Model Misspecification due to Site Specific Rate Heterogeneity: how is tree inference affected?

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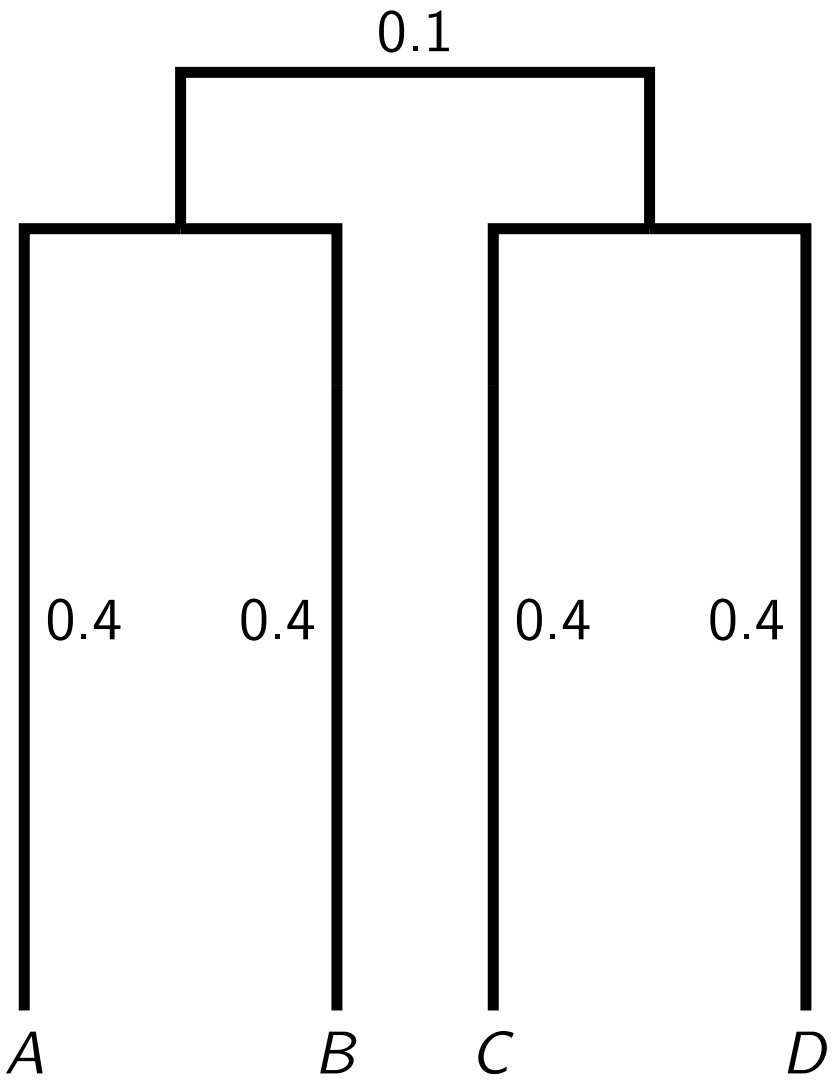
October, 2013

What is Site Specific Rate Heterogeneity (SSRH)?



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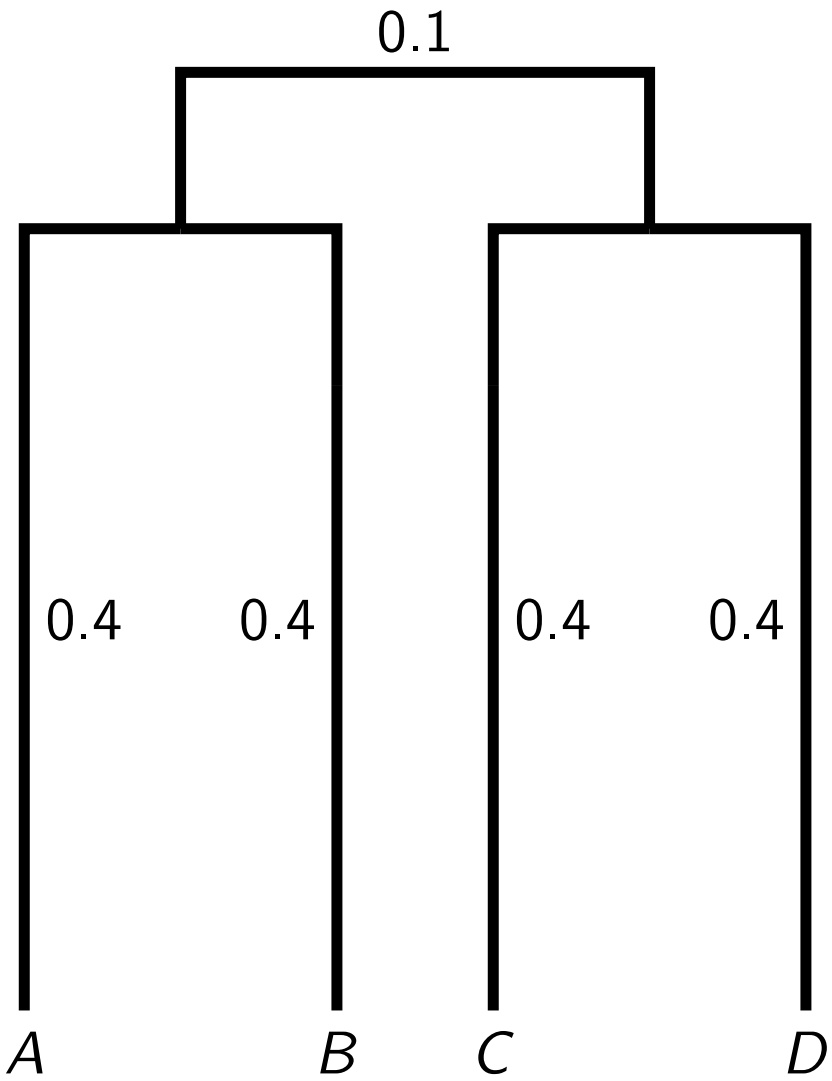

The model contains 3 site types:

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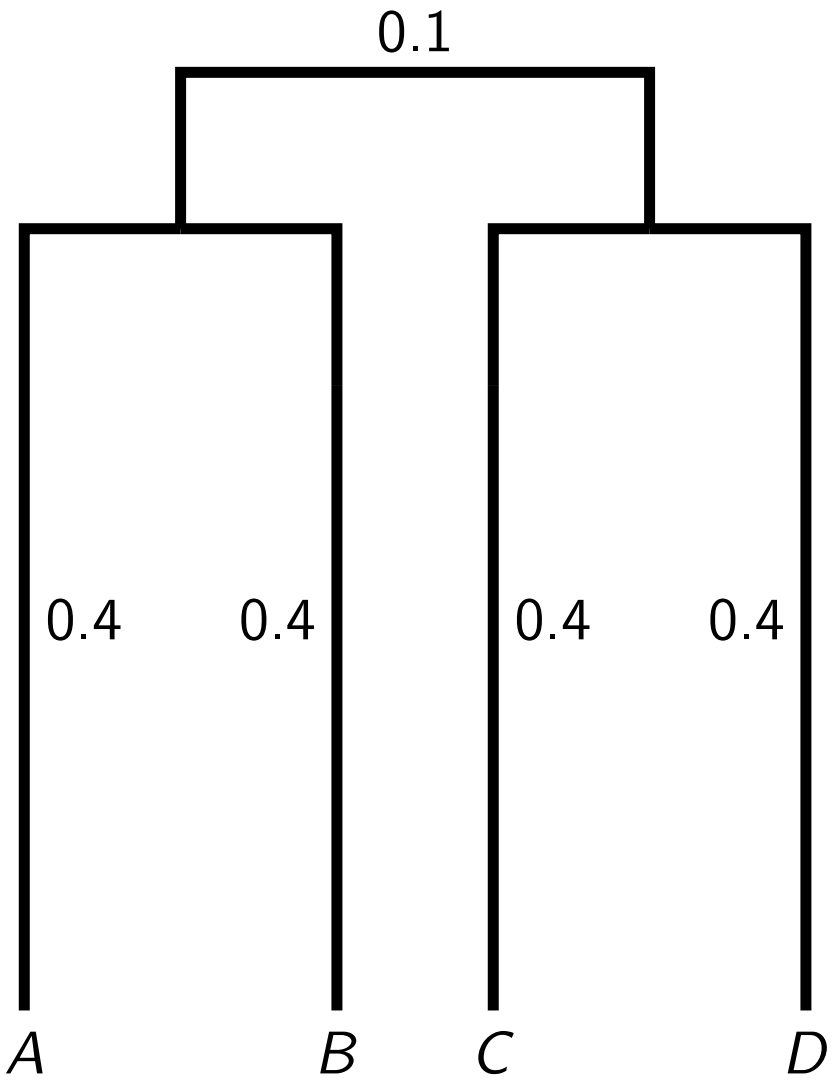

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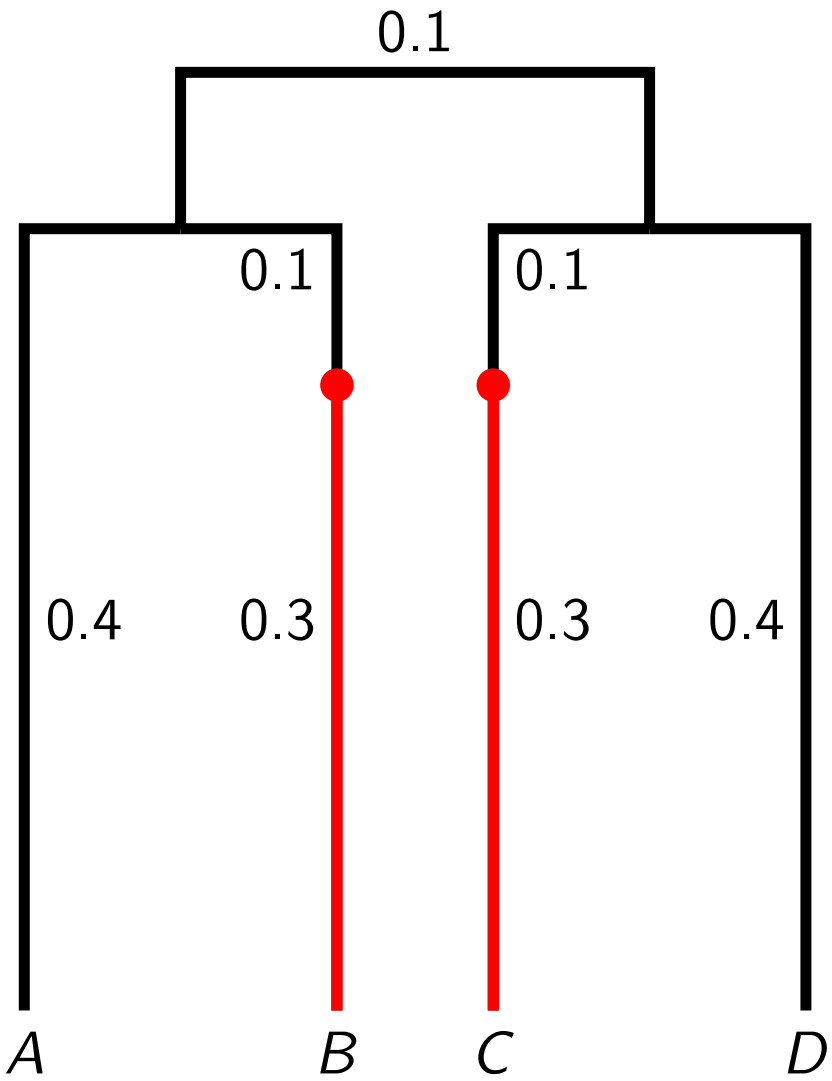

The model contains 3 site types:

- Invariable sites
- Variable sites
- Switching sites

Why should we care about SSRH?

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Tasmanian Pygmy Possum

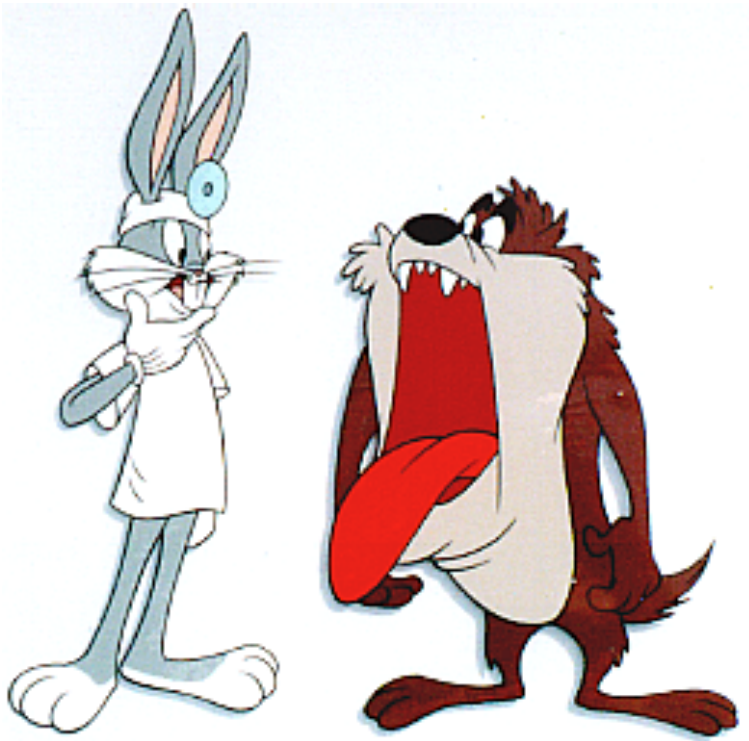
Tasmanian Native Hen

Why should we care about SSRH?

Tasmanian Devil

Why should we care about SSRH?

What's up Doc?



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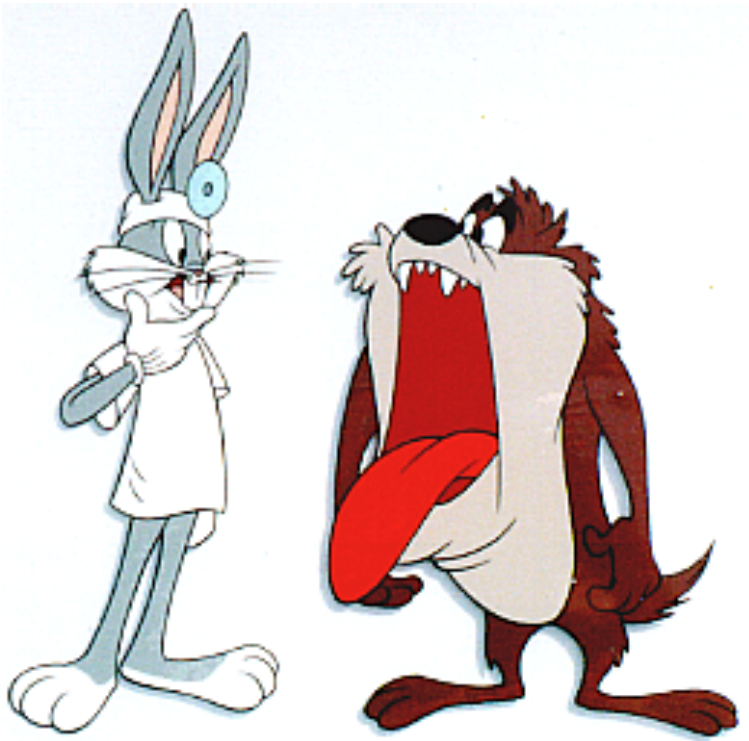

Devil Facial Tumour Syndrome

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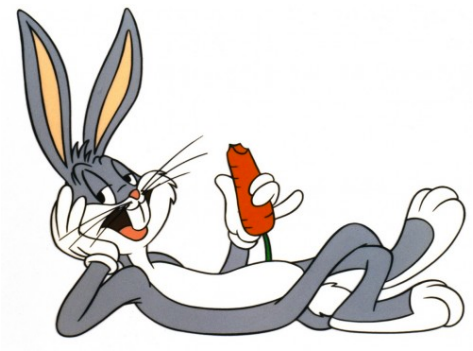

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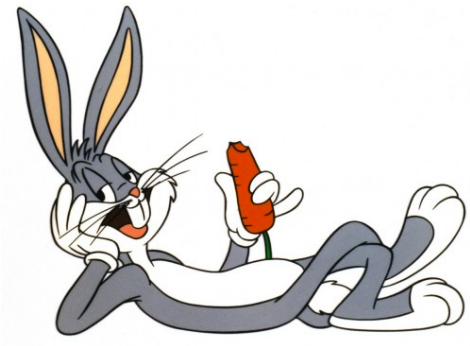

Experimental Procedure

1. Data was simulated using the program LineageSpecificSeqgen[1]

[1]Source: L. Shavit Grievink, D. Penny, M. D. Hendy, and B. R. Holland. BMC Evolutionary Biology, 8:317, 2008.

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Experimental Procedure

1. Data was simulated using the program LineageSpecificSeqgen[1]
2. The Phylip[2] software package was used to perform tree inference using the maximum parsimony (MP), neighbour joining (NJ) and maximum likelihood (ML) methods.
3. A theoretical analysis of each method was carried out in an effort to understand their performance.

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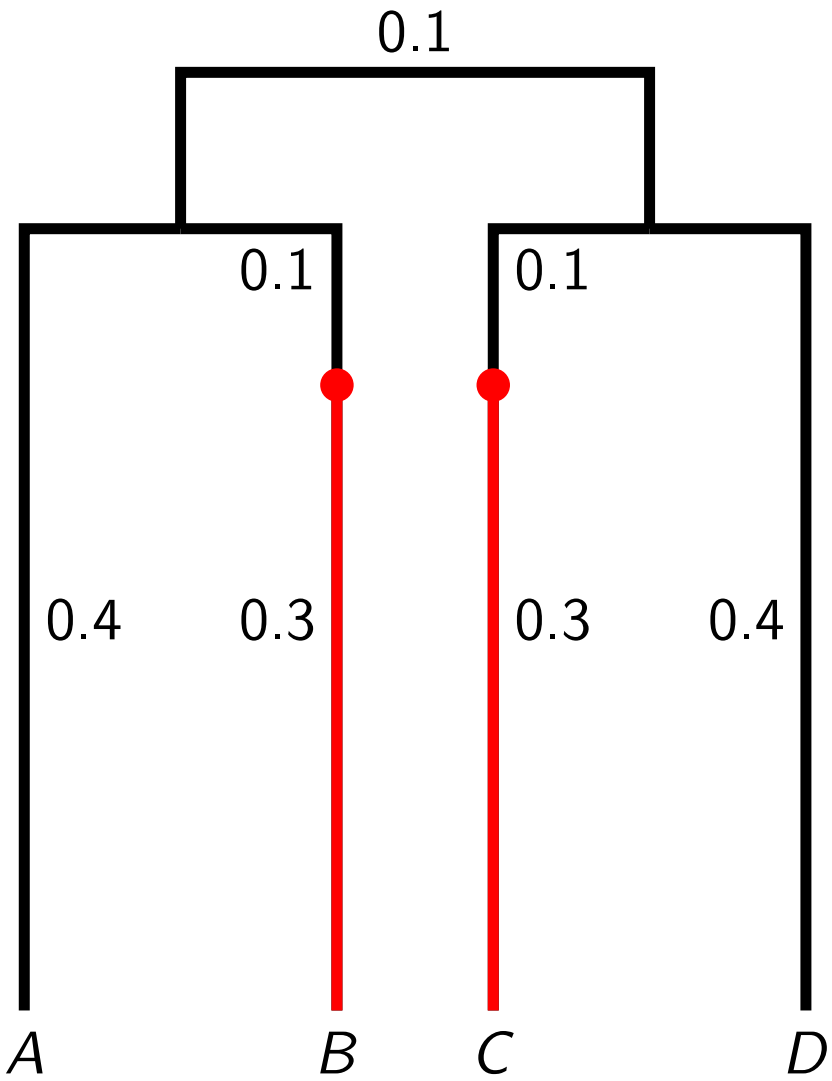
Simulation Parameters



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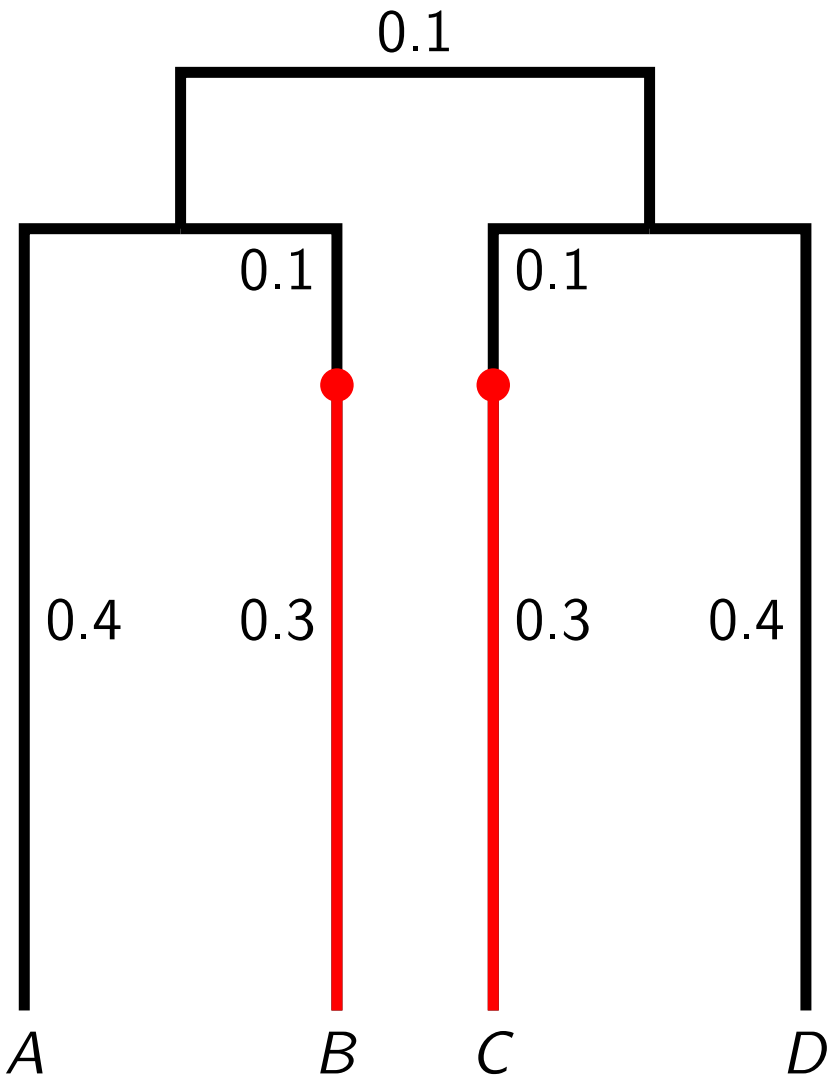

$p_{inv} = 80\%$

$p_{var} = 20\%$

$p_{switch} = 0, 1, 2, \ldots, 100\%$

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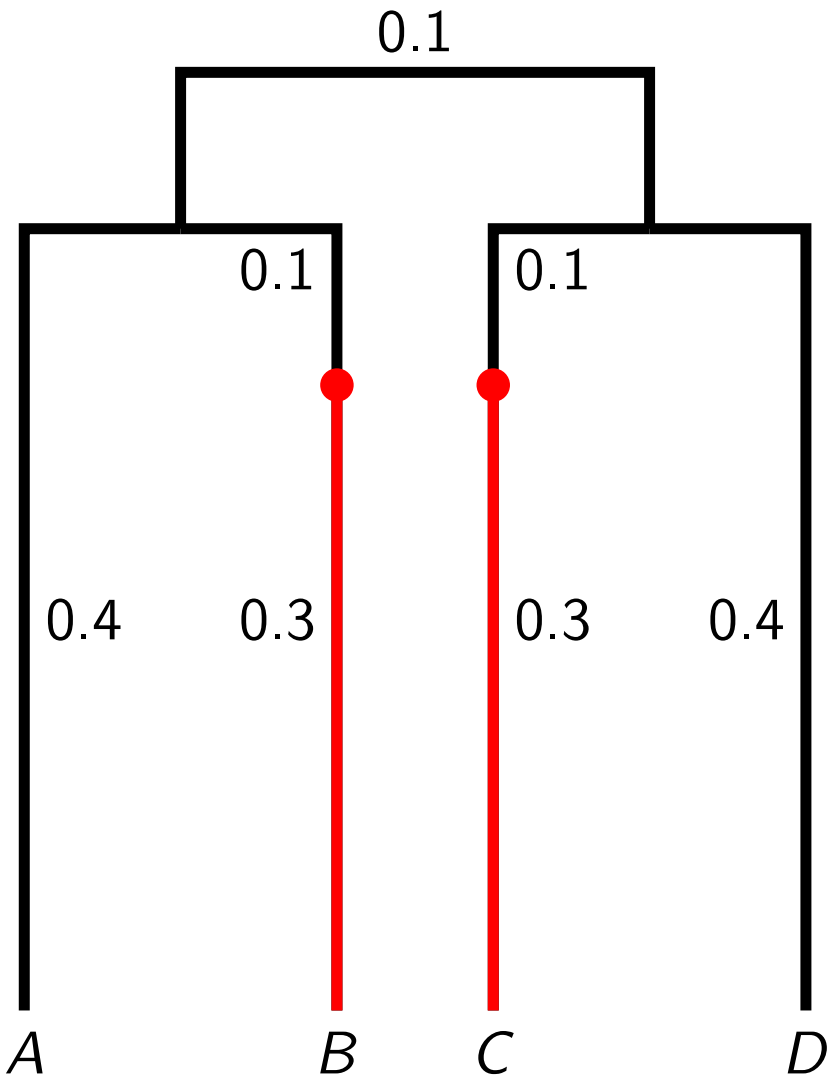

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$p_{var} = 20\%$

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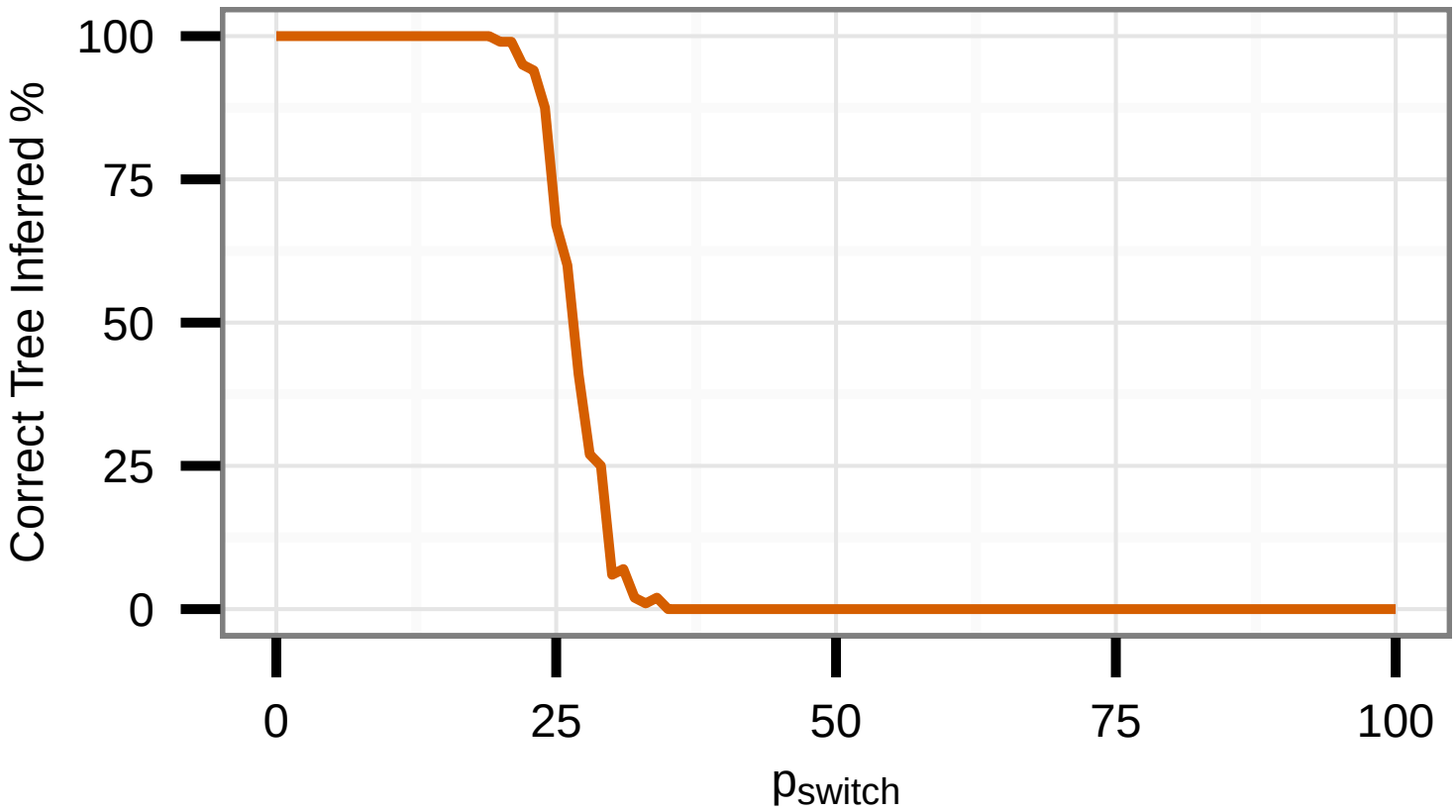
100000 base pairs

Jukes Cantor substitution model

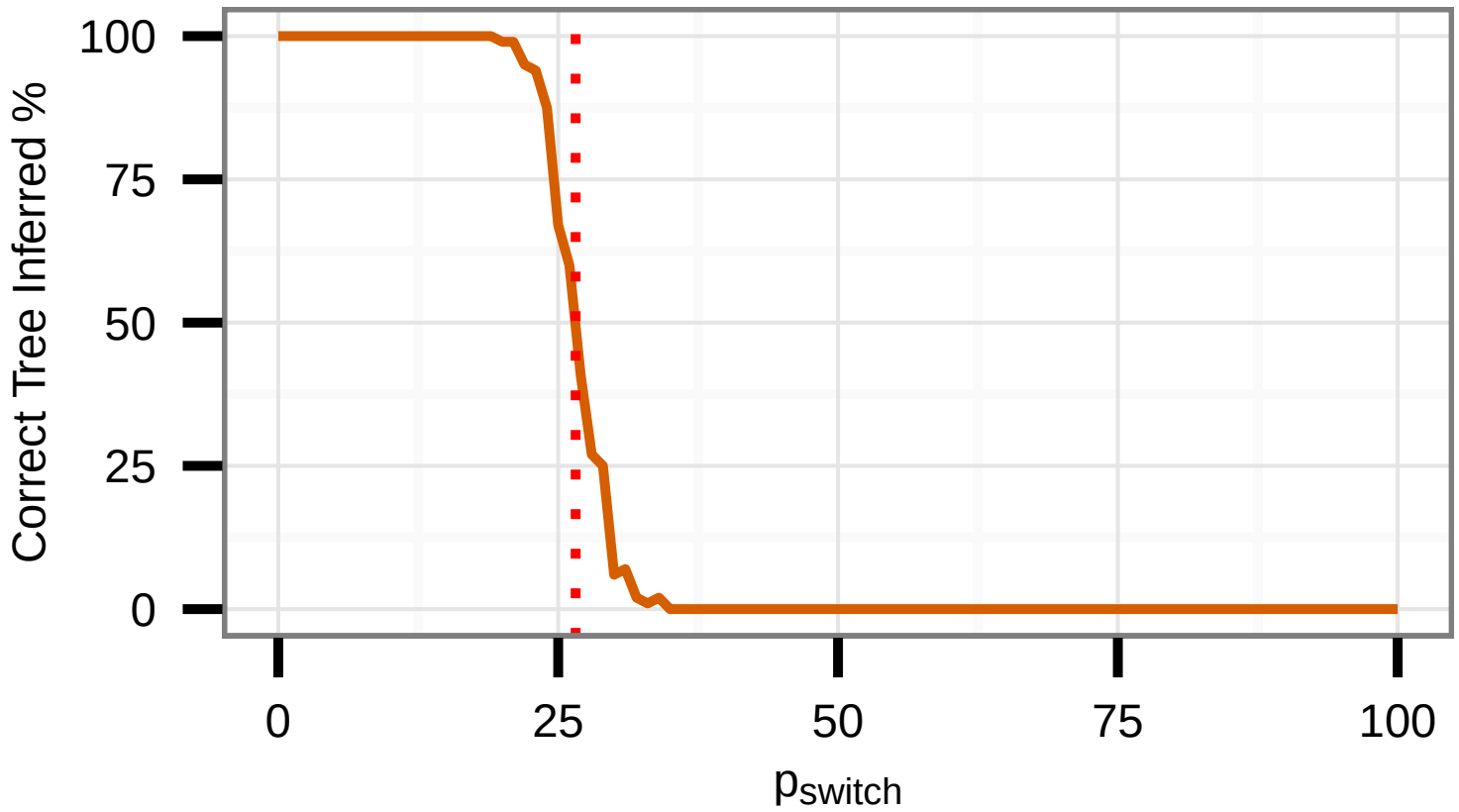
100 replications

Maximum Parsimony

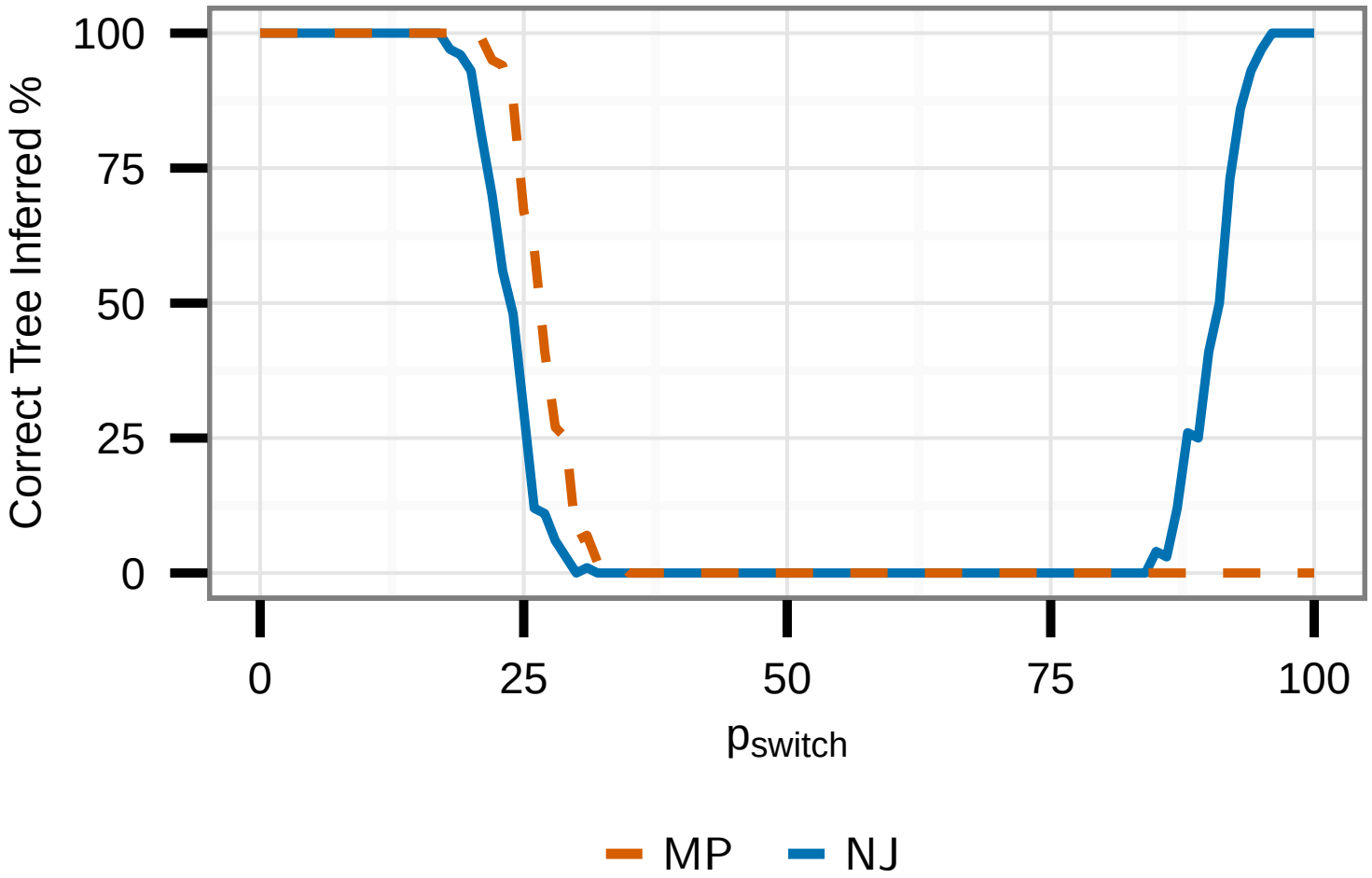


Maximum Parsimony

- Site pattern analysis predicts the asymptotic failure point of MP to be 26.56%.



Neighbour Joining



Neighbour Joining - why the recovery?

The neighbour joining algorithm

$r =$ number of taxa.

$D_{ij} =$ JC distance between taxa i and j.

$Q_{ij} = (r-2)D_{ij} - \sum_{k=1}^{r} D_{ik} - \sum_{k=1}^{r} D_{jk}$

Q is the matrix used by the NJ algorithm: the pair of taxa with the smallest Q_{ij} are joined together and the process is repeated.

The Q matrix for a 4-taxa tree

$$\begin{aligned} Q_{AB} &= (4-2)D_{AB} - \sum_{k\in\{B,C,D\}} D_{Ak} - \sum_{k\in\{A,C,D\}} D_{Bk} \\ &= -(D_{AC} + D_{AD} + D_{BC} + D_{BD}) \end{aligned}$$

Similarly,

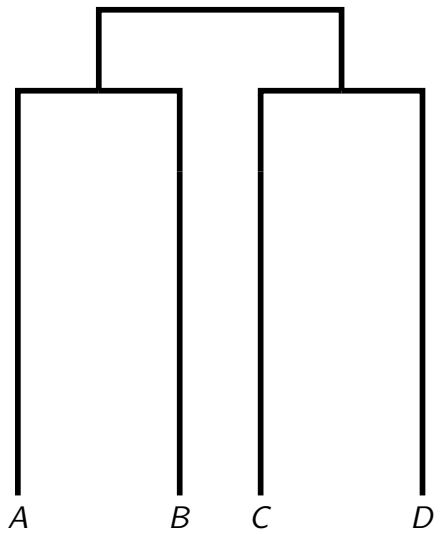
$$Q_{AD} = -(D_{AB} + D_{AC} + D_{BD} + D_{CD})$$

and,

$$Q_{AC} = -(D_{AB} + D_{AD} + D_{BC} + D_{CD})$$

Digression - what tree might we infer?

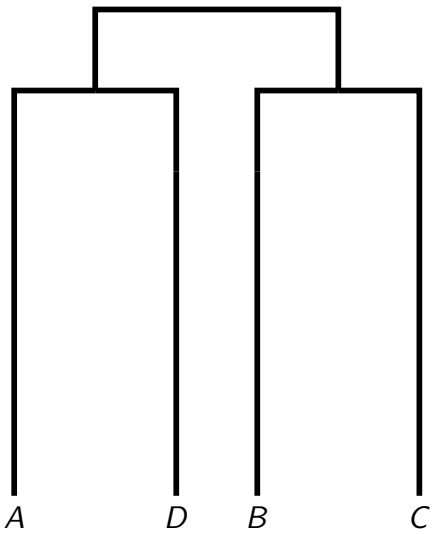
AB|CD



$min(Q_{AB}, Q_{AD}, Q_{AC}) = Q_{AB}$

$\Longrightarrow$ ✔

AD|BC



$min(Q_{AB}, Q_{AD}, Q_{AC}) = Q_{AD}$

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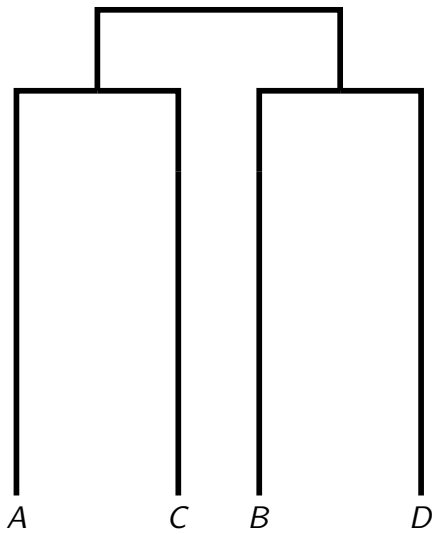
AC|BD



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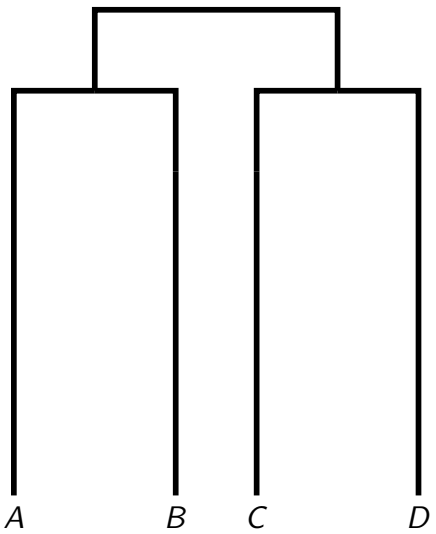
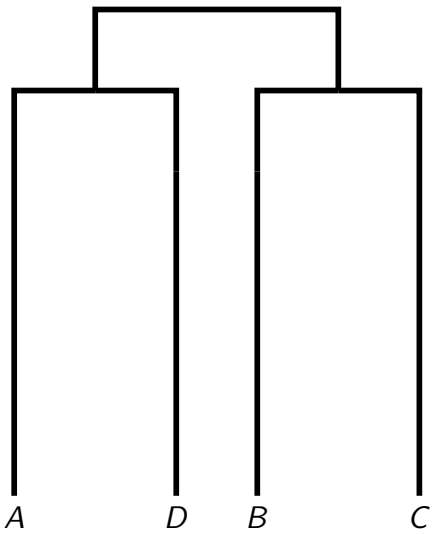


$Q_{AB} < Q_{AD}$

$\Longrightarrow$ ✔

AD|BC



$Q_{AD} < Q_{AB}$

$\Longrightarrow$ ✘

The Q matrix for a 4-taxa tree

The correct tree (AB|CD) will be inferred given the condition:

$$\begin{aligned} & Q_{AB} < Q_{AD} \\ \Longrightarrow \quad & 0 < Q_{AD} - Q_{AB} \\ \Longrightarrow \quad & 0 < D_{AD} + D_{BC} - D_{AB} - D_{CD} \end{aligned}$$

We now define

$$C = D_{AD} + D_{BC} - D_{AB} - D_{CD}$$

so that the correct tree will be inferred when $C > 0$.

Deriving the expected value of C

T = the tree topology

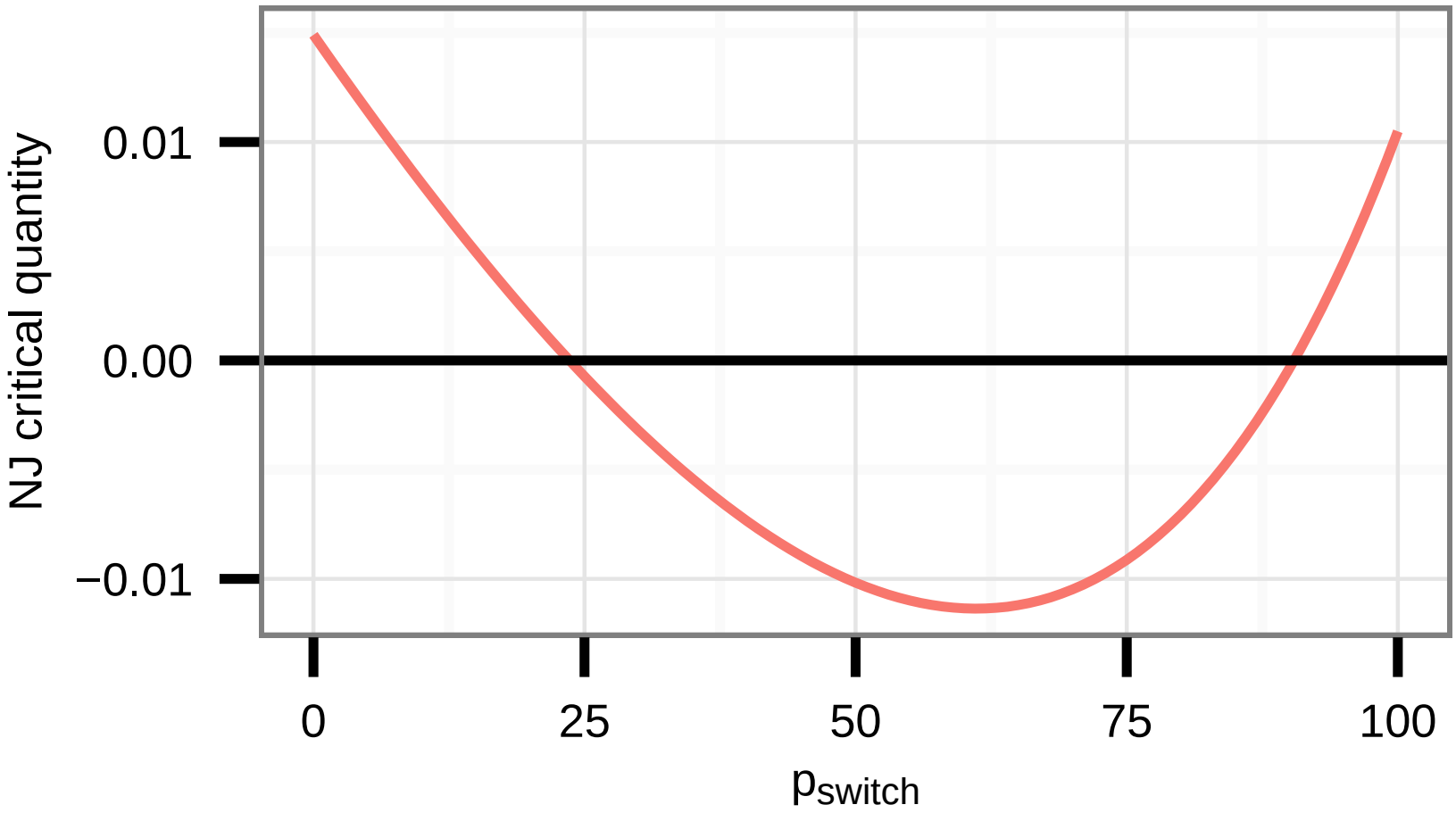
P_{ij} = the proportion of differing sites between taxa i and j

$$E[P_{ij}] = f(p_{switch}, T)$$

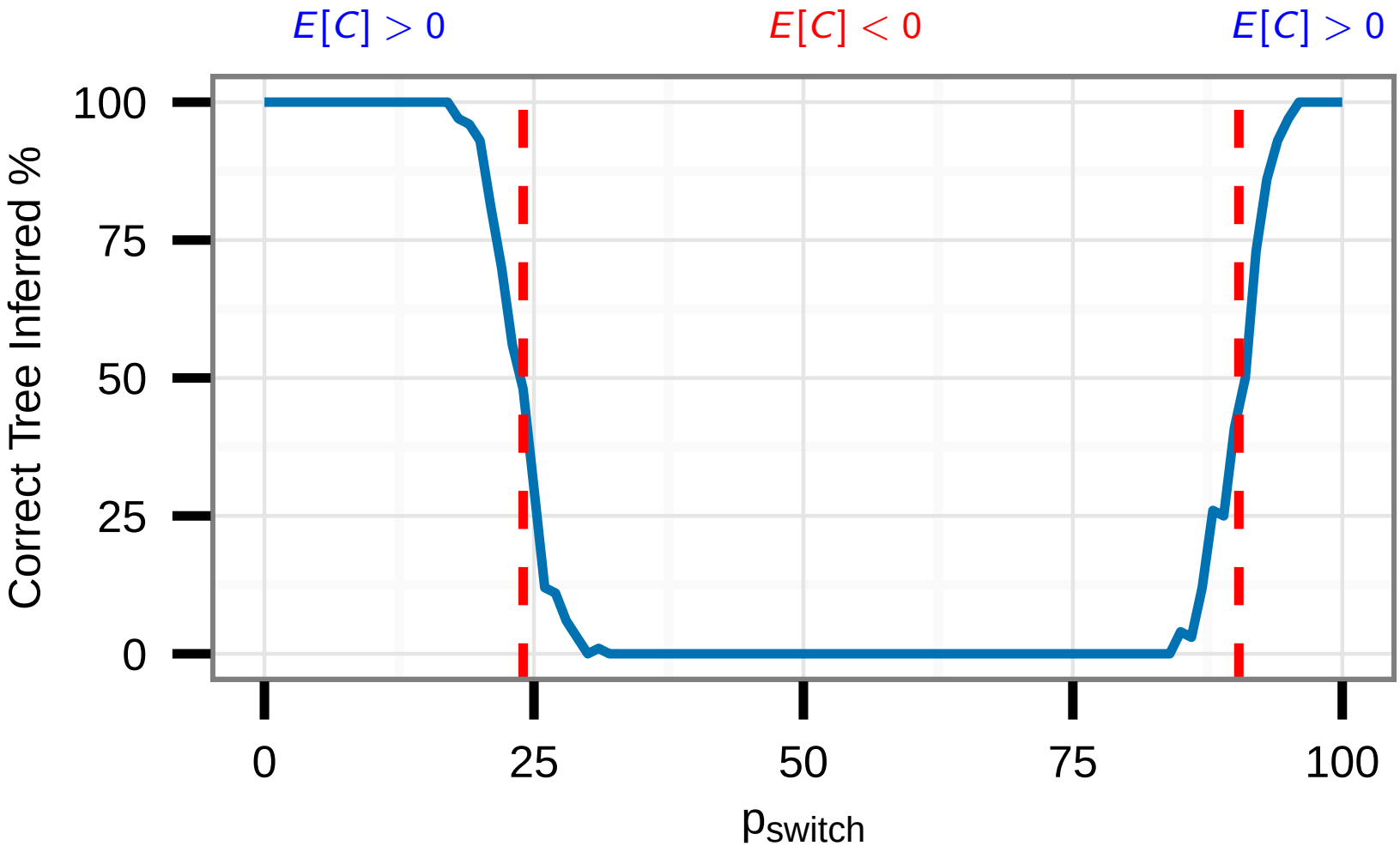
$$E[D_{ij}] = -\frac{3}{4} ln(1 - \frac{4}{3} E[P_{ij}])$$

$$E[C] = E[D_{AD}] + E[D_{BC}] - E[D_{AB}] - E[D_{CD}]$$

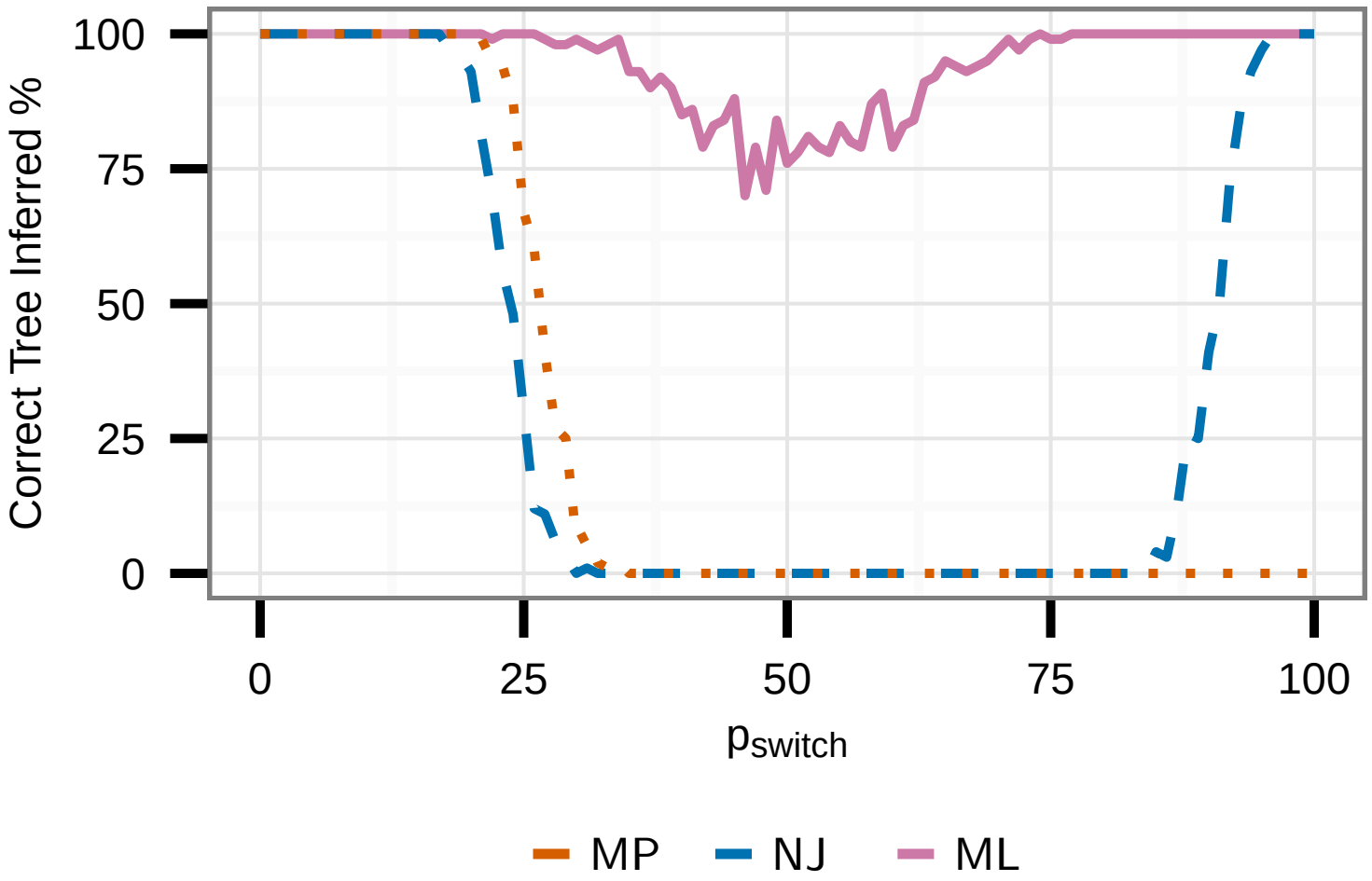
Expected value of C



Neighbour Joining



Maximum Likelihood



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- Traditional methods of phylogenetic inference may be compromised by SSRH.
- Diagnostic tools need to be developed to help identify the presence and extent of SSRH in sequence data.
- Data driven model checking will be the focus of my PhD going forward.

Acknowledgements

I would like to thank my supervisory team for their input and guidance:

- Prof. Nigel Bean - University of Adelaide
- Dr Lars Jermiin - CSIRO
- Dr Barbara Holland - University of Tasmania
- Dr Jono Tuke - University of Adelaide

That's all folks!

Questions?

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$$Q_{AB} - Q_{AC} = D_{AB} + D_{CD} - D_{AC} - D_{BD}$$

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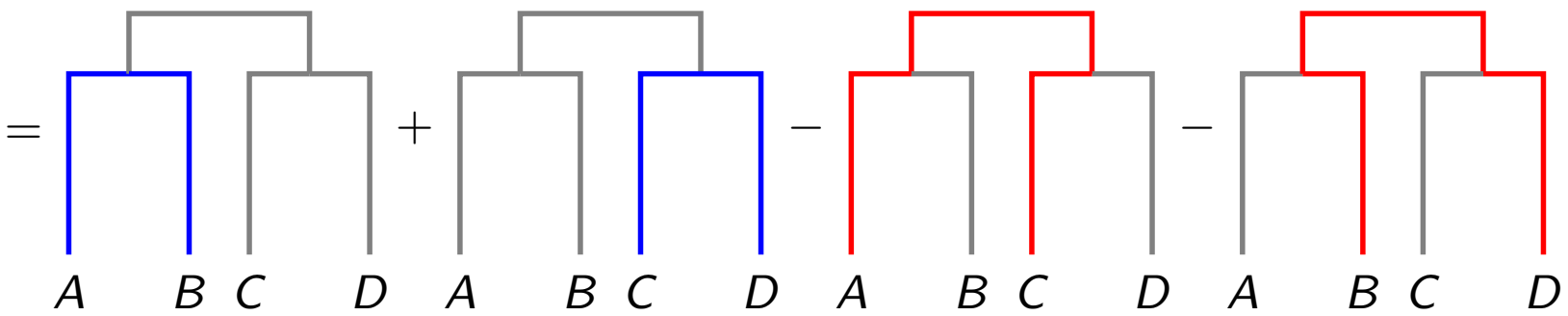

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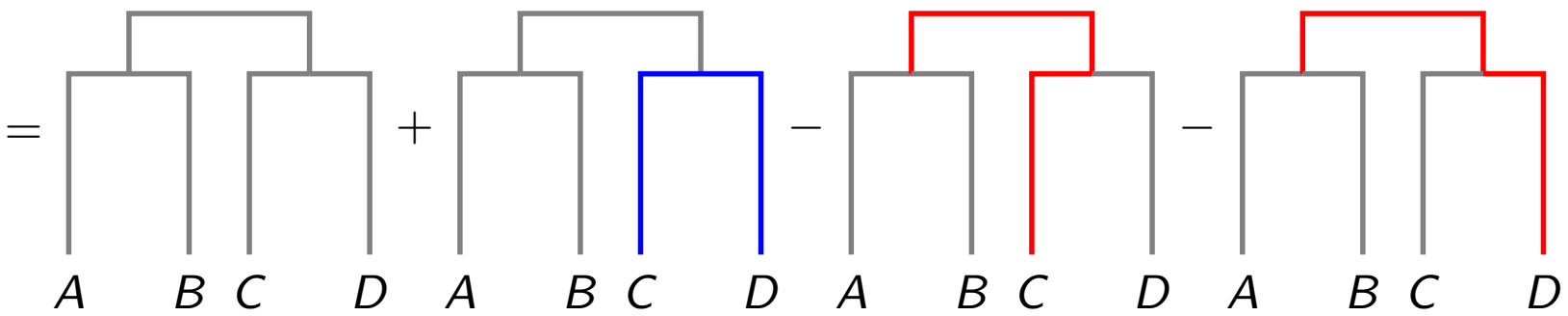

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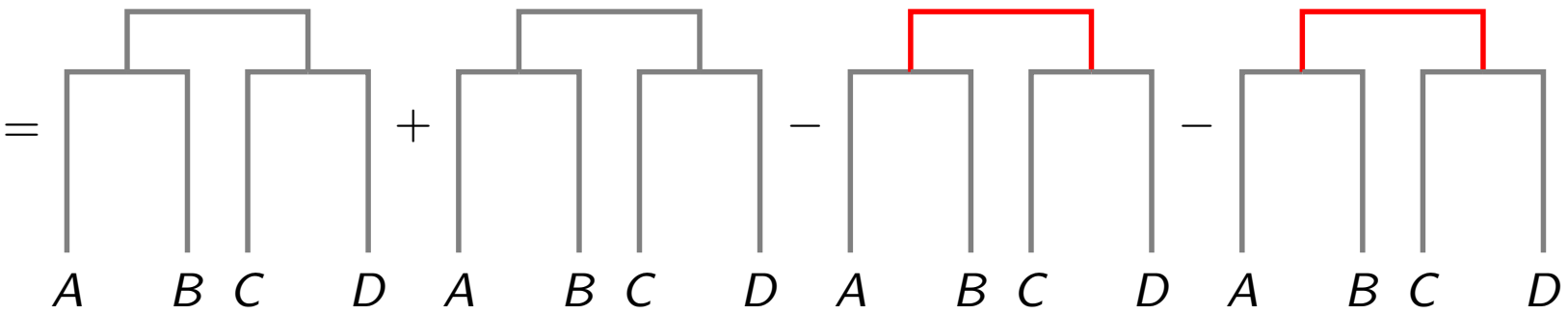

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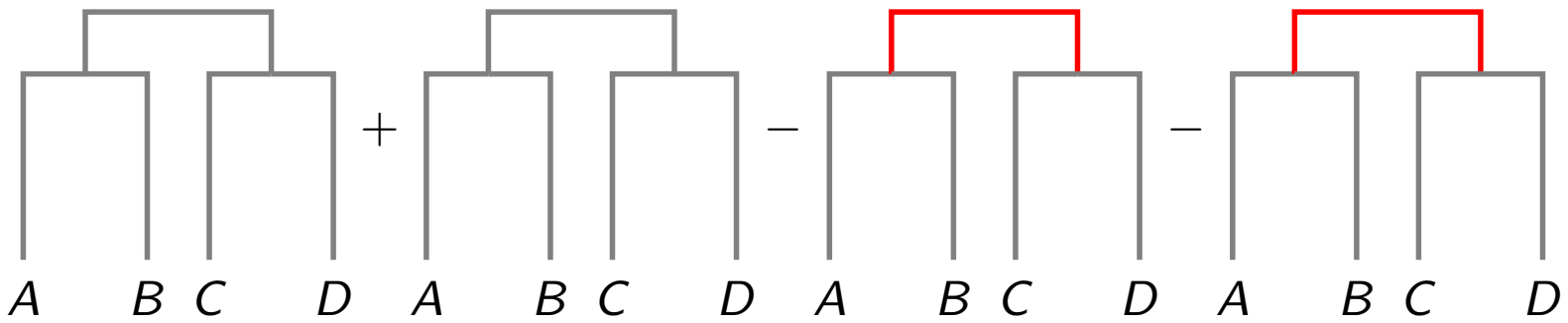
$$=$$ 

$$= -$$  $$-$$ 

$$\leq 0$$

How was the MP crash point derived? I'm glad you asked!

Site Pattern	Correct Tree	Incorrect Tree
xxxx	0	0
xxxy	1	1
xxyx	1	1
xyxx	1	1
yxxx	1	1
xxyy	1	2
xyyx	2	1
xyxy	2	2
xxyz	2	2
xyzx	2	2
xyxz	2	2
yxxz	2	2
yxzx	2	2
yzxx	2	2
wxyz	3	3

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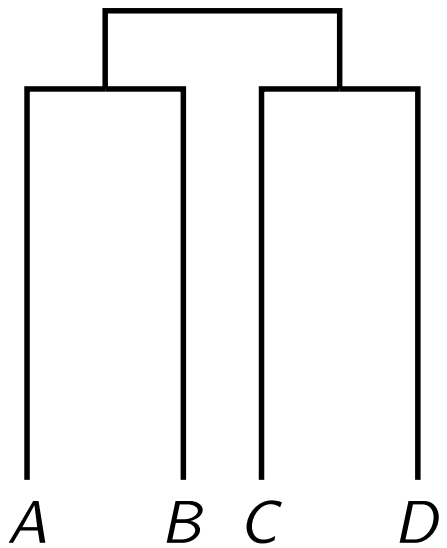
Consider site pattern *xxyy*:



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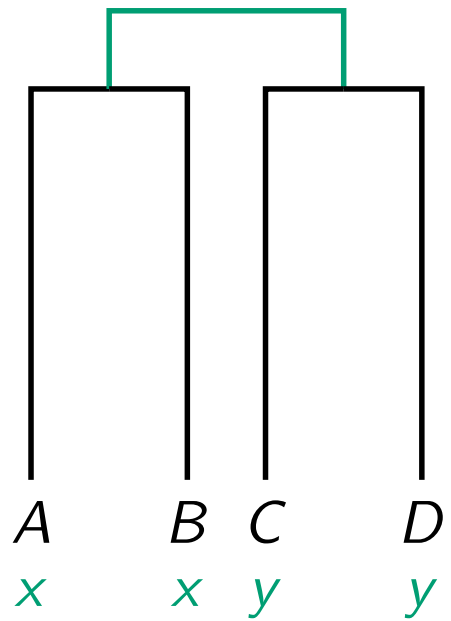

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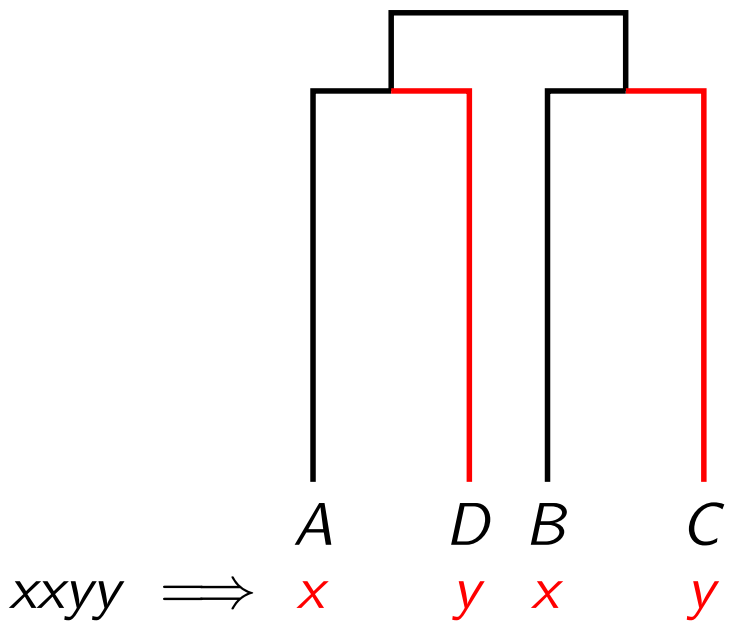

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$$P(xxyy) = f(T)$$

$$P(xyyx) = g(p_{switch}, T)$$

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The failure point of MP is given

by finding p_{switch} such that:

$$P(xxyy) = P(xyyx)$$

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