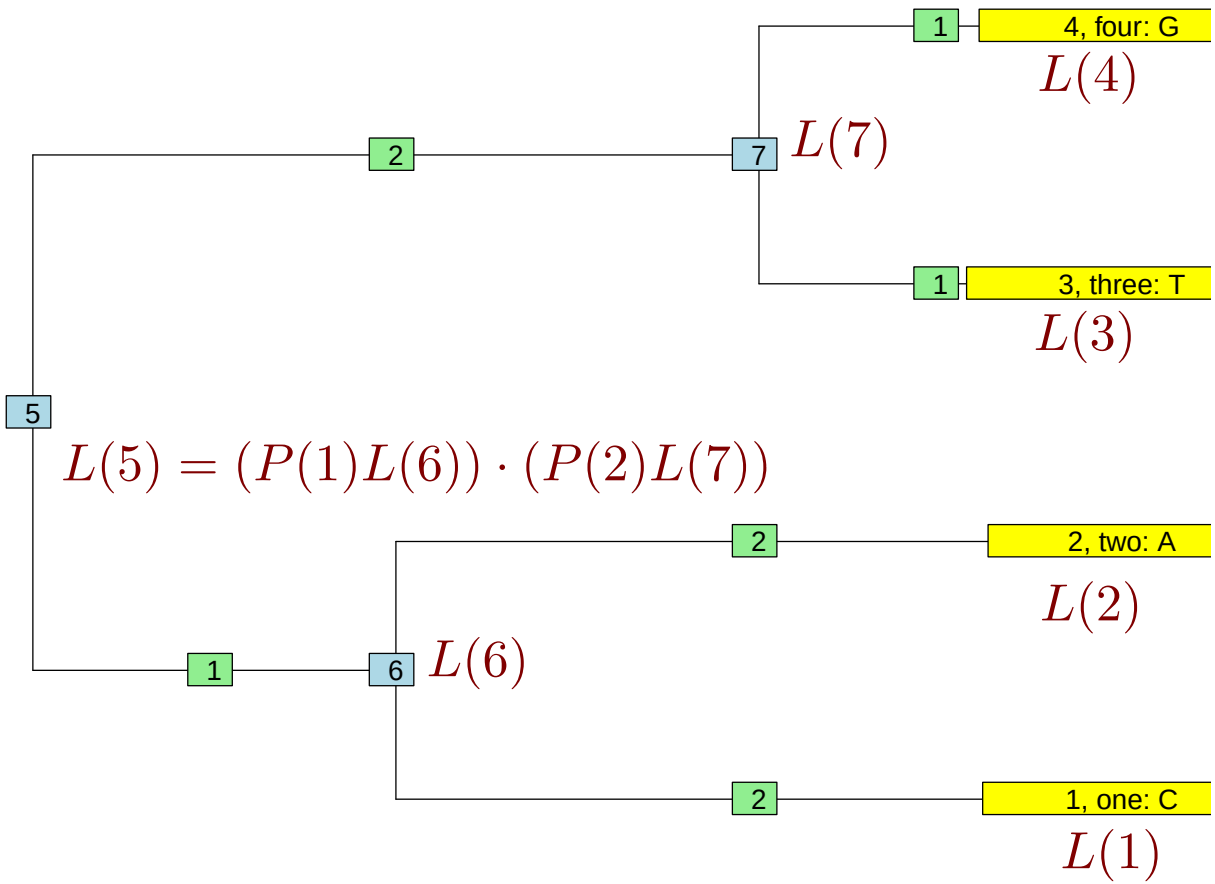

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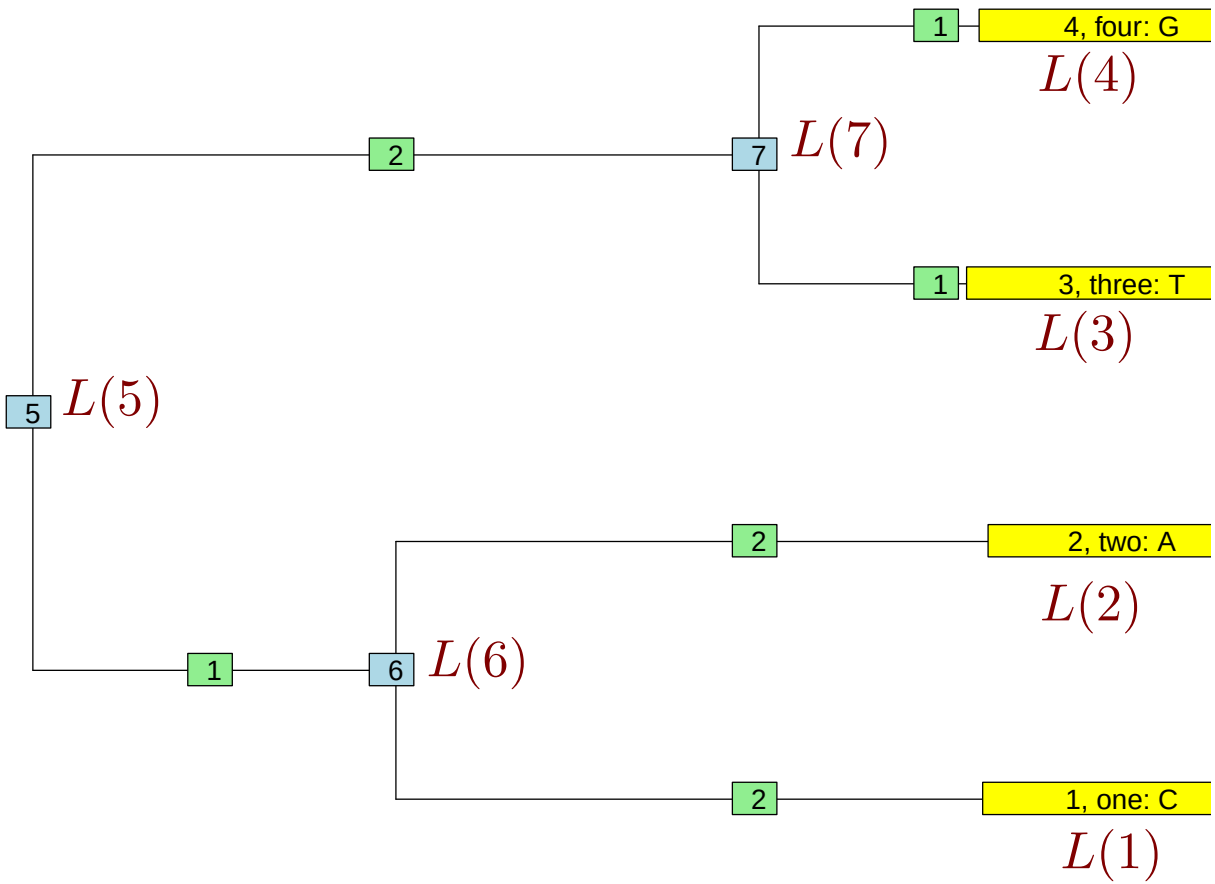
$L = \pi L(5)$



Tree node/nucleotide likelihood computation

For each tree node k, for each site i (1 to N), and for each nucleotide X, we need to compute:

$$L_X^{(i)}(k) := \text{Probability of observing the sequence site } i \text{ among tips descending from node } k \text{ conditioned on node } k \text{ having nucleotide } X$$

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	T	C	A	G
node **k**				
1	?	?	?	?
2	?	?	?	?
...				
N	?	?	?	?

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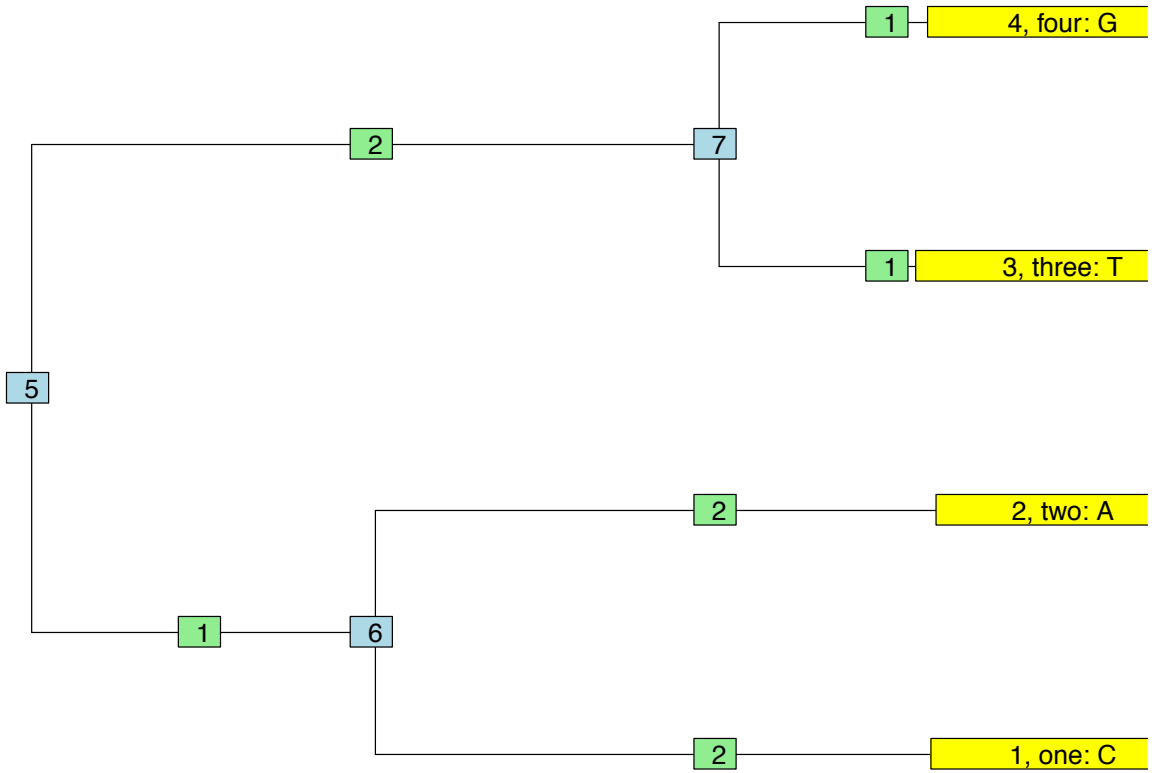
	T	C	A	G
node **k**				
1	?	?	?	?
2	?	?	?	?
...				
N	?	?	?	?

For each node in the tree we need to know the conditional likelihoods of both child nodes.

Felsenstein's pruning algorithm: Example



Alignment:

```
sequences=list(one="C", two="A", three="T", four="G")
```

Felsenstein's pruning algorithm: Tips

4, four: G

3, three: T

2, two: A

1, one: C

if n *is a tip* **then**
  for $i \leftarrow 1$ **to** N **do**
    $L^{(i)}(n) \leftarrow [0, 0, 0, 0]$;
    $L^{(i)}_{A[n,i]}(n) \leftarrow 1$;
  end
else
  ...;
end

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end

	T	C	A	G
node **1**				
1				
node **2**				
1				
node **3**				
1				
node **4**				
1				

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	T	C	A	G
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1	0	0	0	0
node **2**				
1				
node **3**				
1				
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1				

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	T	C	A	G
node **1**				
1	0	**1**	0	0
node **2**				
1				
node **3**				
1				
node **4**				
1				

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	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	**1**	0
node **3**				
1				
node **4**				
1				

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	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **3**				
1	**1**	0	0	0
node **4**				
1				

Felsenstein's pruning algorithm: Tips

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else
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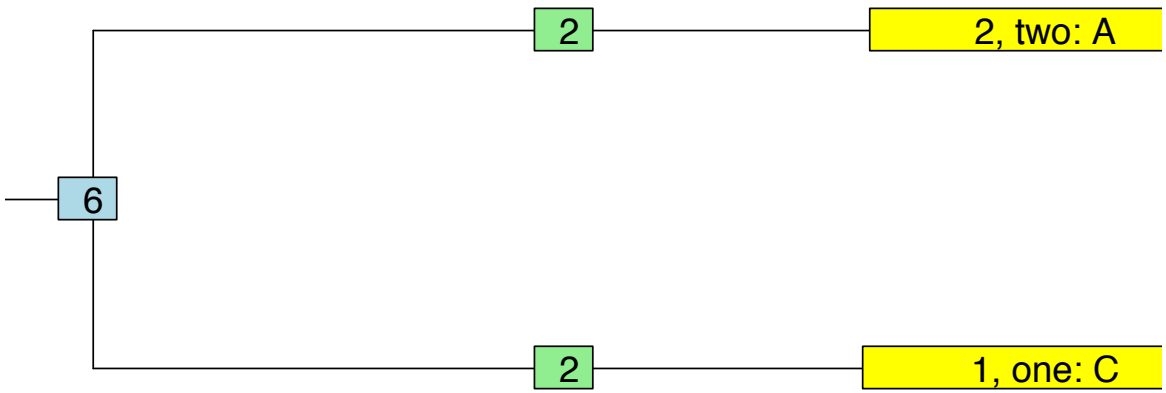
end

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **3**				
1	1	0	0	0
node **4**				
1	0	0	0	**1**

Felsenstein's pruning algorithm: Internal nodes

if n *is a tip* **then**
  ...;
else
  for $i \leftarrow 1$ **to** N **do**
    for X *in* {T, C, A, G} **do**
      $L1 \leftarrow 0$;
      $L2 \leftarrow 0$;
      for Y *in* {T, C, A, G} **do**
        $L1 \leftarrow L1 + P_{XY}(|n, child1|) \cdot L_Y^{(i)}(child1)$;
        $L2 \leftarrow L2 + P_{XY}(|n, child2|) \cdot L_Y^{(i)}(child2)$;
      end
      $L_X^{(i)}(node) = L1 \cdot L2$;
    end
  end
end

Internal node 6



	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1				

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1				

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1				

$$L_T^{(1)}(6) = \left(\sum_{X \in \{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(1) \right) \times \left(\sum_{X \in \{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(2) \right)$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1				

$$
\begin{aligned}
L_T^{(1)}(6) &= \left(\sum_{X \in \{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(1) \right) \times \left(\sum_{X \in \{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(2) \right) \\
&= (P_{TT}(2) \times 0 + P_{TC}(2) \times 1 + P_{TA}(2) \times 0 + P_{TG}(2) \times 0) \\
&\quad \times (P_{TT}(2) \times 0 + P_{TC}(2) \times 0 + P_{TA}(2) \times 1 + P_{TG}(2) \times 0)
\end{aligned}
$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1				

$$
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L_T^{(1)}(6) &= \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(1)\right) \times \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(2)\right) \\
&= (P_{TT}(2)\times 0 + P_{TC}(2)\times 1 + P_{TA}(2)\times 0 + P_{TG}(2)\times 0) \\
&\quad \times (P_{TT}(2)\times 0 + P_{TC}(2)\times 0 + P_{TA}(2)\times 1 + P_{TG}(2)\times 0) \\
&= (0.76\times 0 + 0.24\times 1 + 0.00089\times 0 + 0.00051\times 0) \\
&\quad \times (0.76\times 0 + 0.24\times 0 + 0.00089\times 1 + 0.00051\times 0)
\end{aligned}
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Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1				

$$
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&\quad \times (0.76\times 0 + 0.24\times 0 + 0.00089\times 1 + 0.00051\times 0) \\
&= 0.24\times 0.00089 \approx 0.00021
\end{aligned}
$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1	0.00021			

$$
\begin{aligned}
L_T^{(1)}(6) &= \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(2)L_X^{(1)}(1)\right) \times \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(2)L_X^{(1)}(2)\right) \\
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&= 0.24\times 0.00089 \approx 0.00021
\end{aligned}
$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1	0.00021			

$$L_C^{(1)}(6) = \left(\sum_{X \in \{T,C,A,G\}} P_{CX}(2) L_X^{(1)}(1) \right) \times \left(\sum_{X \in \{T,C,A,G\}} P_{CX}(2) L_X^{(1)}(2) \right)$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1	0.00021			

$$\mathrm{L}_{\mathrm{C}}^{(1)}(6) = \left(\sum_{X \in \{\mathrm{T,C,A,G}\}} \mathrm{P}_{\mathrm{C}X}(2)\mathrm{L}_{X}^{(1)}(1)\right) \times \left(\sum_{X \in \{\mathrm{T,C,A,G}\}} \mathrm{P}_{\mathrm{C}X}(2)\mathrm{L}_{X}^{(1)}(2)\right)$$
$$= (\mathrm{P}_{\mathrm{CC}}(2) \times 1) \times (\mathrm{P}_{\mathrm{CA}}(2) \times 1) = 0.8 \times 0.00089 \approx 0.00071$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1	0.00021	0.00071		

$$\mathrm{L}_{\mathrm{C}}^{(1)}(6) = \left(\sum_{\mathrm{X} \in \{\mathrm{T},\mathrm{C},\mathrm{A},\mathrm{G}\}} \mathrm{P}_{\mathrm{C}\mathrm{X}}(2) \mathrm{L}_{\mathrm{X}}^{(1)}(1) \right) \times \left(\sum_{\mathrm{X} \in \{\mathrm{T},\mathrm{C},\mathrm{A},\mathrm{G}\}} \mathrm{P}_{\mathrm{C}\mathrm{X}}(2) \mathrm{L}_{\mathrm{X}}^{(1)}(2) \right)$$
$$= (\mathrm{P}_{\mathrm{C}\mathrm{C}}(2) \times 1) \times (\mathrm{P}_{\mathrm{C}\mathrm{A}}(2) \times 1) = 0.8 \times 0.00089 \approx 0.00071$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1	0.00021	0.00071		

$$\mathrm{L}_{\mathrm{A}}^{(1)}(6) = \left(\sum_{X \in \{\mathrm{T,C,A,G}\}} \mathrm{P}_{\mathrm{A}X}(2) \mathrm{L}_{X}^{(1)}(1) \right) \times \left(\sum_{X \in \{\mathrm{T,C,A,G}\}} \mathrm{P}_{\mathrm{A}X}(2) \mathrm{L}_{X}^{(1)}(2) \right)$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1	0.00021	0.00071		

$$\mathrm{L}_{\mathrm{A}}^{(1)}(6) = \left(\sum_{X \in \{\mathrm{T,C,A,G}\}} \mathrm{P}_{\mathrm{A}X}(2) \mathrm{L}_{X}^{(1)}(1) \right) \times \left(\sum_{X \in \{\mathrm{T,C,A,G}\}} \mathrm{P}_{\mathrm{A}X}(2) \mathrm{L}_{X}^{(1)}(2) \right)$$
$$= (\mathrm{P}_{\mathrm{AC}}(2) \times 1) \times (\mathrm{P}_{\mathrm{AA}}(2) \times 1) = 0.0007 \times 0.9 \approx 0.00063$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1	0.00021	0.00071	0.00063	

$$\mathrm{L}_{\mathrm{A}}^{(1)}(6) = \left(\sum_{X\in\{\mathrm{T,C,A,G}\}} \mathrm{P}_{\mathrm{A}X}(2)\mathrm{L}_{X}^{(1)}(1)\right) \times \left(\sum_{X\in\{\mathrm{T,C,A,G}\}} \mathrm{P}_{\mathrm{A}X}(2)\mathrm{L}_{X}^{(1)}(2)\right)$$
$$= (\mathrm{P}_{\mathrm{AC}}(2)\times 1)\times(\mathrm{P}_{\mathrm{AA}}(2)\times 1) = 0.0007\times 0.9 \approx 0.00063$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1	0.00021	0.00071	0.00063	

$$\mathrm{L}_{\mathrm{G}}^{(1)}(6) = \left(\sum_{\mathrm{X} \in \{\mathrm{T},\mathrm{C},\mathrm{A},\mathrm{G}\}} \mathrm{P}_{\mathrm{G}\mathrm{X}}(2) \mathrm{L}_{\mathrm{X}}^{(1)}(1) \right) \times \left(\sum_{\mathrm{X} \in \{\mathrm{T},\mathrm{C},\mathrm{A},\mathrm{G}\}} \mathrm{P}_{\mathrm{G}\mathrm{X}}(2) \mathrm{L}_{\mathrm{X}}^{(1)}(2) \right)$$

Internal node 6

	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1	0.00021	0.00071	0.00063	

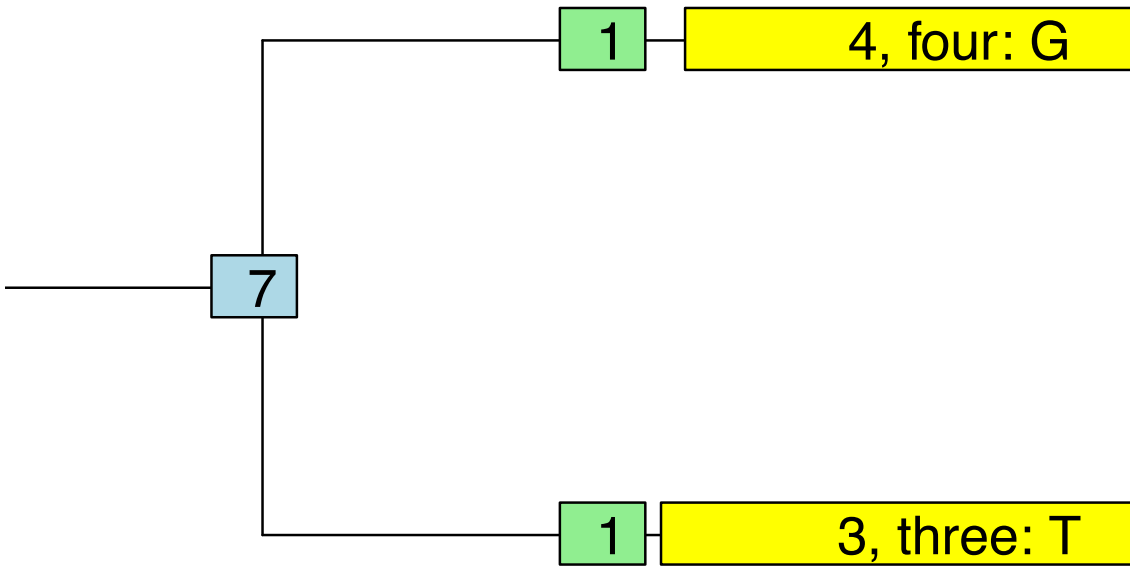
$$\mathrm{L}_{\mathrm{G}}^{(1)}(6) = \left(\sum_{X\in\{\mathrm{T,C,A,G}\}} \mathrm{P}_{\mathrm{G}X}(2)\mathrm{L}_{X}^{(1)}(1)\right) \times \left(\sum_{X\in\{\mathrm{T,C,A,G}\}} \mathrm{P}_{\mathrm{G}X}(2)\mathrm{L}_{X}^{(1)}(2)\right)$$
$$= (\mathrm{P}_{\mathrm{GC}}(2)\times 1)\times(\mathrm{P}_{\mathrm{GA}}(2)\times 1) = 0.0007\times 0.17 \approx 0.00012$$

Internal node 6

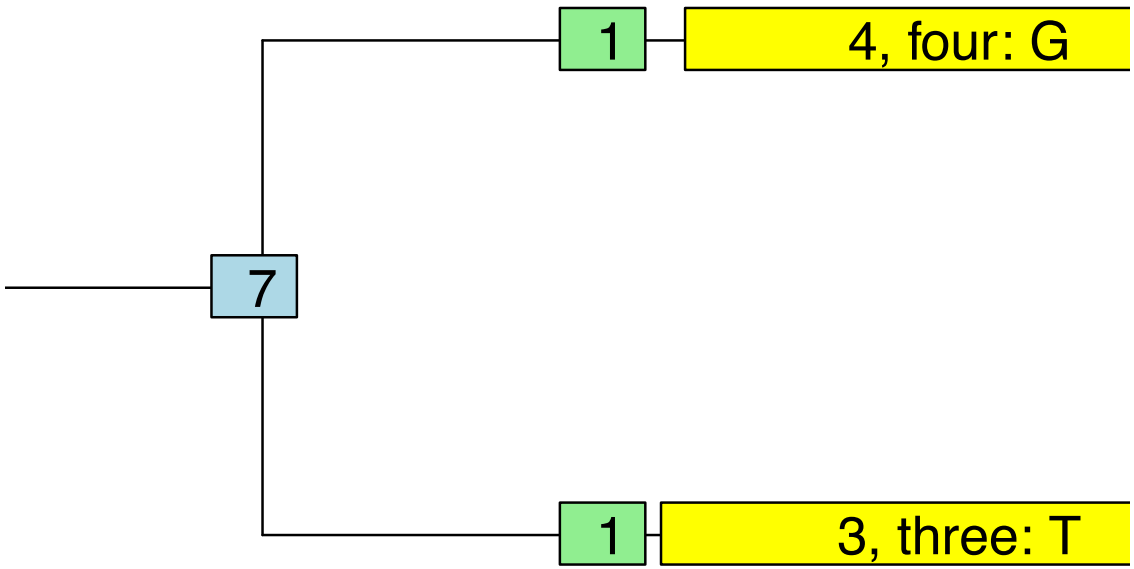
	T	C	A	G
node **1**				
1	0	1	0	0
node **2**				
1	0	0	1	0
node **6**				
1	0.00021	0.00071	0.00063	0.00012

$$L_G^{(1)}(6) = \left(\sum_{X \in \{T,C,A,G\}} P_{GX}(2) L_X^{(1)}(1) \right) \times \left(\sum_{X \in \{T,C,A,G\}} P_{GX}(2) L_X^{(1)}(2) \right)$$
$$= (P_{GC}(2) \times 1) \times (P_{GA}(2) \times 1) = 0.0007 \times 0.17 \approx 0.00012$$

Internal node 7



Internal node 7



	T	C	A	G
node **3**				
1	1	0	0	0
node **4**				
1	0	0	0	1
node **7**				
1	0.00022	0.000029	0.000015	0.00027

Internal node 5

	T	C	A	G
node **6**				
1	0.00021	0.00071	0.00063	0.00012
node **7**				
1	0.00022	0.000029	0.000015	0.00027
node **5**				
1				

Internal node 5

	T	C	A	G
node **6**				
1	0.00021	0.00071	0.00063	0.00012
node **7**				
1	0.00022	0.000029	0.000015	0.00027
node **5**				
1				

$$L_T^{(1)}(5) = \left(\sum_{X \in \{T,C,A,G\}} P_{TX}(1) L_X^{(1)}(6) \right) \times \left(\sum_{X \in \{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(7) \right)$$

Internal node 5

	T	C	A	G
node **6**				
1	0.00021	0.00071	0.00063	0.00012
node **7**				
1	0.00022	0.000029	0.000015	0.00027
node **5**				
1				

$$L_T^{(1)}(5) = \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(1) L_X^{(1)}(6)\right) \times \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(7)\right)$$
$$= (0.861 \times 0.00021 + 0.13 \times 0.00071 + 0.00045 \times 0.00063 + 0.00026 \times 0.00012)$$
$$\times (0.76 \times 0.00022 + 0.24 \times 0.000029 + 0.00089 \times 0.000015 + 0.00051 \times 0.00027)$$

Internal node 5

	T	C	A	G
node **6**				
1	0.00021	0.00071	0.00063	0.00012
node **7**				
1	0.00022	0.000029	0.000015	0.00027
node **5**				
1				

$$\begin{aligned} L_T^{(1)}(5) &= \left(\sum_{X \in \{T,C,A,G\}} P_{TX}(1) L_X^{(1)}(6) \right) \times \left(\sum_{X \in \{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(7) \right) \\ &= (0.861 \times 0.00021 + 0.13 \times 0.00071 + 0.00045 \times 0.00063 + 0.00026 \times 0.00012) \\ &\quad \times (0.76 \times 0.00022 + 0.24 \times 0.000029 + 0.00089 \times 0.000015 + 0.00051 \times 0.00027) \\ &\approx 4.89e{-}08 \end{aligned}$$

Internal node 5

	T	C	A	G
node **6**				
1	0.00021	0.00071	0.00063	0.00012
node **7**				
1	0.00022	0.000029	0.000015	0.00027
node **5**				
1	4.89e-08			

$$\begin{aligned} L_T^{(1)}(5) &= \left(\sum_{X \in \{T,C,A,G\}} P_{TX}(1) L_X^{(1)}(6) \right) \times \left(\sum_{X \in \{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(7) \right) \\ &= (0.861 \times 0.00021 + 0.13 \times 0.00071 + 0.00045 \times 0.00063 + 0.00026 \times 0.00012) \\ &\quad \times (0.76 \times 0.00022 + 0.24 \times 0.000029 + 0.00089 \times 0.000015 + 0.00051 \times 0.00027) \\ &\approx 4.89e{-}08 \end{aligned}$$

Internal node 5

	T	C	A	G
node **6**				
1	0.00021	0.00071	0.00063	0.00012
node **7**				
1	0.00022	0.000029	0.000015	0.00027
node **5**				
1	4.89e-08	4.43e-08		

$$\begin{aligned} L_T^{(1)}(5) &= \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(1) L_X^{(1)}(6)\right) \times \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(7)\right) \\ &= (0.861 \times 0.00021 + 0.13 \times 0.00071 + 0.00045 \times 0.00063 + 0.00026 \times 0.00012) \\ &\quad \times (0.76 \times 0.00022 + 0.24 \times 0.000029 + 0.00089 \times 0.000015 + 0.00051 \times 0.00027) \\ &\approx 4.89e{-}08 \end{aligned}$$

Internal node 5

	T	C	A	G
node **6**				
1	0.00021	0.00071	0.00063	0.00012
node **7**				
1	0.00022	0.000029	0.000015	0.00027
node **5**				
1	4.89e-08	4.43e-08	2.42e-08	

$$L_T^{(1)}(5) = \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(1)L_X^{(1)}(6)\right) \times \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(2)L_X^{(1)}(7)\right)$$
$$= (0.861 \times 0.00021 + 0.13 \times 0.00071 + 0.00045 \times 0.00063 + 0.00026 \times 0.00012)$$
$$\times (0.76 \times 0.00022 + 0.24 \times 0.000029 + 0.00089 \times 0.000015 + 0.00051 \times 0.00027)$$
$$\approx 4.89e{-}08$$

Internal node 5

	T	C	A	G
node **6**				
1	0.00021	0.00071	0.00063	0.00012
node **7**				
1	0.00022	0.000029	0.000015	0.00027
node **5**				
1	4.89e-08	4.43e-08	2.42e-08	3.72e-08

$$
\begin{aligned}
L_T^{(1)}(5) &= \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(1) L_X^{(1)}(6)\right) \times \left(\sum_{X\in\{T,C,A,G\}} P_{TX}(2) L_X^{(1)}(7)\right) \\
&= (0.861 \times 0.00021 + 0.13 \times 0.00071 + 0.00045 \times 0.00063 + 0.00026 \times 0.00012) \\
&\quad \times (0.76 \times 0.00022 + 0.24 \times 0.000029 + 0.00089 \times 0.000015 + 0.00051 \times 0.00027) \\
&\approx 4.89e{-}08
\end{aligned}
$$

From conditional likelihood to likelihood

	T	C	A	G
node **5**				
1	4.89e-08	4.43e-08	2.42e-08	3.72e-08

$$\pi = (0.22, 0.26, 0.33, 0.19)$$

From conditional likelihood to likelihood

	T	C	A	G
node **5**				
1	4.89e-08	4.43e-08	2.42e-08	3.72e-08

$$\pi = (0.22, 0.26, 0.33, 0.19)$$

$$\mathrm{logL} = \sum_{i=1}^{N} \log \left(\sum_{X \in \{T,C,A,G\}} \pi_X L_X^{(i)}(5) \right)$$

From conditional likelihood to likelihood

	T	C	A	G
node **5**				
1	4.89e-08	4.43e-08	2.42e-08	3.72e-08

$$\pi = (0.22, 0.26, 0.33, 0.19)$$

$$\begin{aligned} \mathrm{logL} &= \sum_{i=1}^{N} \log \left(\sum_{X \in \{T,C,A,G\}} \pi_X L_X^{(i)}(5) \right) \\ &= \log \left(\sum_{X \in \{T,C,A,G\}} \pi_X L_X^{(1)}(5) \right) \end{aligned}$$

From conditional likelihood to likelihood

	T	C	A	G
node **5**				
1	4.89e-08	4.43e-08	2.42e-08	3.72e-08

$$\pi = (0.22, 0.26, 0.33, 0.19)$$

$$\begin{aligned}
\mathrm{logL} &= \sum_{i=1}^{N} \log \left(\sum_{X \in \{T,C,A,G\}} \pi_X L_X^{(i)}(5) \right) \\
&= \log \left(\sum_{X \in \{T,C,A,G\}} \pi_X L_X^{(1)}(5) \right) \\
&= \log \left(\pi_T L_T^{(1)}(5) + \pi_C L_C^{(1)}(5) + \pi_A L_A^{(1)}(5) + \pi_G L_G^{(1)}(5) \right)
\end{aligned}$$

From conditional likelihood to likelihood

	T	C	A	G
node **5**				
1	4.89e-08	4.43e-08	2.42e-08	3.72e-08

$$\pi = (0.22, 0.26, 0.33, 0.19)$$

$$\begin{aligned}
\log L &= \sum_{i=1}^{N} \log \left(\sum_{X \in \{T,C,A,G\}} \pi_X L_X^{(i)}(5) \right) \\
&= \log \left(\sum_{X \in \{T,C,A,G\}} \pi_X L_X^{(1)}(5) \right) \\
&= \log \left(\pi_T L_T^{(1)}(5) + \pi_C L_C^{(1)}(5) + \pi_A L_A^{(1)}(5) + \pi_G L_G^{(1)}(5) \right) \\
&= \log(0.22 \times 4.89e{-}08 + 0.26 \times 4.43e{-}08 \\
&\quad + 0.33 \times 2.42e{-}08 + 0.19 \times 3.72e{-}08)
\end{aligned}$$

From conditional likelihood to likelihood

	T	C	A	G
node **5**				
1	4.89e-08	4.43e-08	2.42e-08	3.72e-08

$$\pi = (0.22, 0.26, 0.33, 0.19)$$

$$\begin{aligned}
\log L &= \sum_{i=1}^{N} \log \left(\sum_{X \in \{T,C,A,G\}} \pi_X L_X^{(i)}(5) \right) \\
&= \log \left(\sum_{X \in \{T,C,A,G\}} \pi_X L_X^{(1)}(5) \right) \\
&= \log \left(\pi_T L_T^{(1)}(5) + \pi_C L_C^{(1)}(5) + \pi_A L_A^{(1)}(5) + \pi_G L_G^{(1)}(5) \right) \\
&= \log(0.22 \times 4.89e{-}08 + 0.26 \times 4.43e{-}08 \\
&\quad + 0.33 \times 2.42e{-}08 + 0.19 \times 3.72e{-}08) \\
&= \log(3.73e{-}08) \approx -17.1
\end{aligned}$$

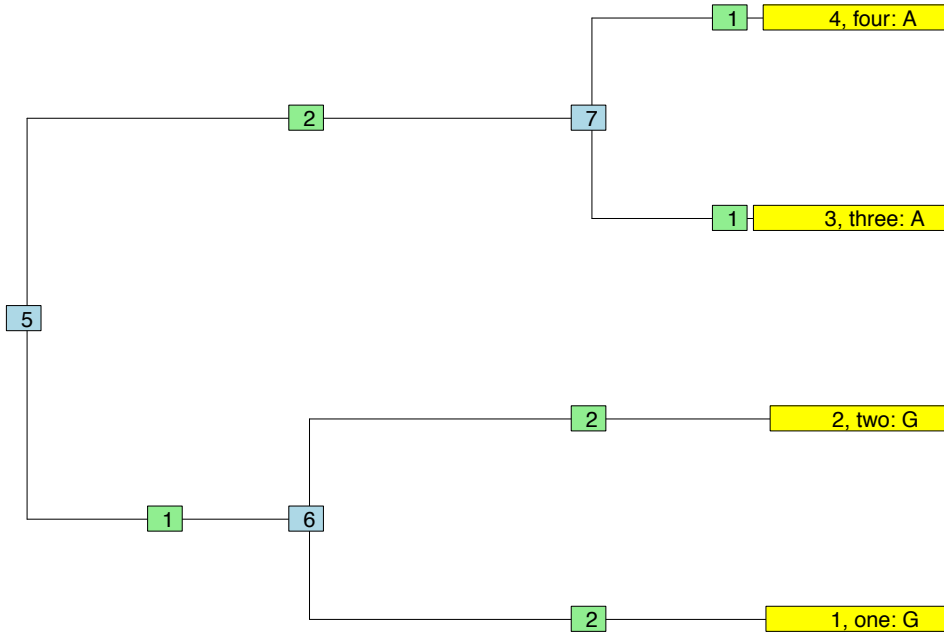
Full tree log-likelihood computation

Data: Sequence alignment A, tree τ
Result: $\log L$
$\log L \leftarrow 0$;
for $i \leftarrow 1$ **to** N **do**
  $L \leftarrow 0$;
  for X *in* $\{T, C, A, G\}$ **do**
    $L \leftarrow L + \pi_X L_X^{(i)}(\text{root})$;
  end
  $\log L \leftarrow \log L + \log(L)$;
end
return($\log L$);

Tree node/nucleotide likelihood computation

Data: Node n, sequence alignment A, tree τ, transition probability matrices $P_{TN93}(t)$ for each branch length t in τ
Result: $L_i(n)$
if n *is a tip* **then**
  for $i \leftarrow 1$ **to** N **do**
    $L^{(i)}(n) \leftarrow [0, 0, 0, 0]$;
    $L^{(i)}_{A[n,i]}(n) \leftarrow 1$;
  end
else
  for $i \leftarrow 1$ **to** N **do**
    for X *in* $\{T, C, A, G\}$ **do**
      $L1 \leftarrow 0$;
      $L2 \leftarrow 0$;
      for Y *in* $\{T, C, A, G\}$ **do**
        $L1 \leftarrow L1 + P_{XY}(|n, child1|) \cdot L^{(i)}_Y(child1)$;
        $L2 \leftarrow L2 + P_{XY}(|n, child2|) \cdot L^{(i)}_Y(child2)$;
      end
      $L^{(i)}_X(node) = L1 \times L2$;
    end
  end

Pen and paper exercise



$\pi = (0.22, 0.26, 0.33, 0.19)$

P(1):

	T	C	A	G
T	0.86	0.13	0.00045	0.00026
C	0.11	0.89	0.00045	0.00026
A	0.0003	0.00035	0.95	0.052
G	0.0003	0.00035	0.09	0.91

P(2):

	T	C	A	G
T	0.76	0.24	0.00089	0.00051
C	0.2	0.8	0.00089	0.00051
A	0.00059	0.0007	0.9	0.096
G	0.00059	0.0007	0.17	0.83

Pen and paper solution

	T	C	A	G
node 1				
1	0	0	0	1
node 2				
1	0	0	0	1
node 6				
1	2.601e-07	2.601e-07	9.216e-03	0.6889
node 3				
1	0	0	1	0
node 4				
1	0	0	1	0
node 7				
1	2.025e-07	2.025e-07	0.9025	8.1e-03
node 5				
1	1.482021e-07	1.448554e-07	0.036	0.099

$$\begin{aligned}\mathbf{LogL} &= \log(\pi_T \times L_1(5|T) + \pi_C \times L_1(5|C) + \pi_A \times L_1(5|A) + \pi_G \times L_1(5|G)) \\ &= \log(0.22 \times 1.482021e{-}07 + 0.26 \times 1.448554e{-}07 \\ &+ 0.33 \times 0.03624314450 + 0.19 \times 0.1005294544) \\ &= \log(0.0310609) \approx -3.471805\end{aligned}$$