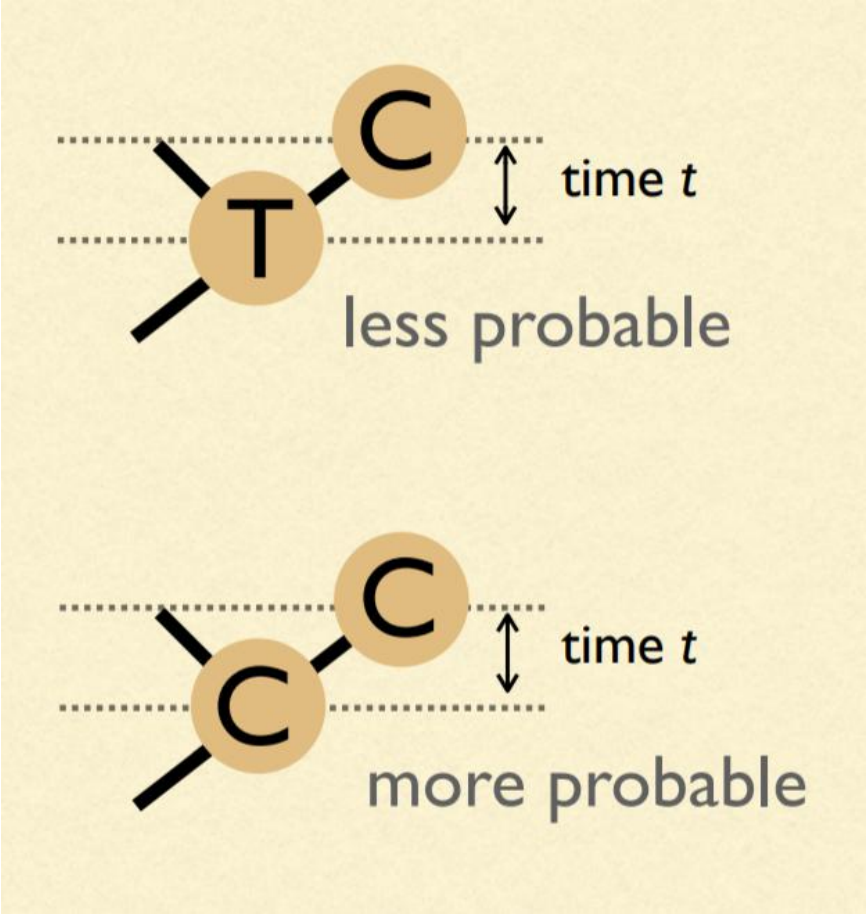
Continuous-Time Markov Models

Markov assumption **= probability of change depends only on current state, not how long it has been in that state**

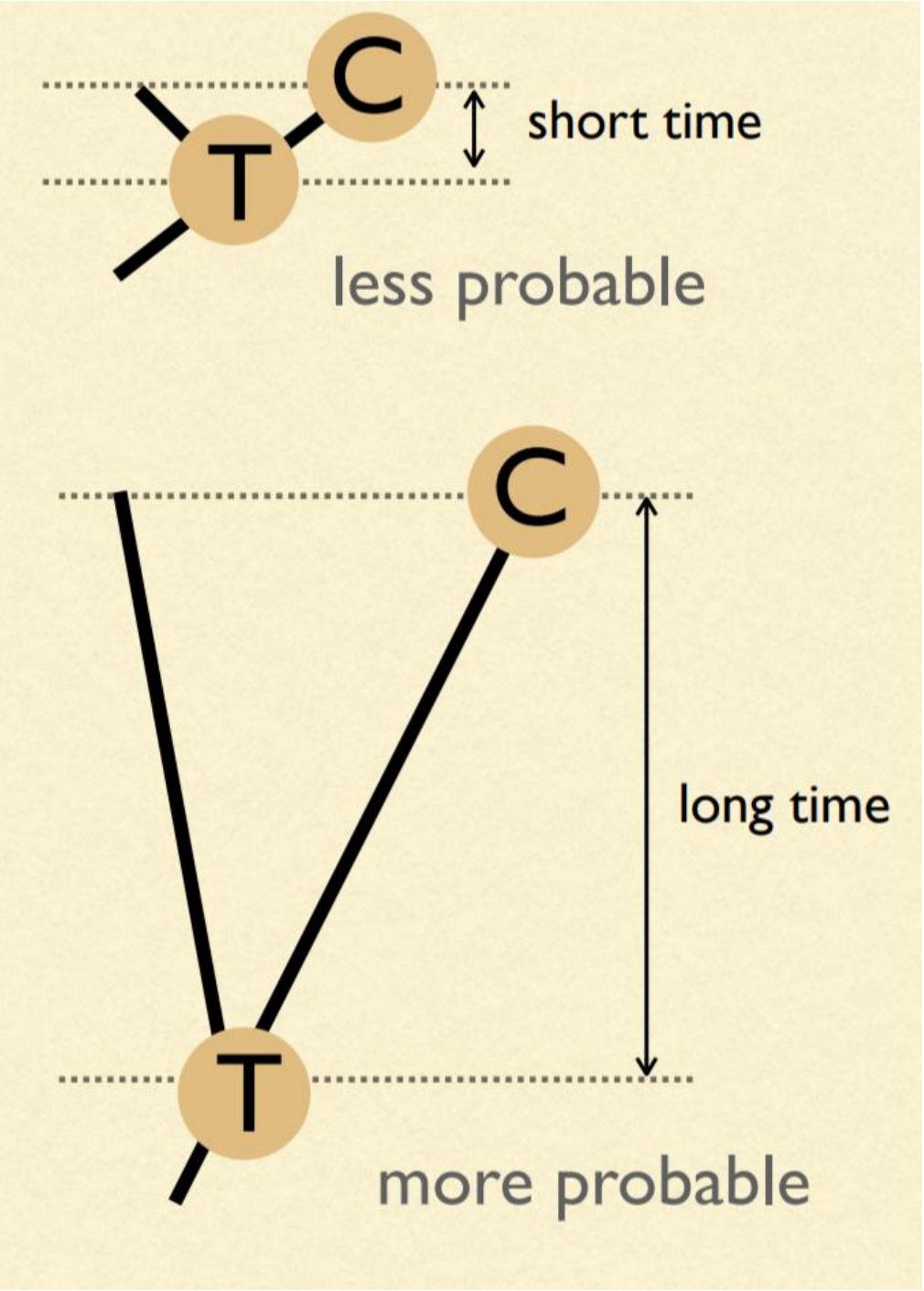
Our model of change depends on time: We must estimate branch lengths

Units of branch length will be expected number of substitutions per site

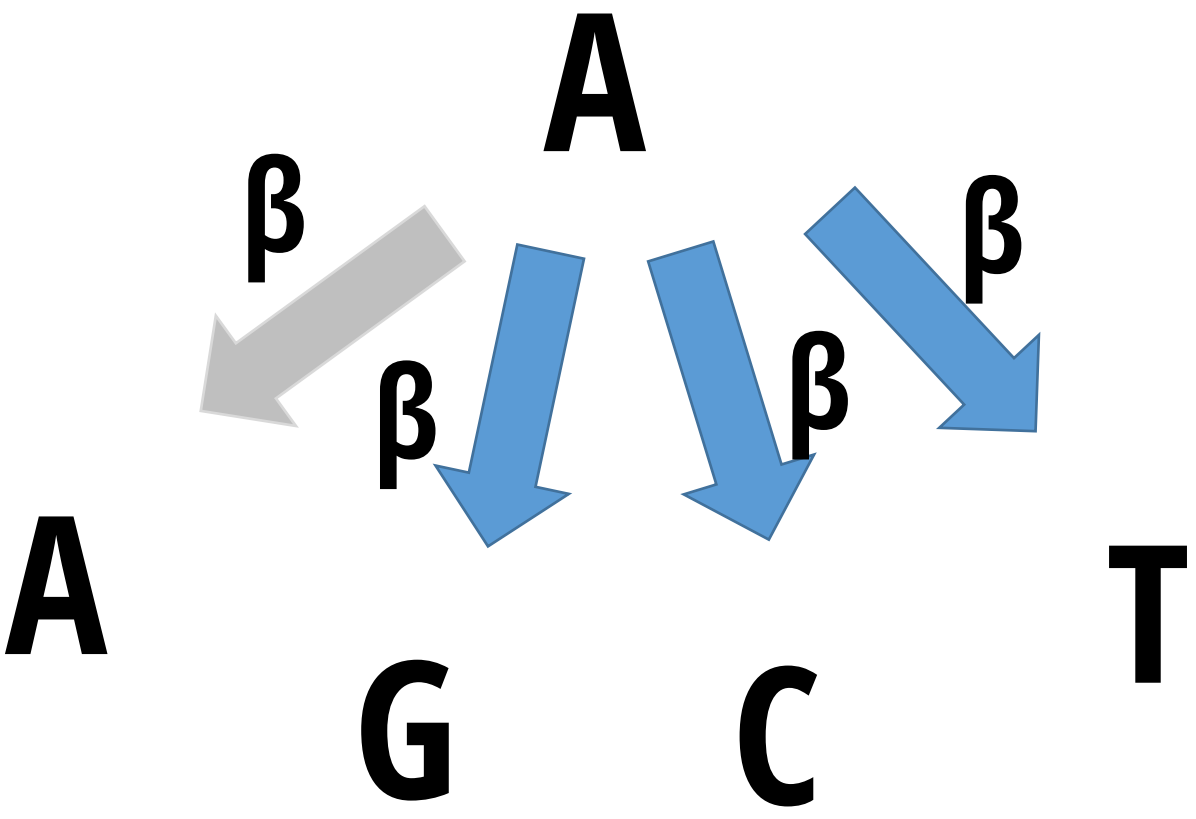
(= rate of substitions x time)



Probabilities are dependent on time



$\mu = 4\beta$



A (very) simple phylogeny…

P_{AA} =

Probability nothing happened +

Probability something happened, but that the last thing that happened ended in an A

A (very) simple phylogeny...

$$P_{AA} = (e^{-\mu t}) + (1 - e^{-\mu t})(1/4)$$

Probability something doesn't happen

Probability at least one thing happens

Probability that the last thing that happened ends in an A

A (very) simple phylogeny…

P_{AG} =

$(1 - e^{-\mu t})(1/4)$

Probability at least one thing happens

Probability that the last thing that happened ends in an G

A (very) simple phylogeny…

P_{AC} =

$(1 - e^{-\mu t})(1/4)$

Probability at least one thing happens

Probability that the last thing that happened ends in an C

A (very) simple phylogeny…

$P_{AT} = (1 - e^{-\mu t})(1/4)$

Probability at least one thing happens

Probability that the last thing that happened ends in an T

One last bit...substitutions vs. "events"

$$\nu = (3/4)\mu t = 3\beta t$$

$$4\nu/3 = \mu t$$

Only 3 out of 4 events results in a substitution. Thus, we can define the expected number of substitutions for a given time interval t as ν.

$$P_{AA} = (e^{-\mu t}) + (1 - e^{-\mu t})(1/4)$$

$$P_{AG} = (1 - e^{-\mu t})(1/4)$$

$$P_{AC} = (1 - e^{-\mu t})(1/4)$$

$$P_{AT} = (1 - e^{-\mu t})(1/4)$$

$$P_{AA} = (1/4) + (3/4)(e^{-4v/3})$$

$$P_{AG} = (1/4) - (1/4)(e^{-4v/3})$$

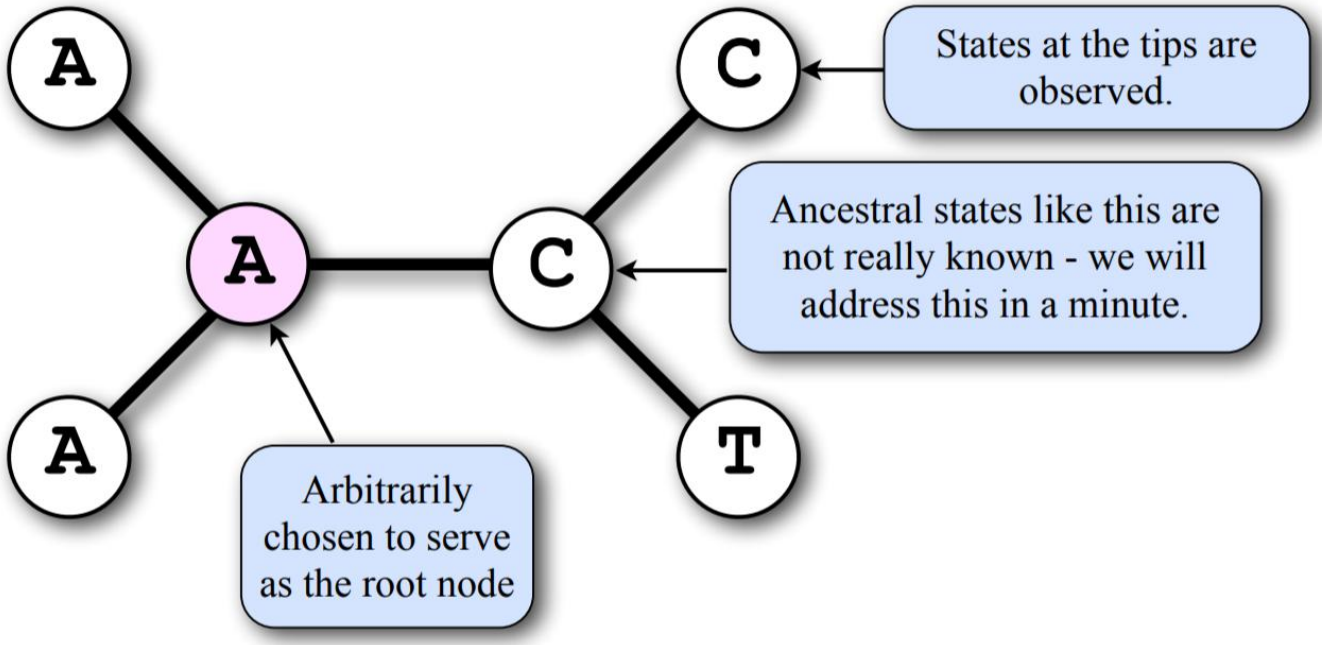
$$P_{AC} = (1/4) - (1/4)(e^{-4v/3})$$

$$P_{AT} = (1/4) - (1/4)(e^{-4v/3})$$

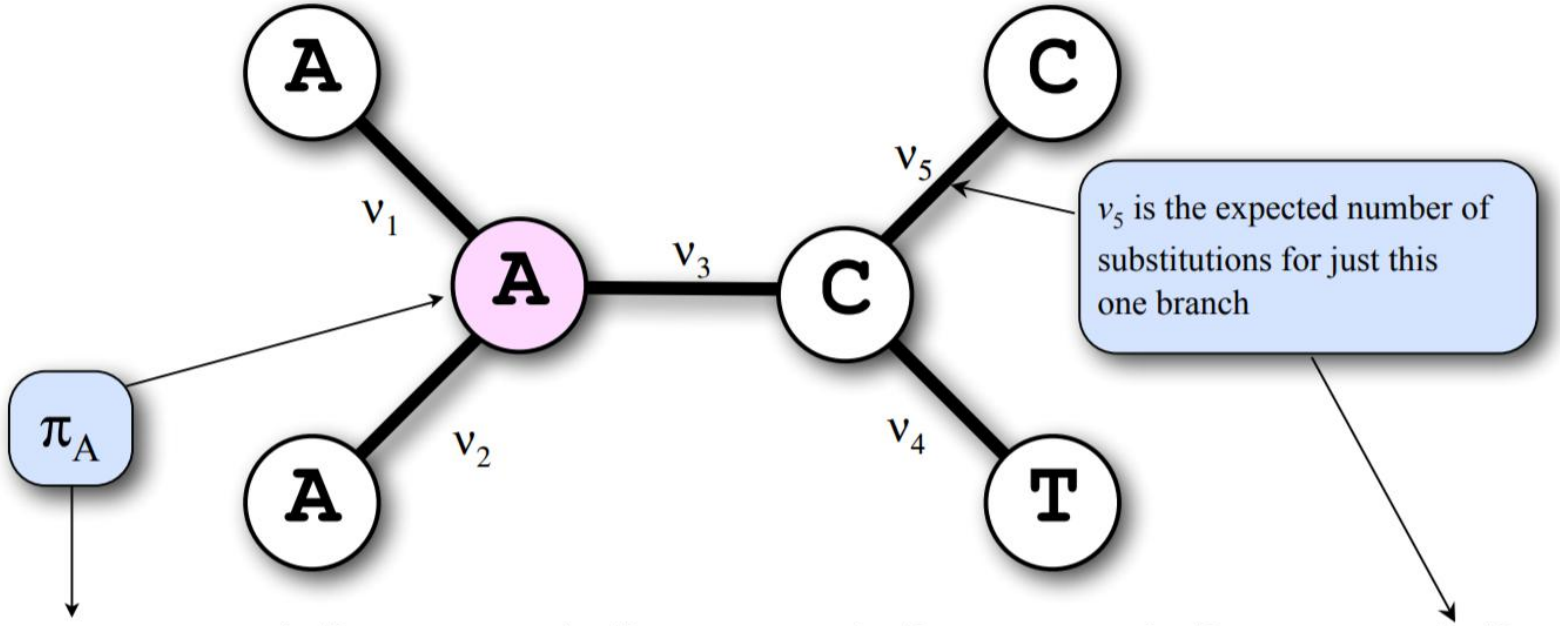
Sanity check:
Do they all add to 1?

Likelihood of an unrooted tree

(data shown for only one site)



Likelihood for site k

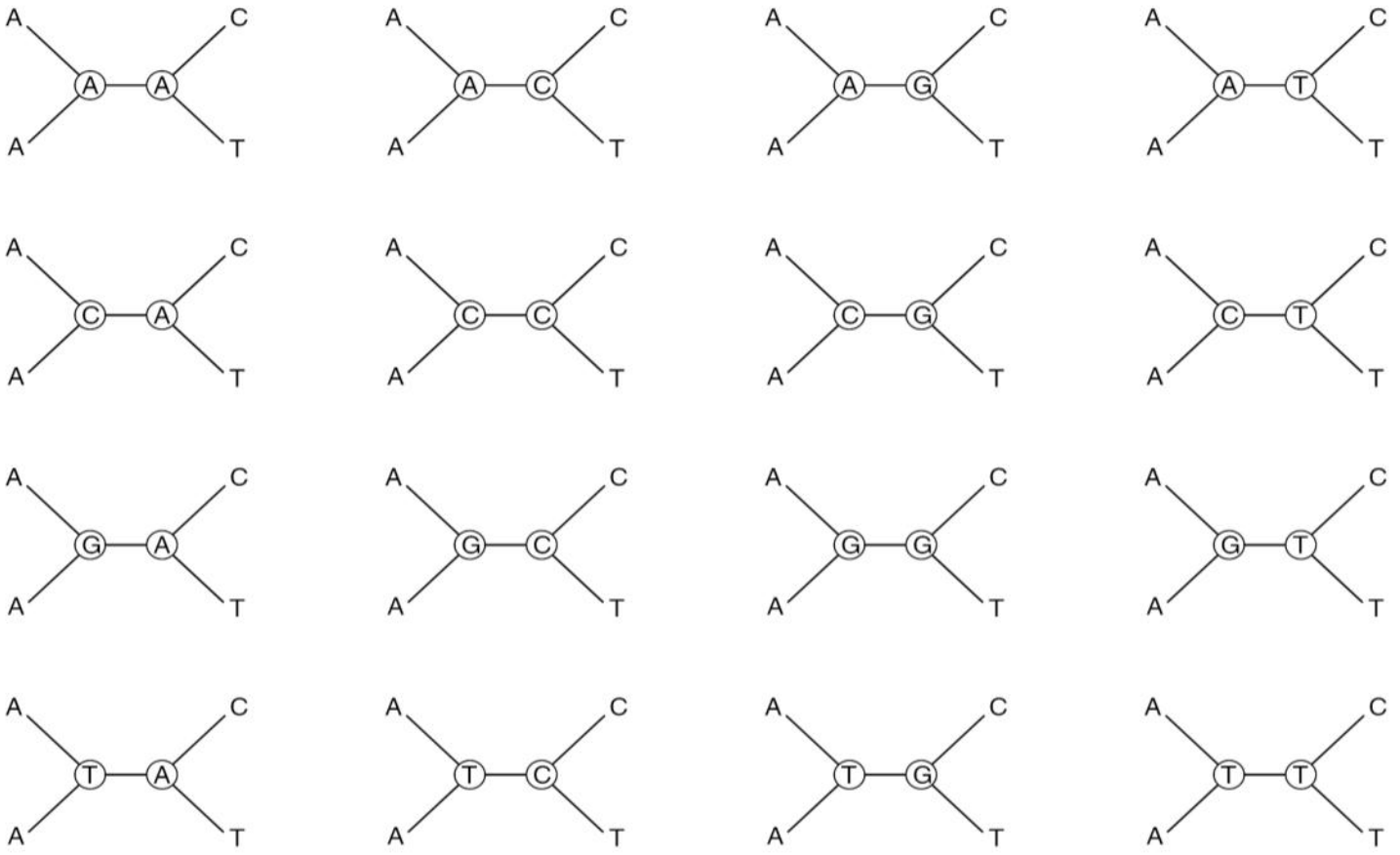


$$L_k = \tfrac{1}{4}\left[\tfrac{1}{4}+\tfrac{3}{4}e^{-4\nu_1/3}\right]\left[\tfrac{1}{4}+\tfrac{3}{4}e^{-4\nu_2/3}\right]\left[\tfrac{1}{4}-\tfrac{1}{4}e^{-4\nu_3/3}\right]\left[\tfrac{1}{4}-\tfrac{1}{4}e^{-4\nu_4/3}\right]\left[\tfrac{1}{4}+\tfrac{3}{4}e^{-4\nu_5/3}\right]$$

$P_{AA}(v_1)$ $P_{AA}(v_2)$ $P_{AC}(v_3)$ $P_{CT}(v_4)$ $P_{CC}(v_5)$

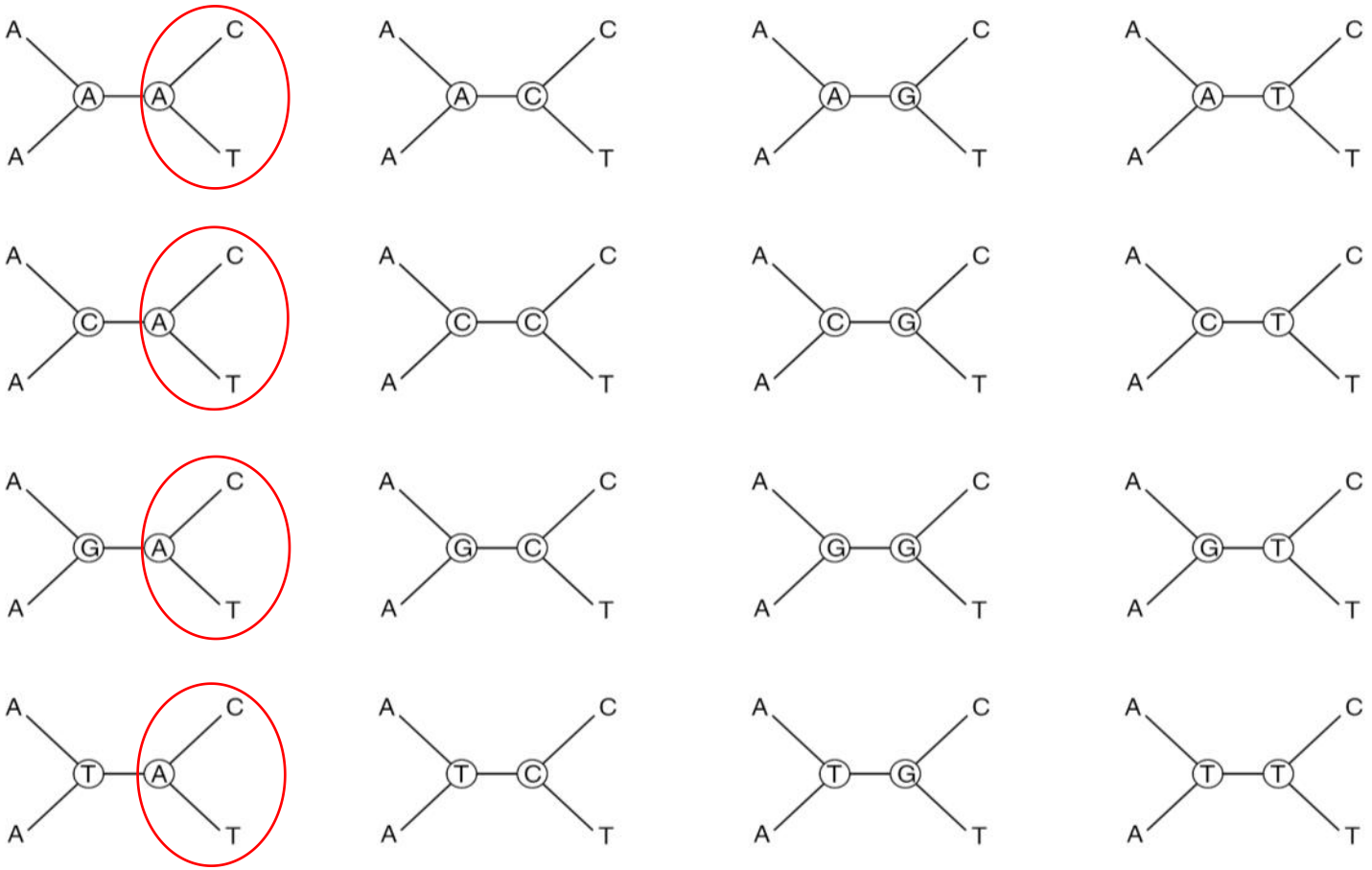
Note use of the AND probability rule

Brute force approach would be to calculate L_k for all 16 combinations of ancestral states and sum them



Note use of the OR probability rule

Pruning algorithm



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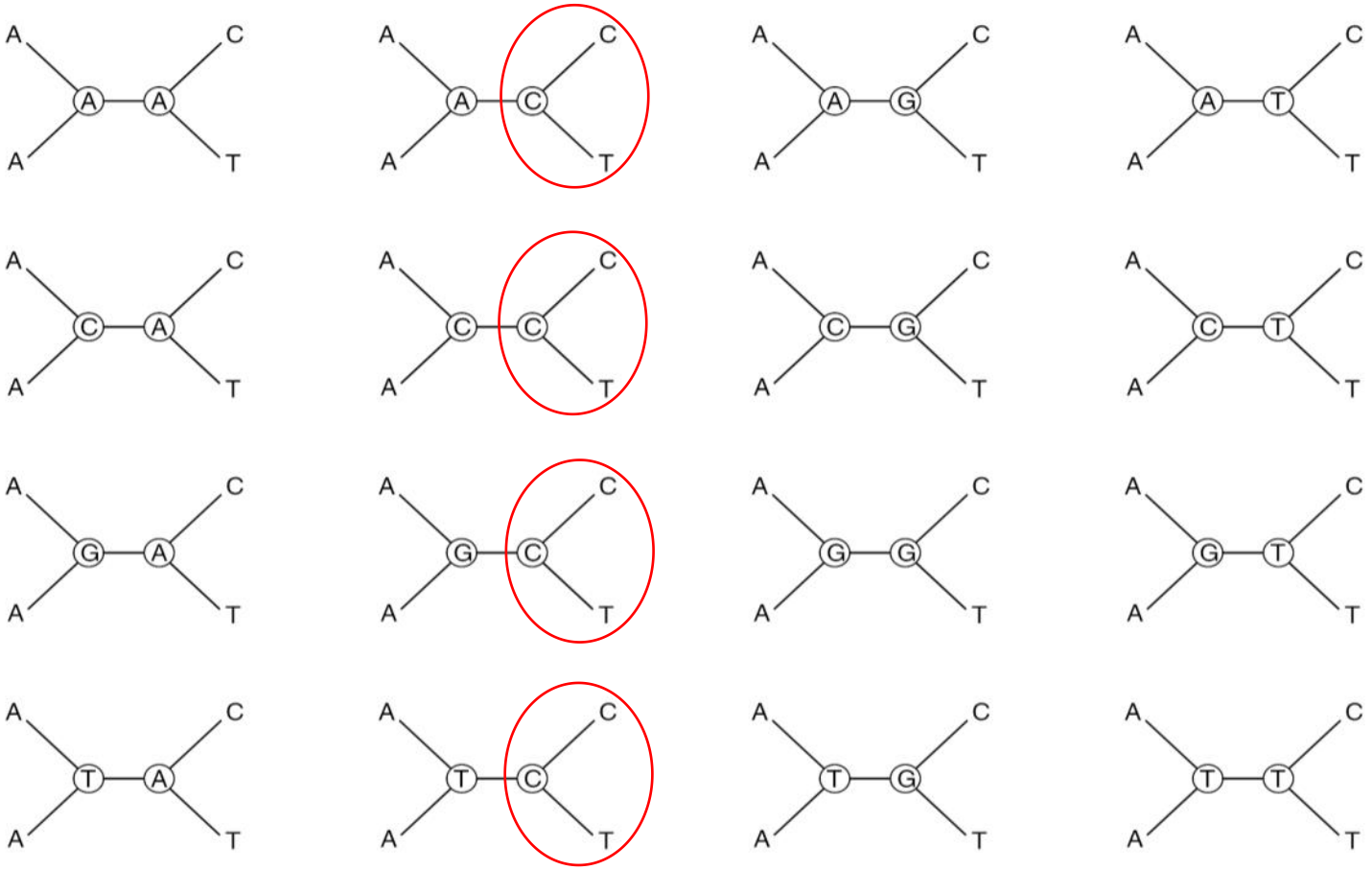

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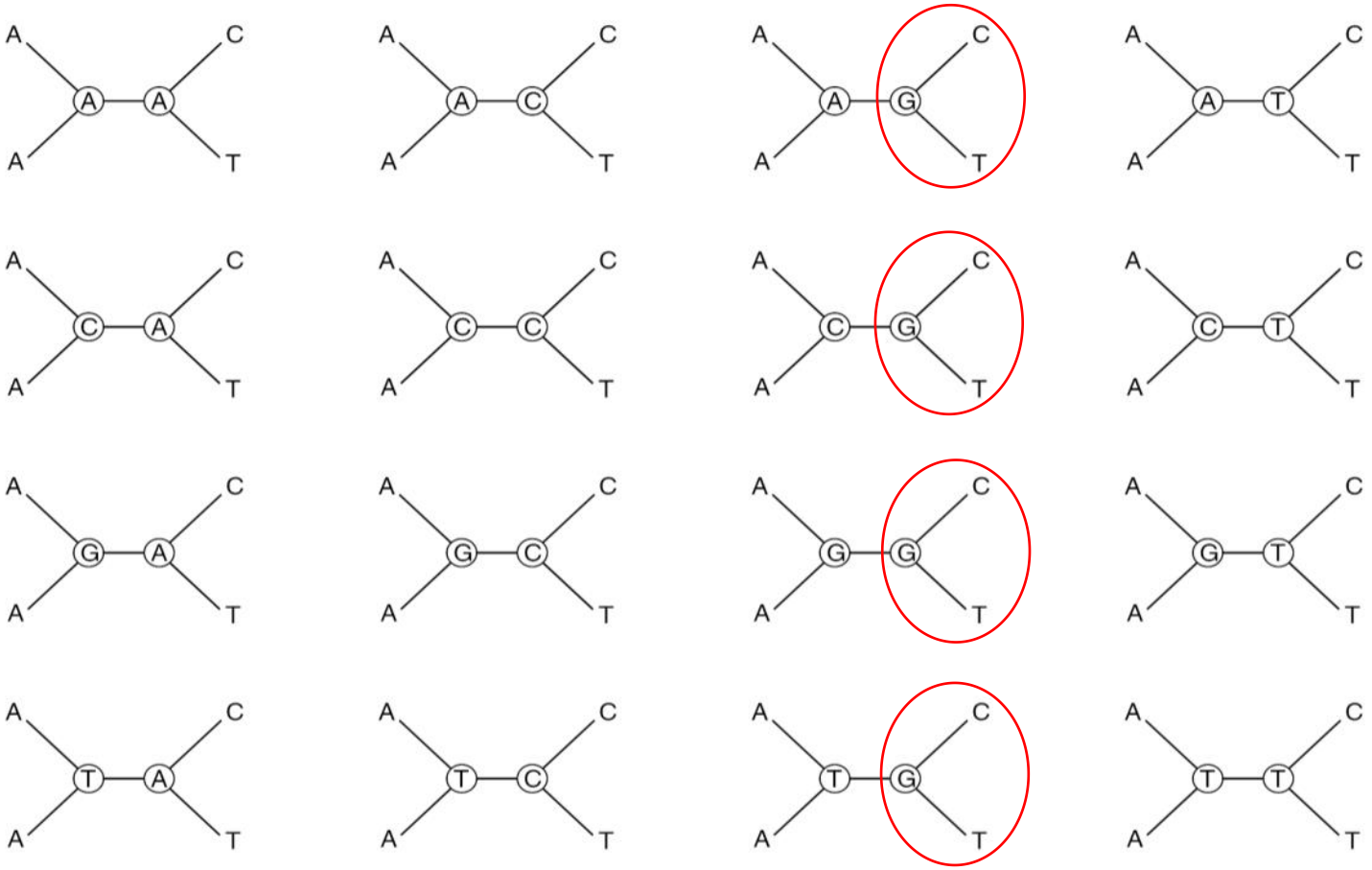

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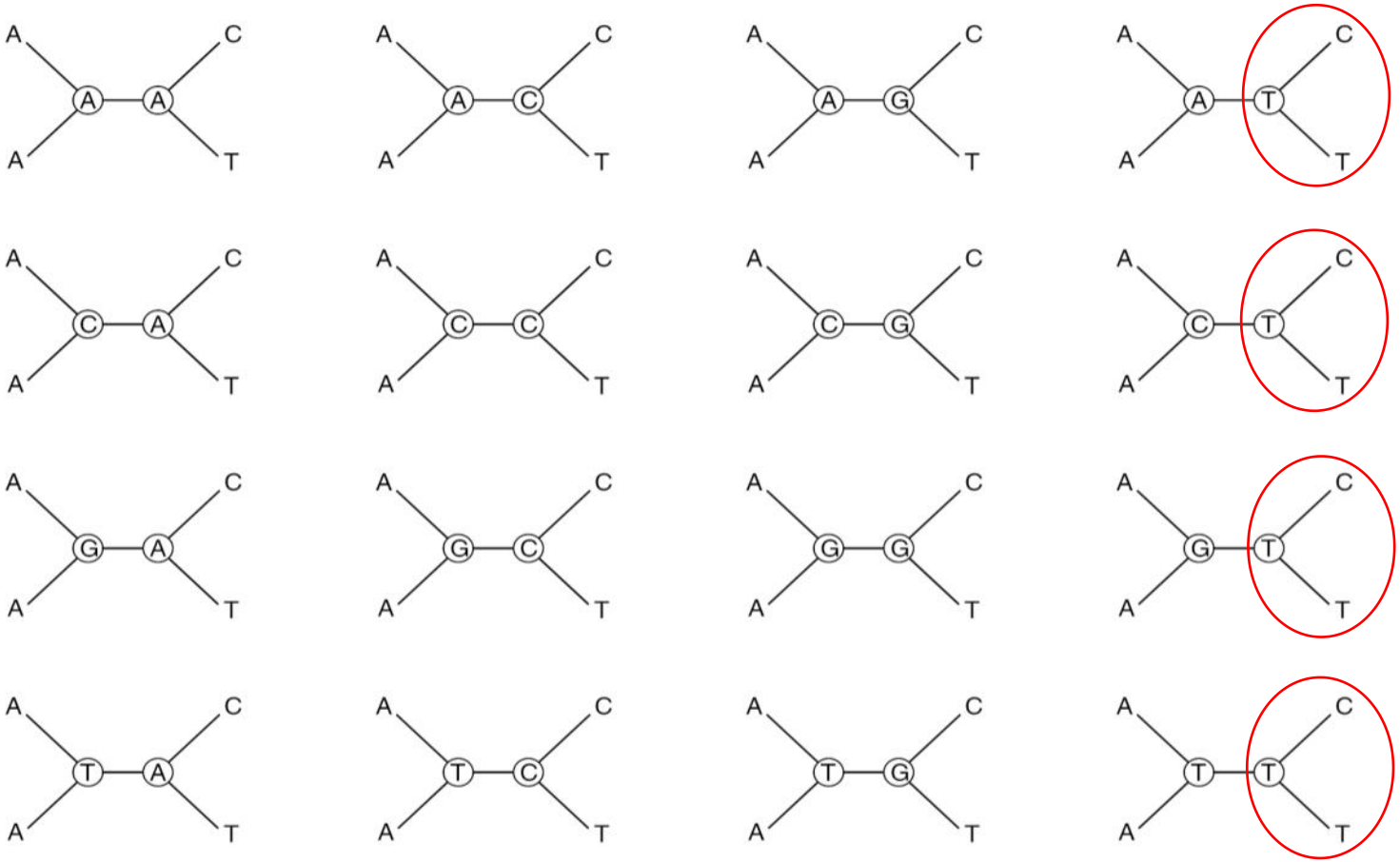

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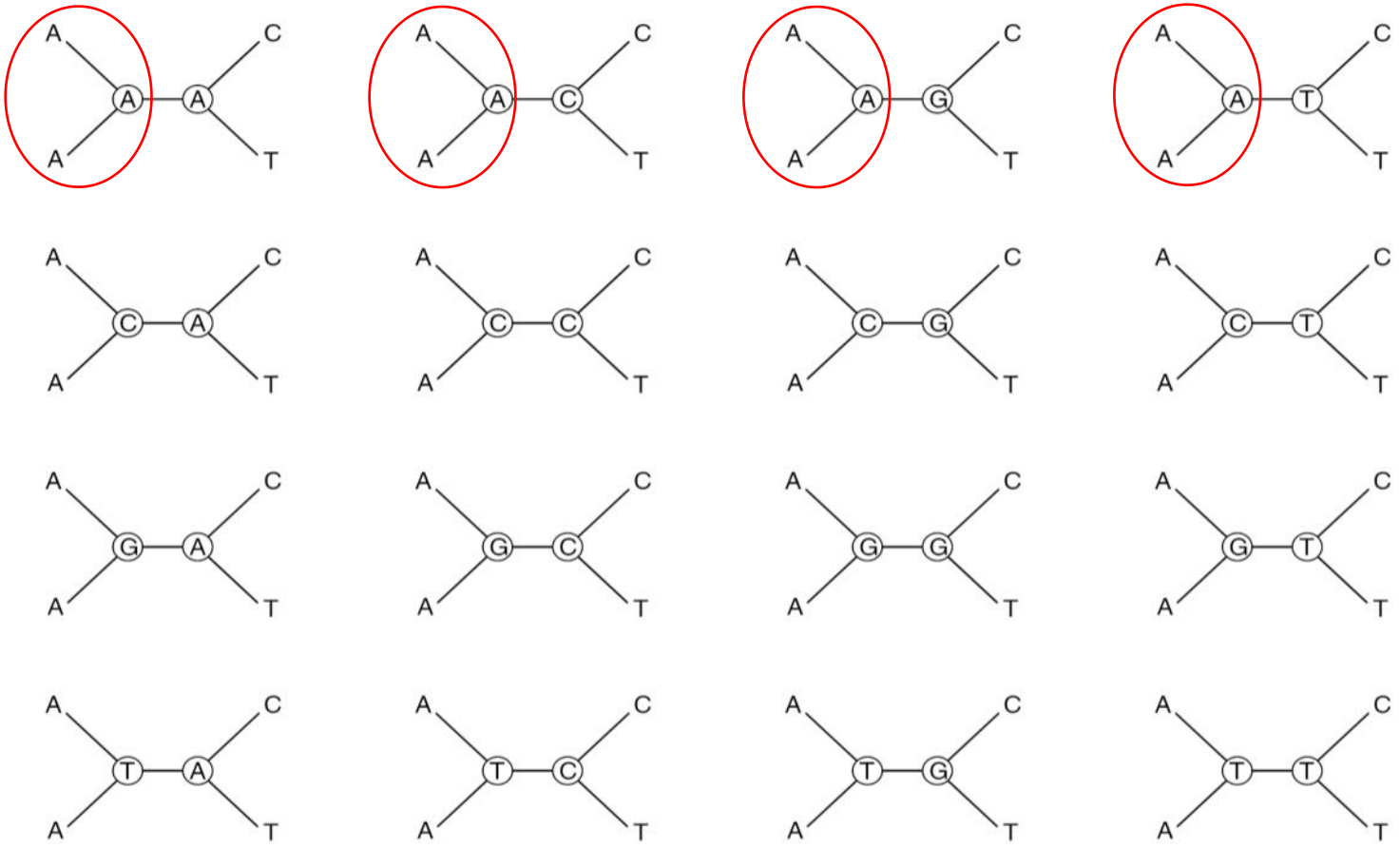

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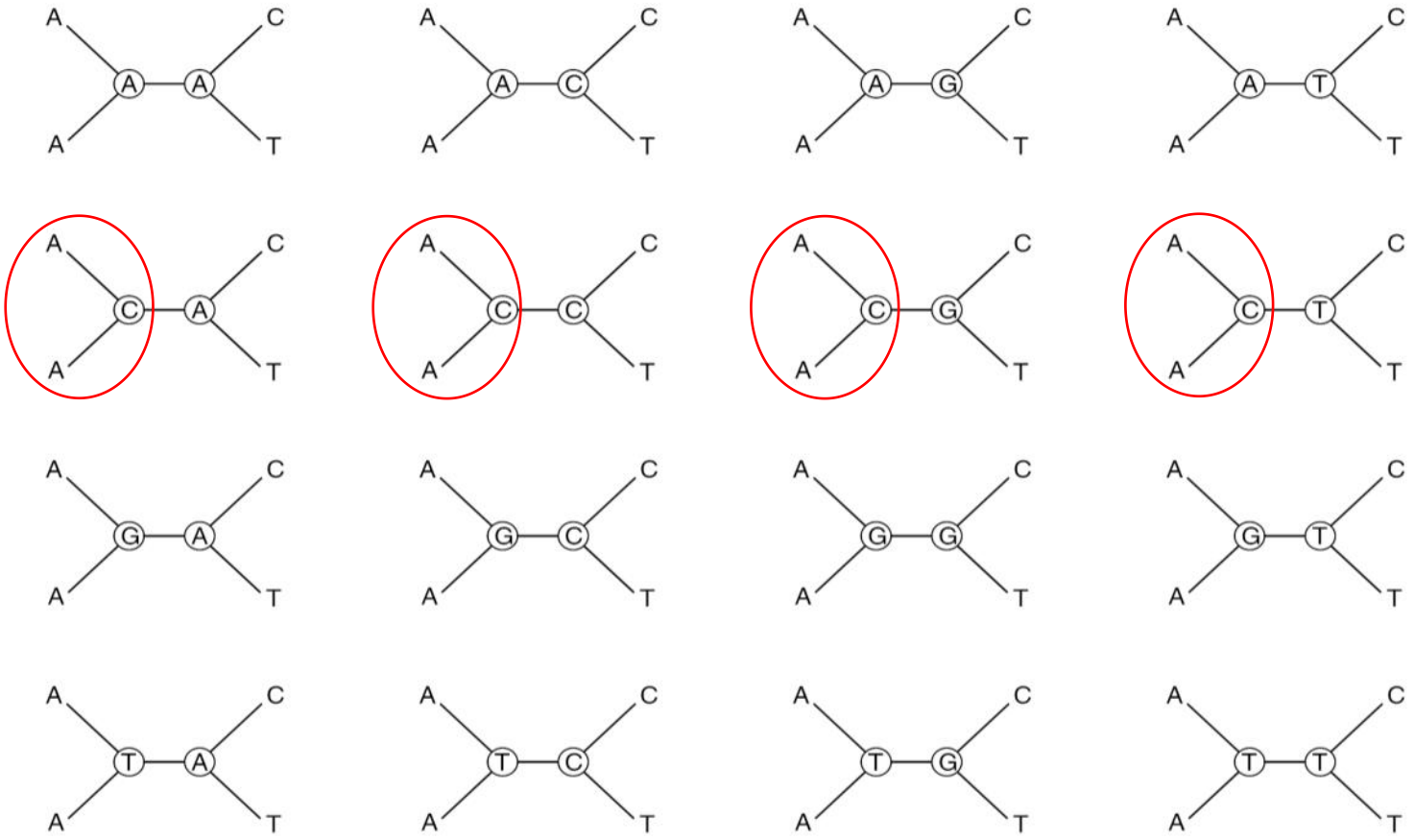

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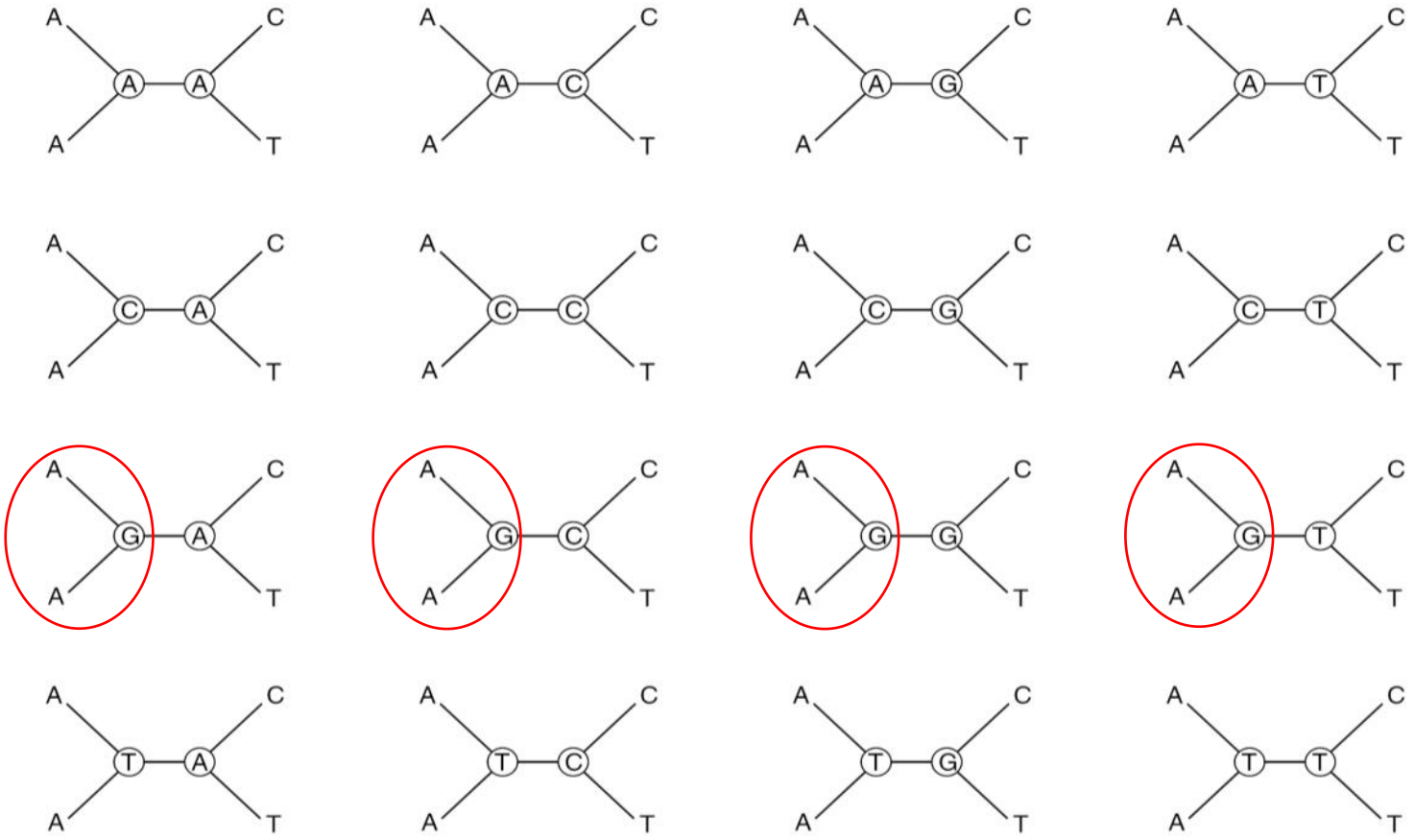

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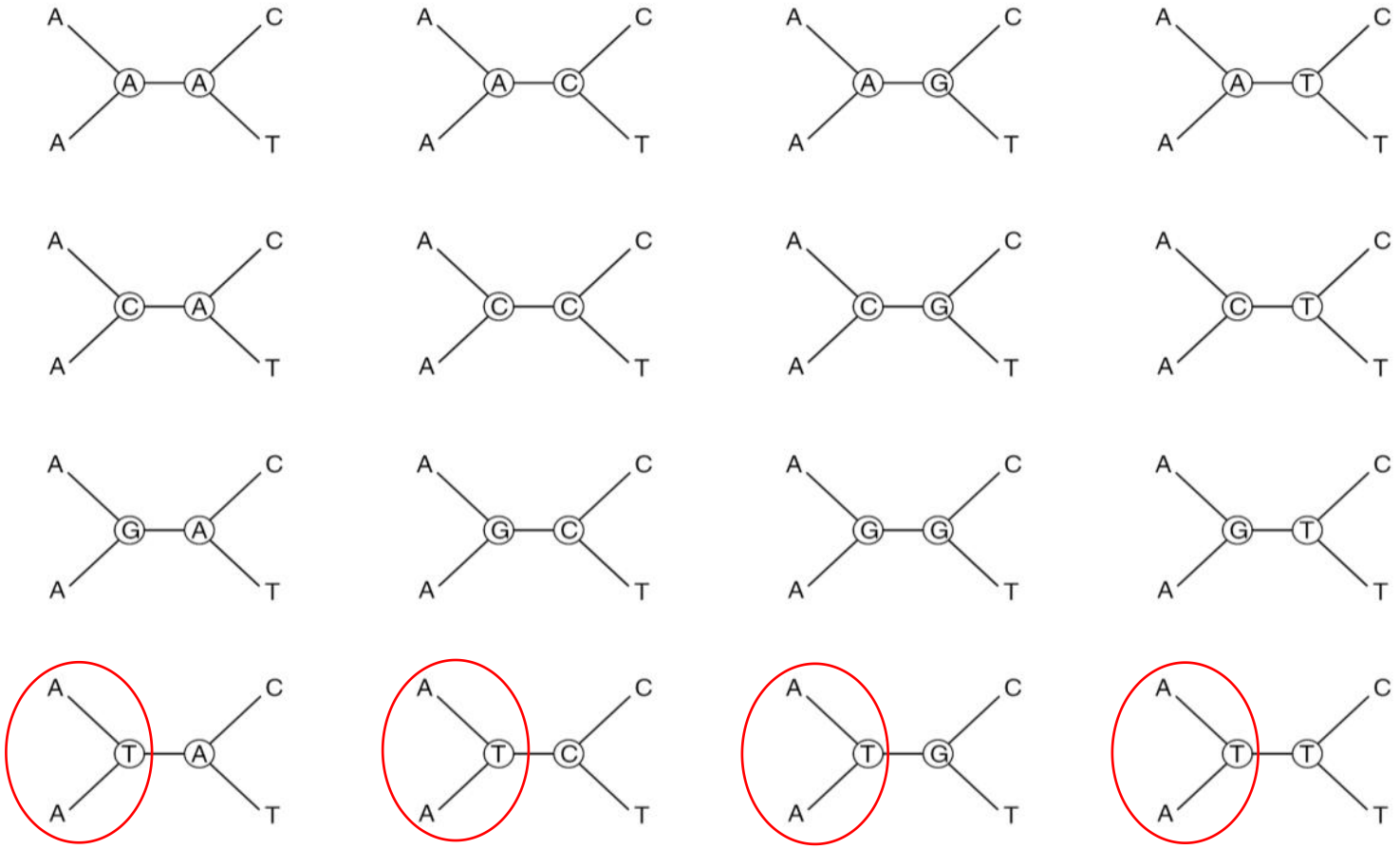

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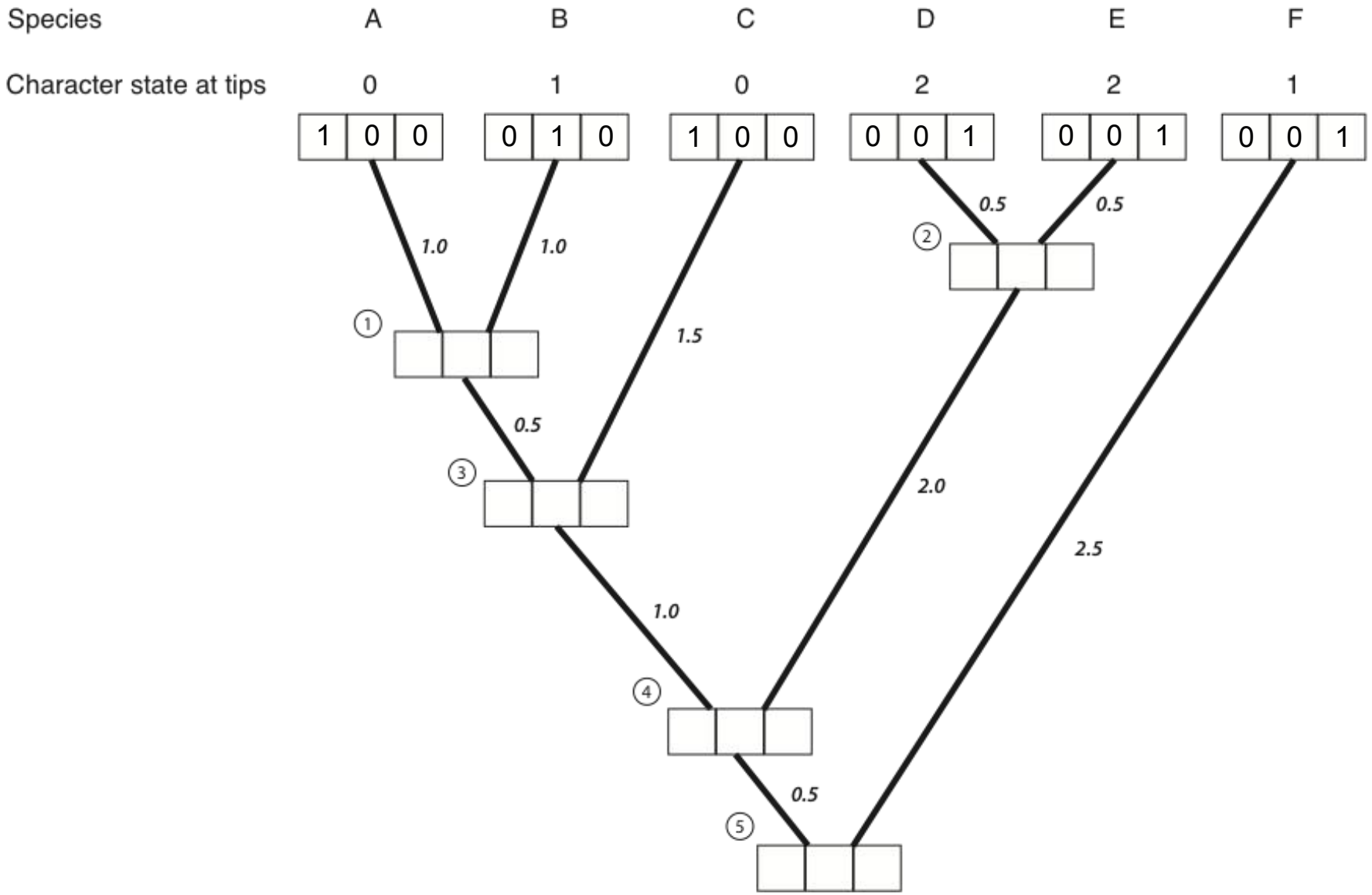
Species
A
B
C
D
E
F
Character state at tips
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1 0 0
0 0 1
0 0 1
0 0 1
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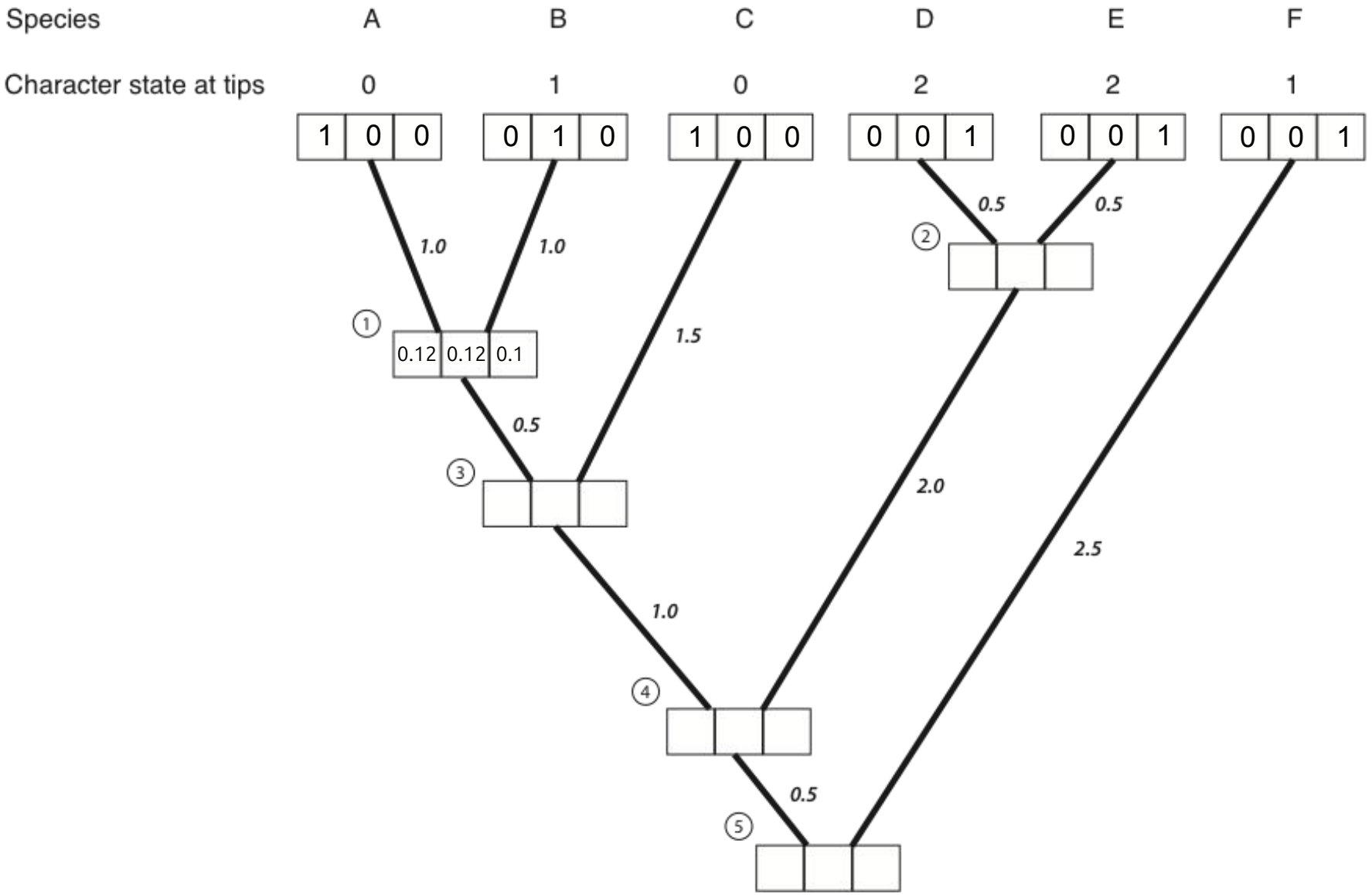
5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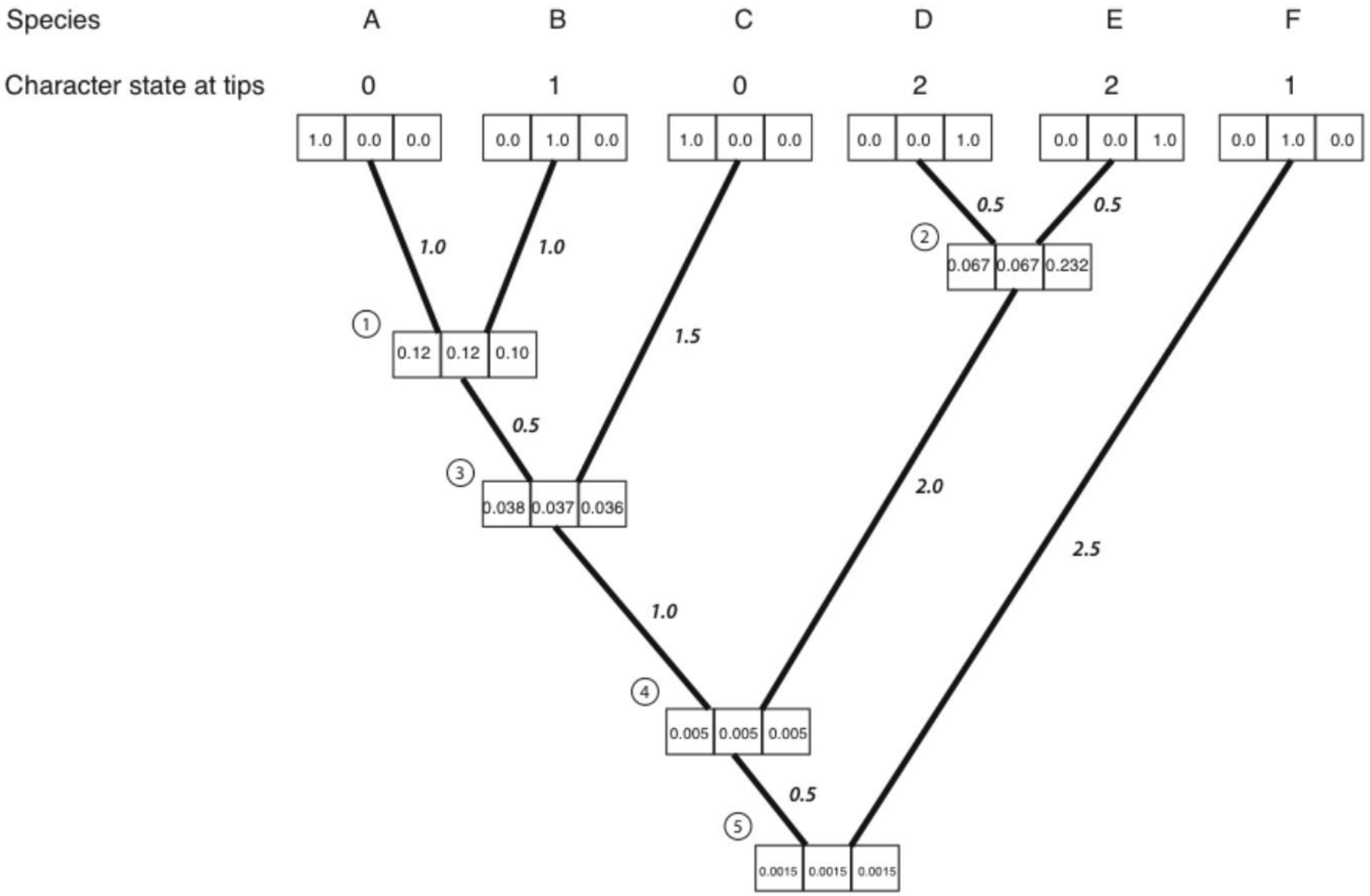
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Lab Exercise in R

Goal:

Get some experience R

Understand probability, likelihoods, and Bayesian inference using non-phylogenetic models (linear regression)