
Introduction to Phylogenetics

Part 2

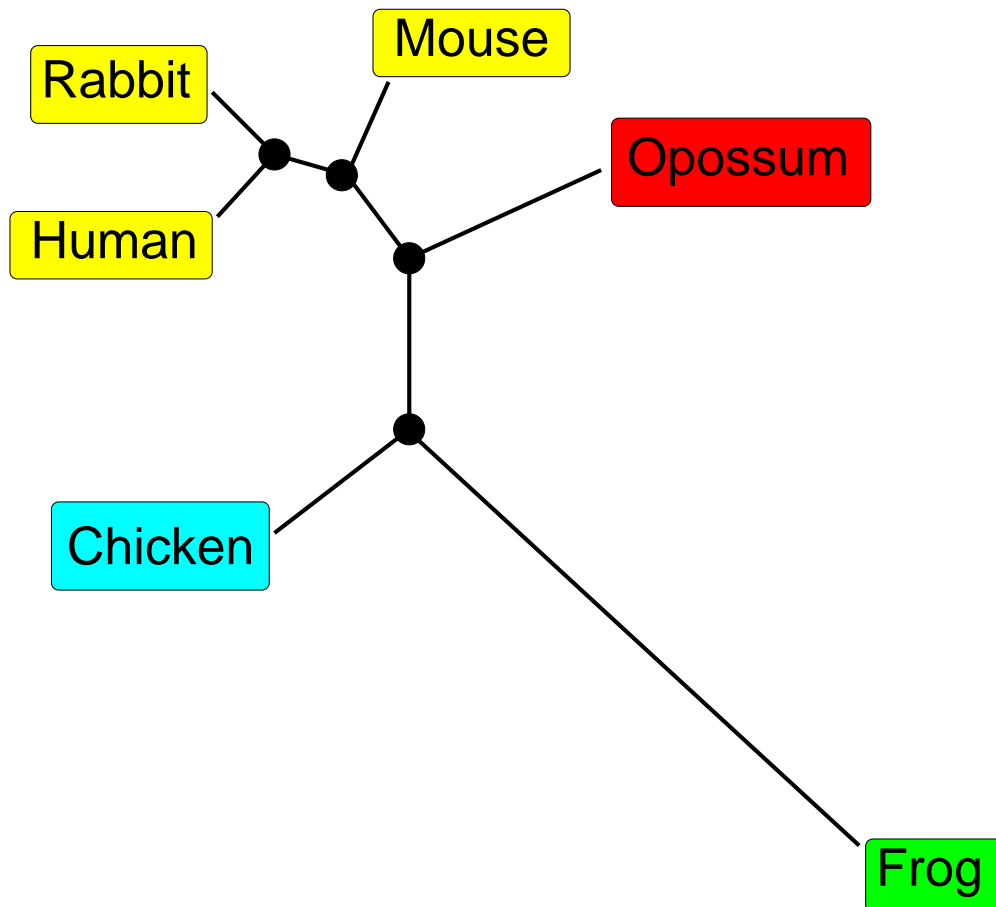
Dirk Husmeier

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Invergowrie, Dundee DD2 5DA, UK

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<http://www.bioss.ac.uk/~dirk>

Phylogenetic tree

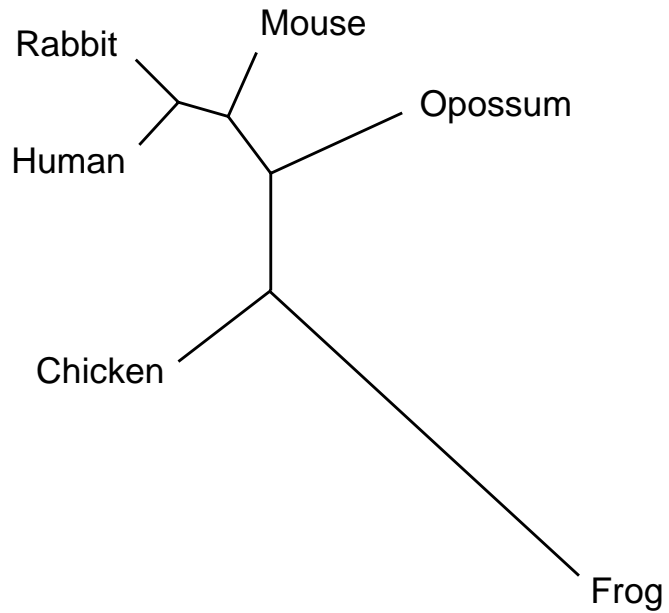


--> Topology

--> Branch lengths

Probabilistic models of evolution

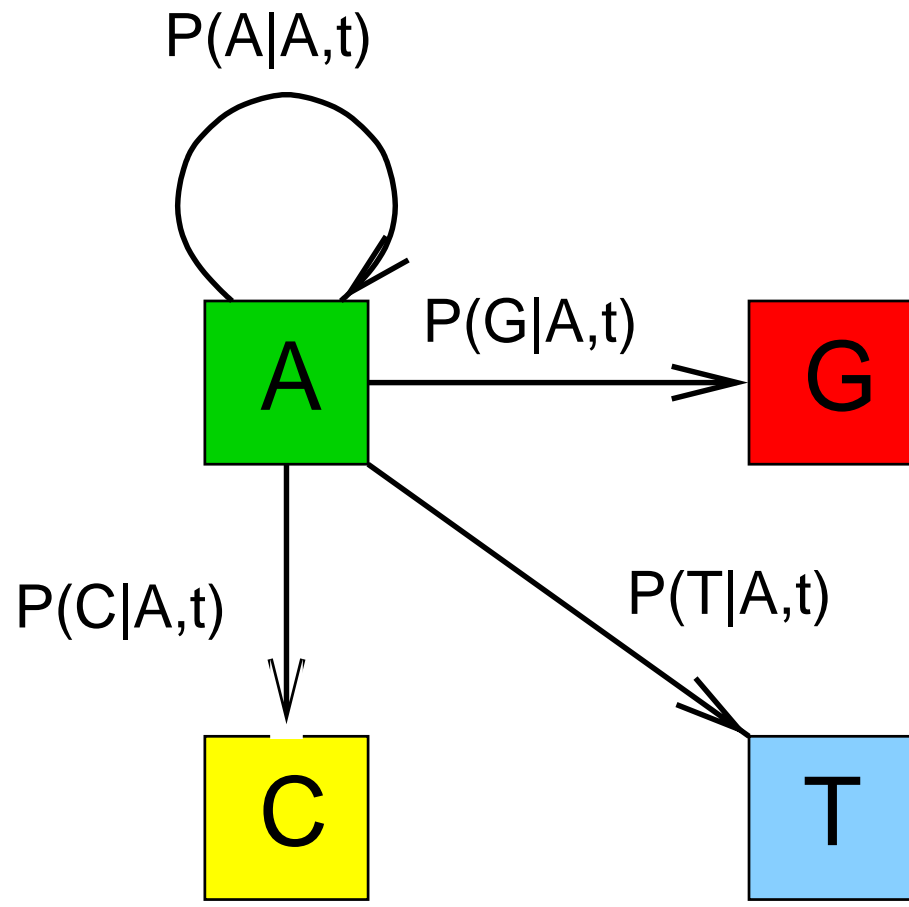
Frog	G	C	T	T	G	A	C	T	T	C	T	G	A	G	G	T	T
Chicken	G	C	G	T	A	A	C	T	T	C	A	C	A	T	G	A	T
Human	G	C	G	T	C	A	C	T	T	G	A	G	A	C	G	C	T
Rabbit	G	C	G	T	C	A	C	T	T	G	A	G	A	C	G	C	T
Mouse	G	C	G	T	C	A	C	T	T	G	A	C	A	G	G	C	T
Opossum	G	C	G	T	C	A	C	T	T	G	A	G	A	C	G	C	T



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--> Branch lengths

Mutation probabilities



Markov model of evolution

$$\mathbf{P}(t) = \begin{bmatrix} P(y(t) = A|y(0) = A) & P(y(t) = A|y(0) = G) & \dots \\ P(y(t) = G|y(0) = A) & P(y(t) = G|y(0) = G) & \dots \\ P(y(t) = C|y(0) = A) & P(y(t) = C|y(0) = G) & \dots \\ P(y(t) = T|y(0) = A) & P(y(t) = T|y(0) = G) & \dots \end{bmatrix}$$

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$$P[y(t + \Delta t)|y(t), y(t - \Delta t), \dots] = P[y(t + \Delta t)|y(t)]$$

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- The Markov process is the **same for all positions**
- Substitutions at different positions are **independent** of each other:

$$P[(y_1(t), \dots, y_N(t)|y_1(0), \dots, y_N(0))] = \prod_{i=1}^N P[y_i(t)|y_i(0)]$$

Transition Rates

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Transition Rates

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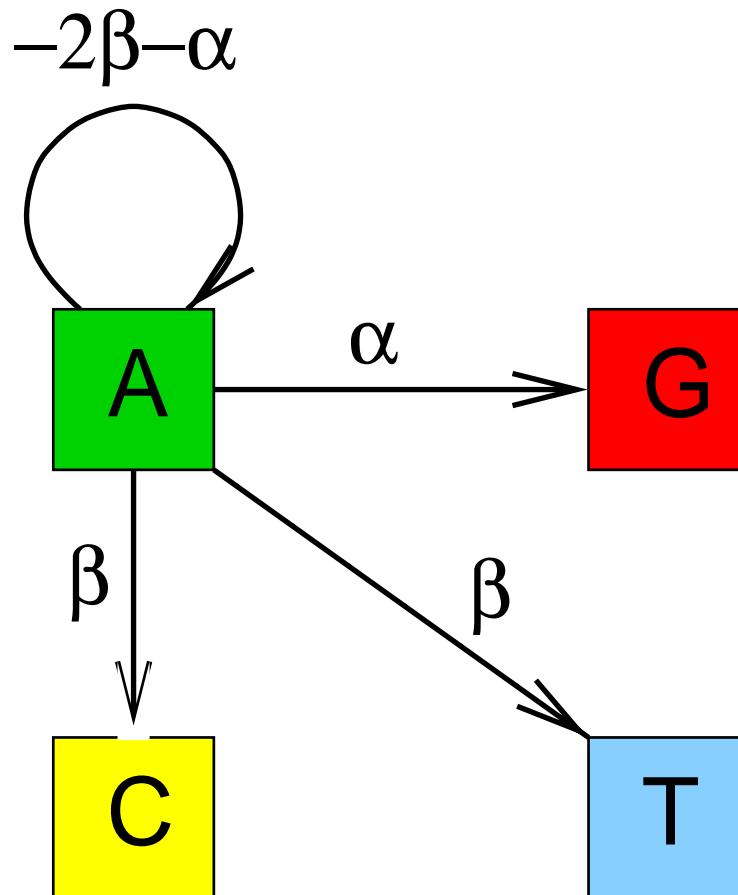
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$$\frac{d\mathbf{P}}{dt} = \mathbf{R}\mathbf{P} \implies \mathbf{P}(t) = e^{\mathbf{R}t}$$

$$\mathbf{R} = \begin{bmatrix} -2\beta - \alpha & \beta & \alpha & \beta \\ \beta & -2\beta - \alpha & \beta & \alpha \\ \alpha & \beta & -2\beta - \alpha & \beta \\ \beta & \alpha & \beta & -2\beta - \alpha \end{bmatrix}$$

Transition Rates



Transition Probabilities

$$\mathbf{P}(t) = e^{\mathbf{R}t} = \begin{bmatrix} d(t) & f(t) & g(t) & f(t) \\ f(t) & d(t) & f(t) & g(t) \\ g(t) & f(t) & d(t) & f(t) \\ f(t) & g(t) & f(t) & d(t) \end{bmatrix}$$

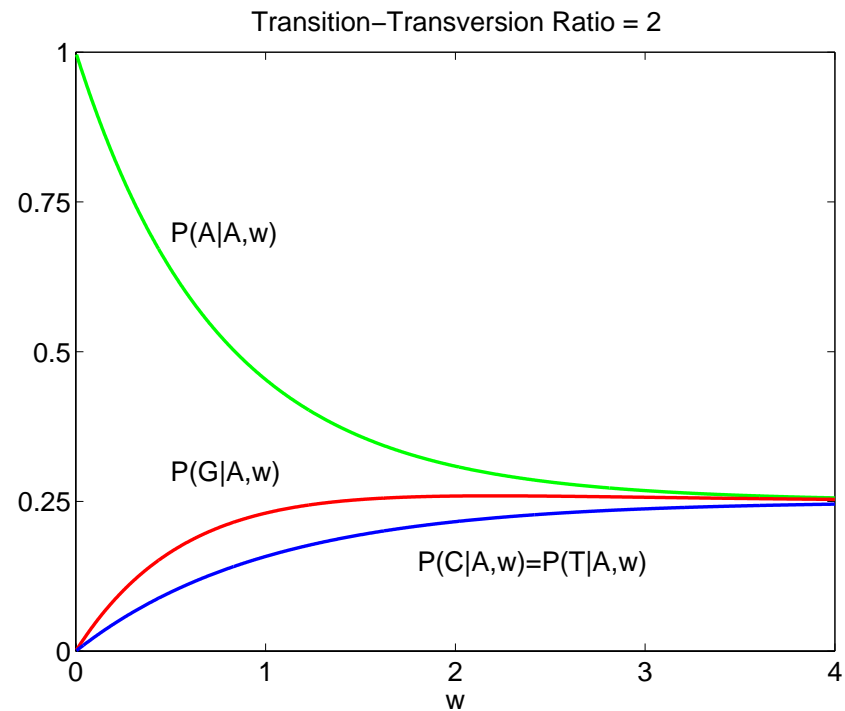
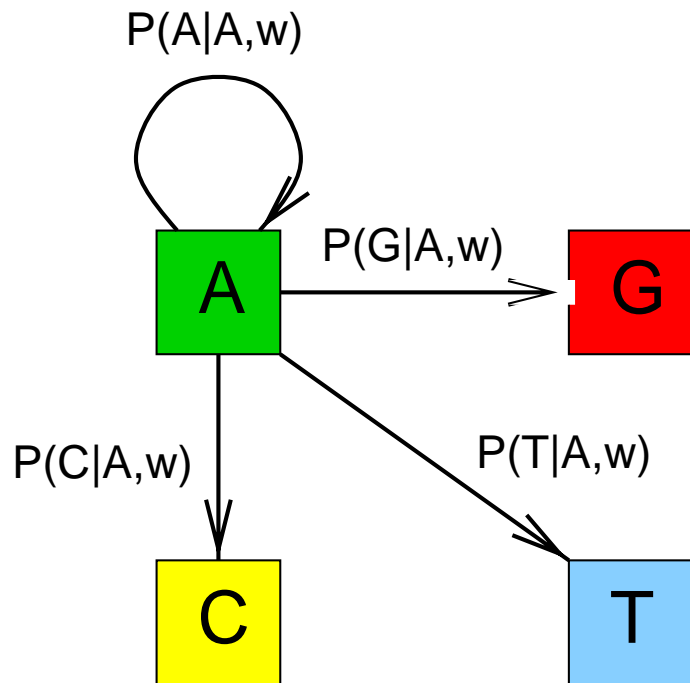
$$f(t) = \frac{1}{4}(1 - e^{-4\beta t}) \quad g(t) = \frac{1}{4}(1 + e^{-4\beta t} - 2e^{-2(\alpha+\beta)t}) \quad d(t) = 1 - 2f(t) - g(t)$$

Molecular time: $w = 4\beta t$

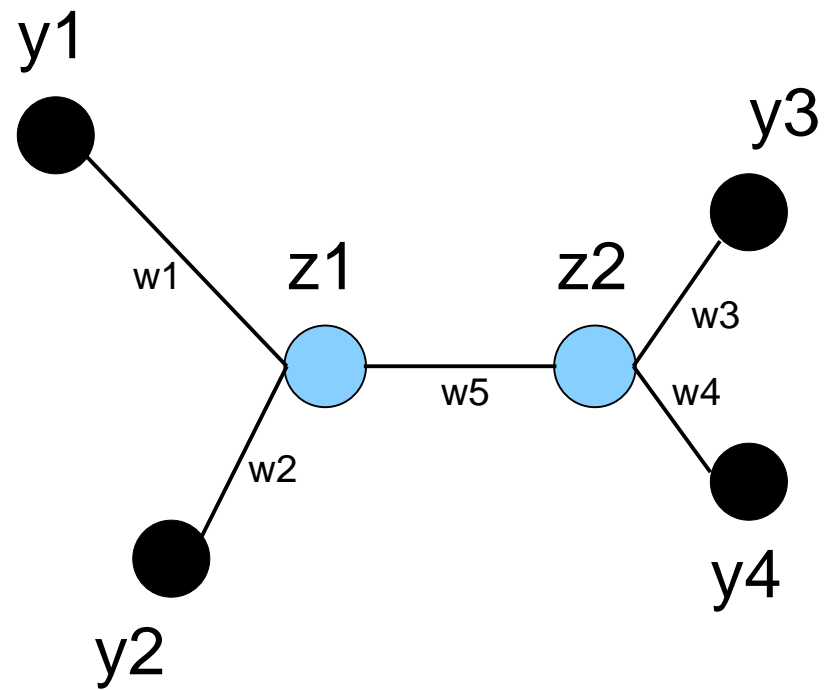
$$\begin{aligned} f(w) &= \frac{1}{4}(1 - e^{-w}) \\ g(w) &= \frac{1}{4}(1 + e^{-w} - 2e^{-\frac{\tau+1}{2}w}) \\ d(w) &= 1 - 2f(w) - g(w) \end{aligned}$$

Transition-transversion ratio: $\tau = \frac{\alpha}{\beta}$

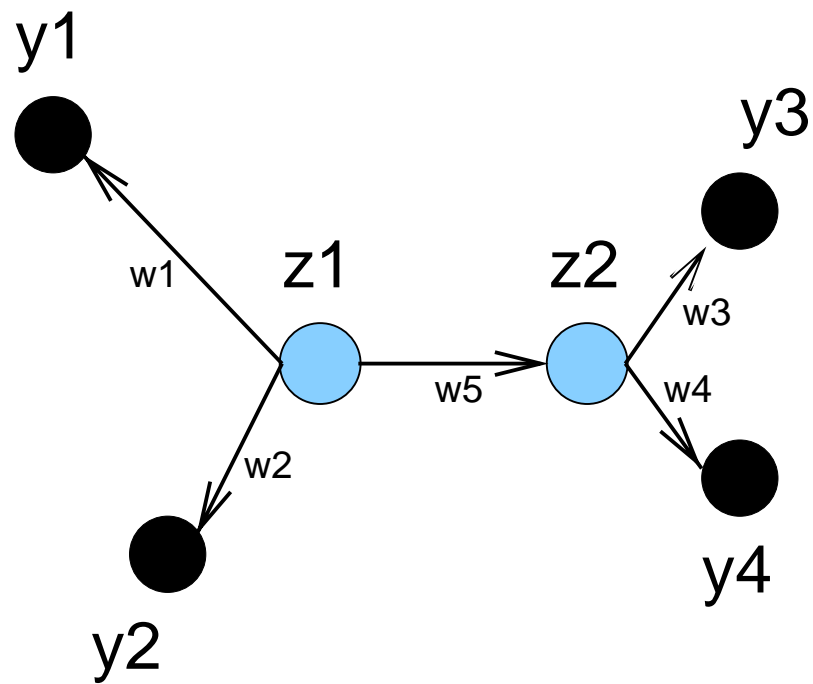
Transition probabilities



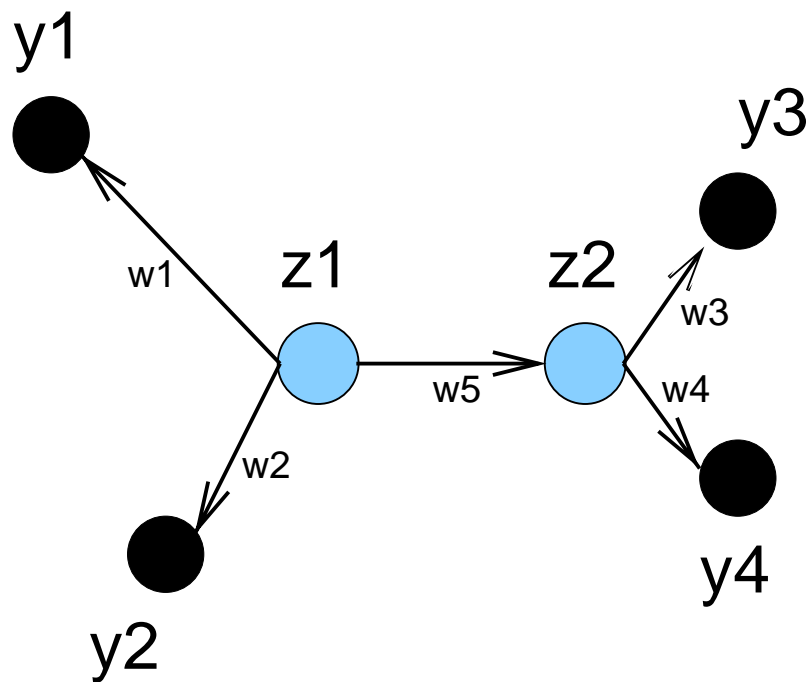
Phylogenetic tree as an undirected graph



Phylogenetic tree as a directed graph

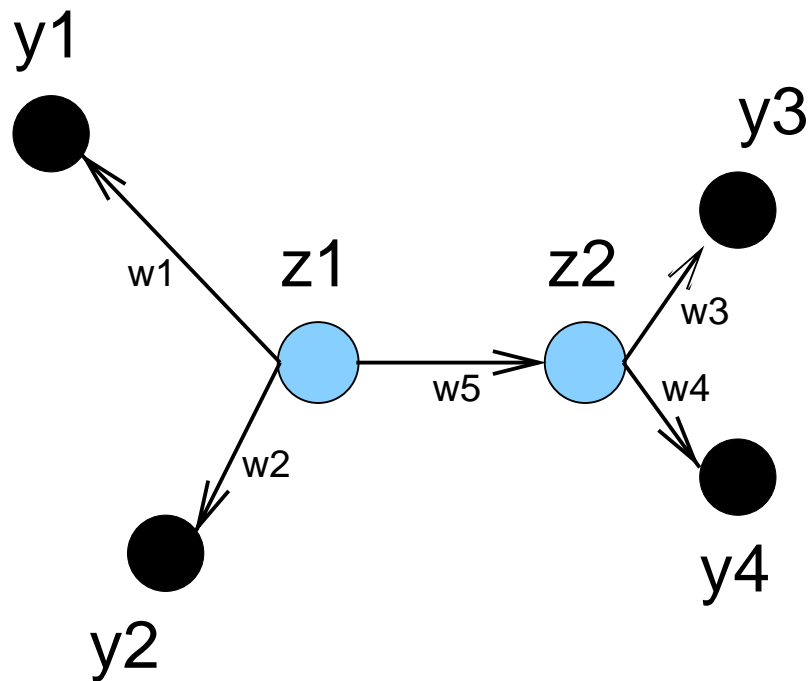


Phylogenetic tree as a directed graph



$$P(y_1, y_2, y_3, y_4, z_1, z_2 | \mathbf{w})$$

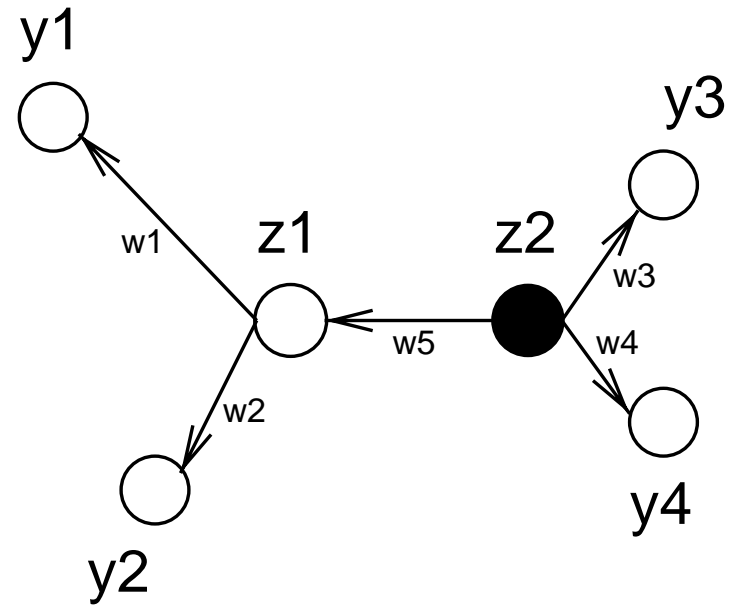
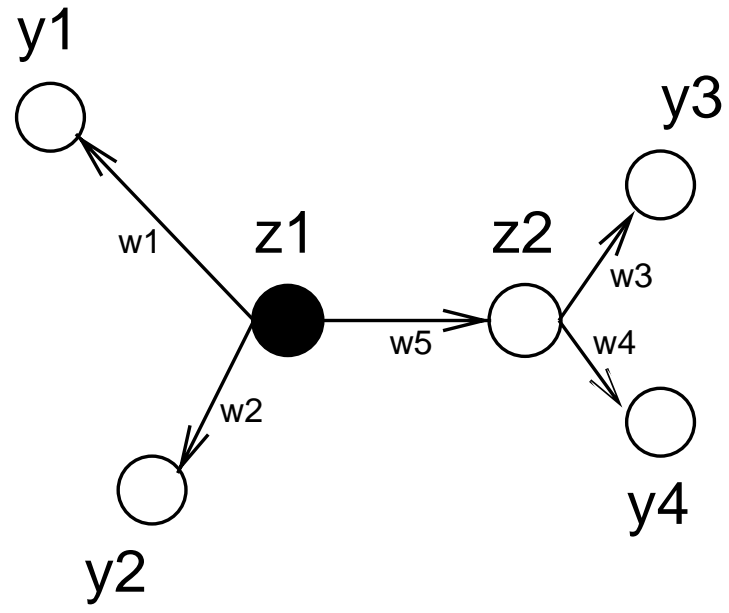
Phylogenetic tree as a directed graph



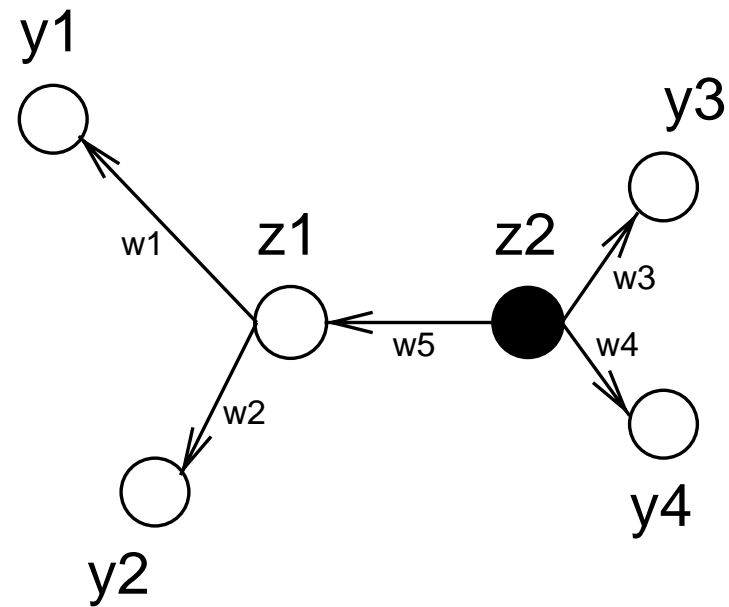
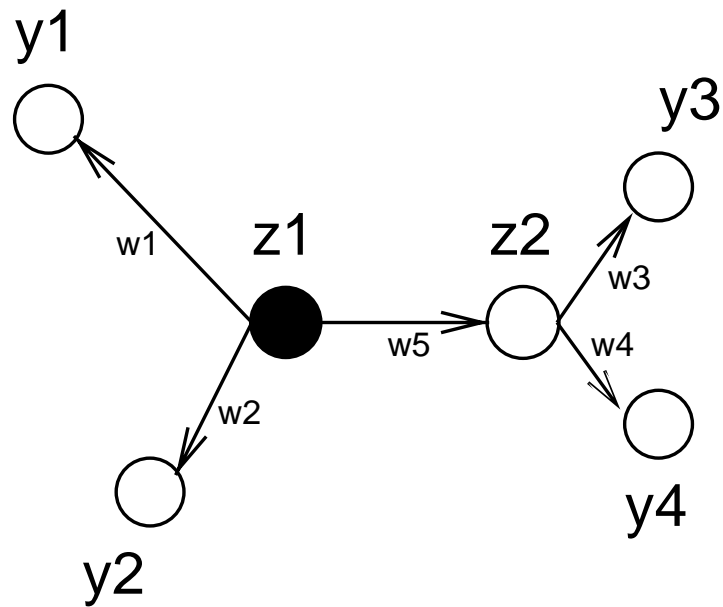
$$P(y_1, y_2, y_3, y_4, z_1, z_2 | \mathbf{w})$$

$$= P(y_1 | z_1, w_1) P(y_2 | z_1, w_2) P(z_2 | z_1, w_5) P(y_3 | z_2, w_3) P(y_4 | z_2, w_4) P(z_1)$$

Different directed graphs

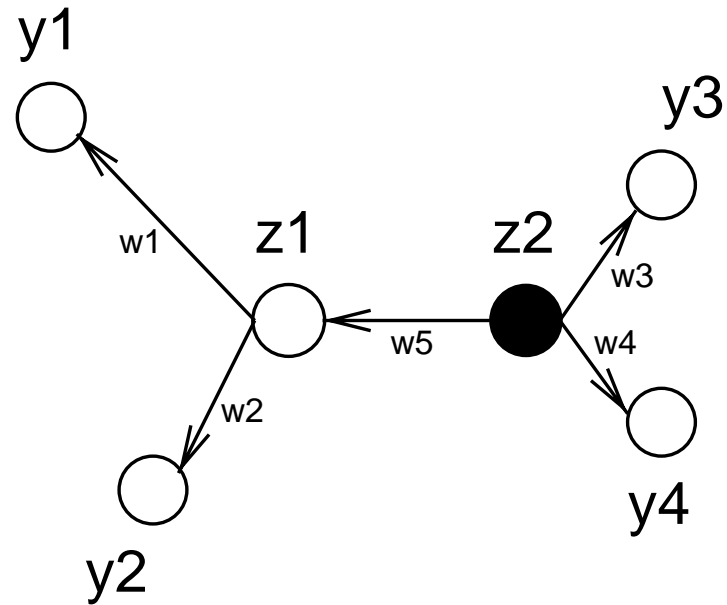
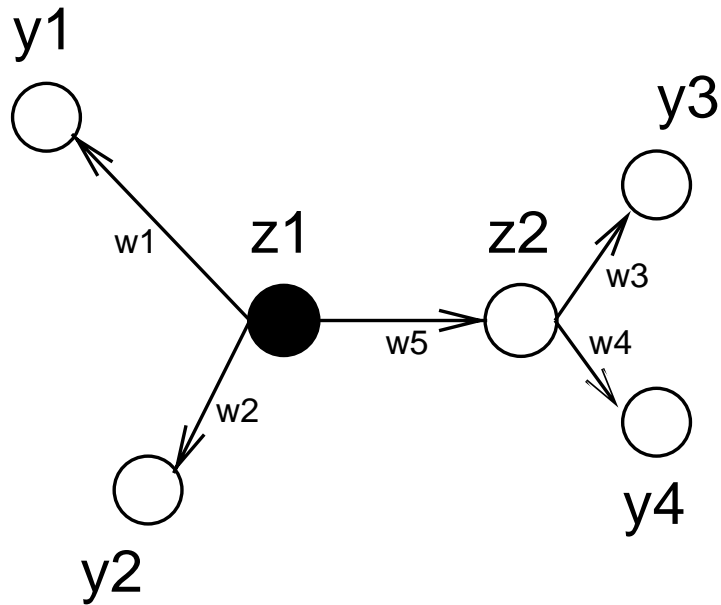


Different directed graphs



Left : $P(y_1, y_2, y_3, y_4, z_1, z_2 | \mathbf{w}) =$
 $P(y_1 | z_1, w_1) P(y_2 | z_1, w_2) P(y_3 | z_2, w_3) P(y_4 | z_2, w_4) P(z_2 | z_1, w_5) P(z_1)$

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Right : $P(y_1, y_2, y_3, y_4, z_1, z_2 | \mathbf{w}) =$
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Reversibility

We can *not* decide on the direction of evolutionary processes.

$$P(z_1|z_2, w_5)P(z_2) = P(z_2|z_1, w_5)P(z_1)$$

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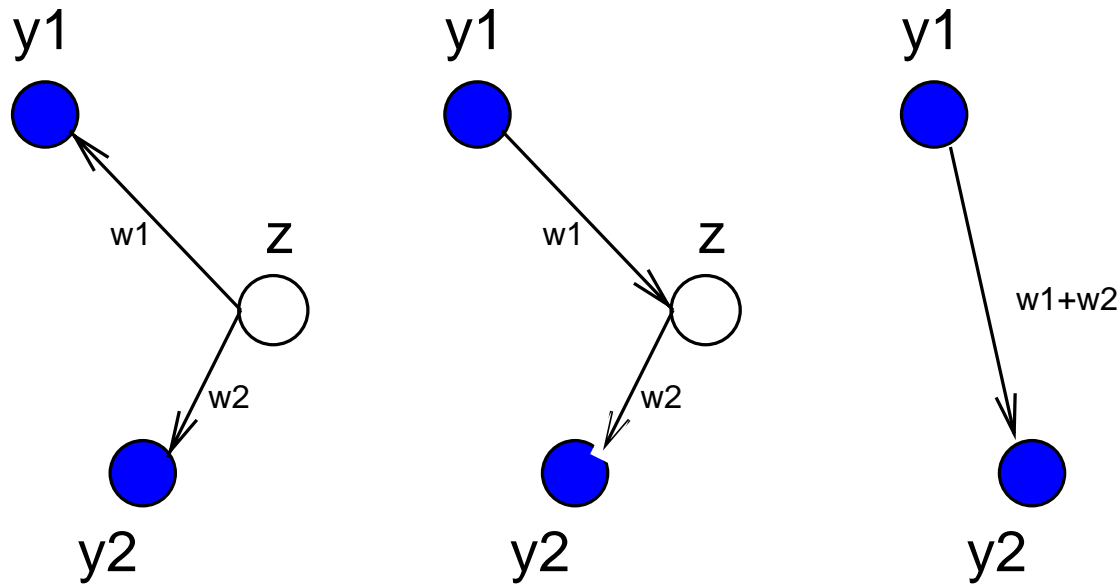
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- Changing the position of the root and the direction of the arcs does not affect the probability.
- All directed graphs are in the same equivalence class .

Root elimination

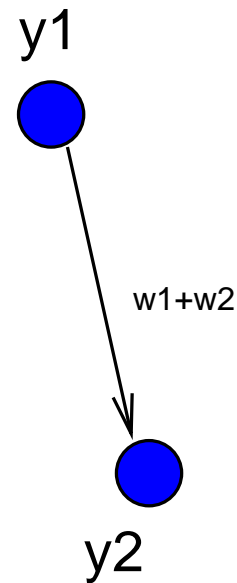
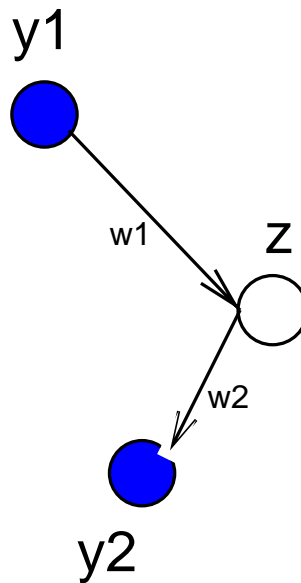
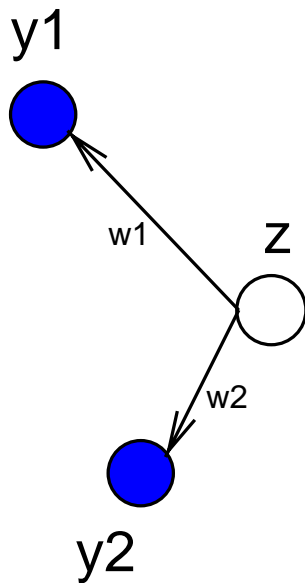
Homogeneous Markov chain \implies Multiplicativity of the substitution matrices:
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$$\sum_z P(y_2|z, w_2)P(y_1|z, w_1)P(z)$$

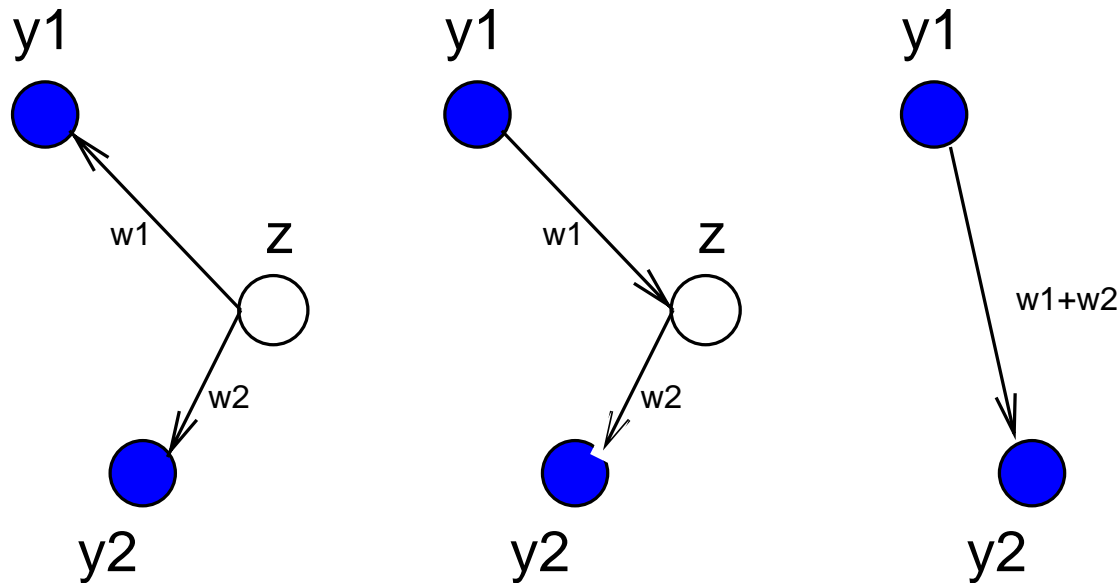
$$\sum_z P(y_2|z, w_2)P(z|y_1, w_1)P(y_1)$$

$$P(y_2|y_1, w_1+w_2)P(y_1)$$

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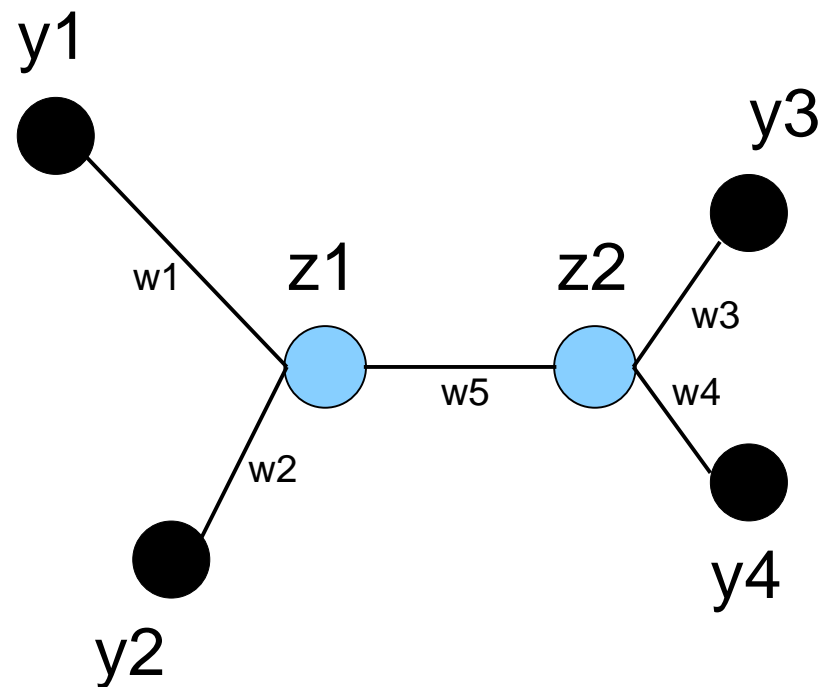


$$\sum_z P(y_2|z, w_2)P(y_1|z, w_1)P(z) \quad \sum_z P(y_2|z, w_2)P(z|y_1, w_1)P(y_1) \quad P(y_2|y_1, w_1+w_2)P(y_1)$$

Reversibility \implies left = middle

Multiplicativity \implies middle = right

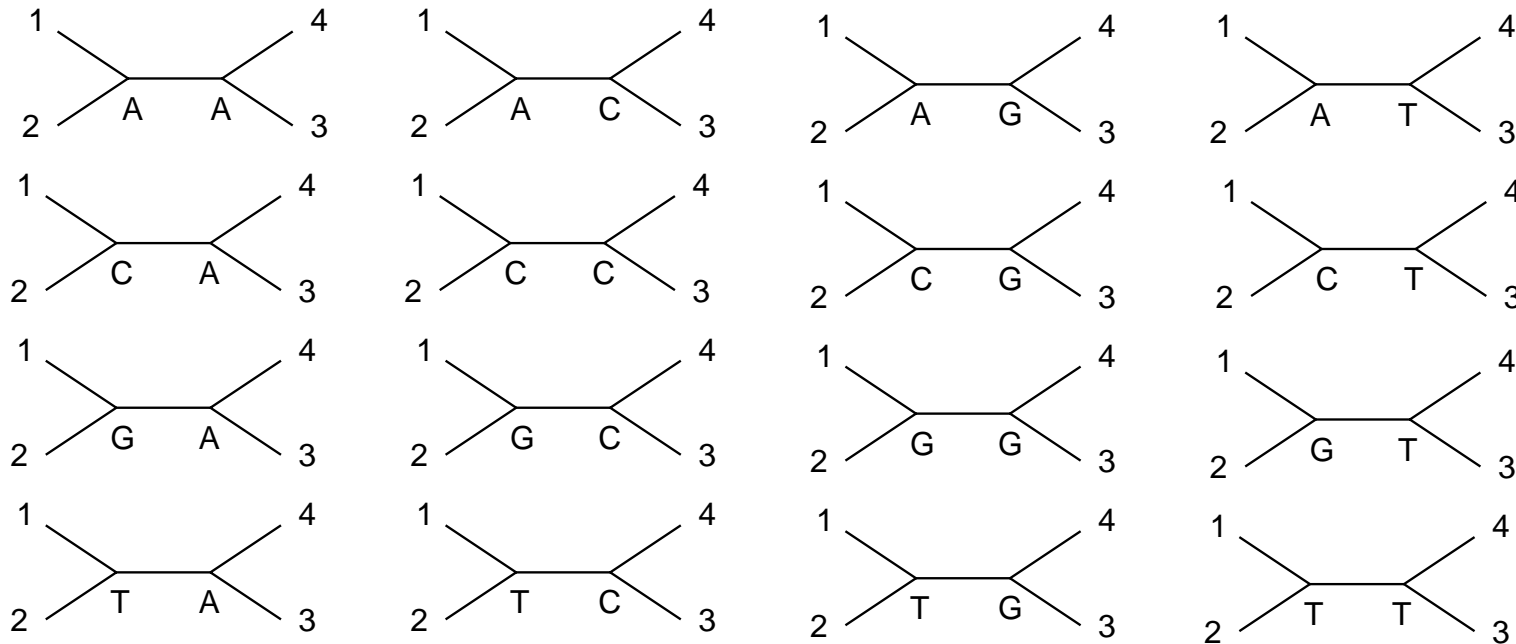
Expansion of the joint probability



$$P(y_1, y_2, y_3, y_4, z_1, z_2 | \mathbf{w})$$

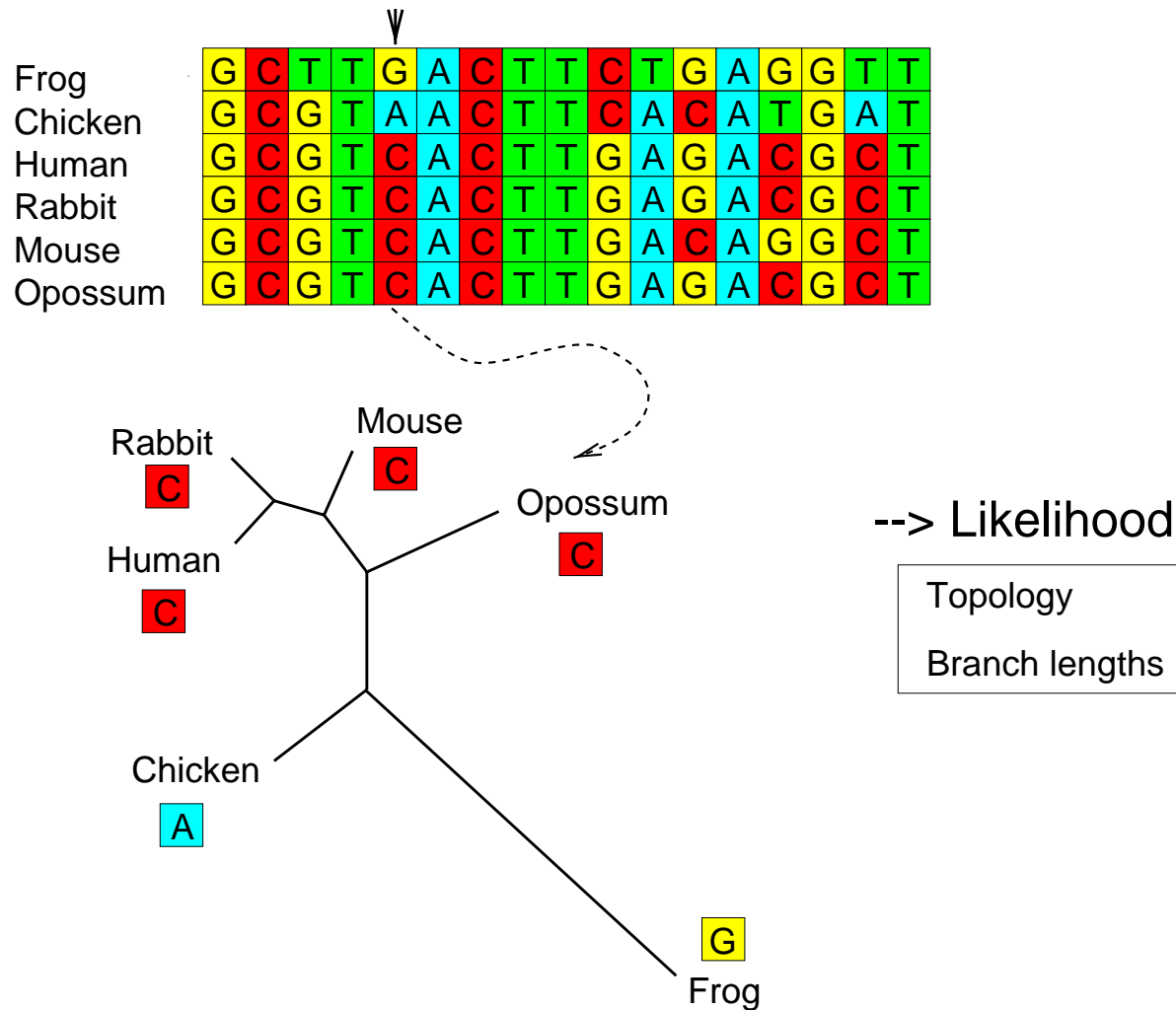
$$= P(y_1 | z_1, w_1) P(y_2 | z_1, w_2) P(z_2 | z_1, w_5) P(y_3 | z_2, w_3) P(y_4 | z_2, w_4) P(z_1)$$

Marginalisation



$$P(y_1, y_2, y_3, y_4 | \mathbf{w}) = \sum_{z_1} \sum_{z_2} P(y_1, y_2, y_3, y_4, z_1, z_2 | \mathbf{w})$$

Statistical approach to phylogenetics



Maximum likelihood

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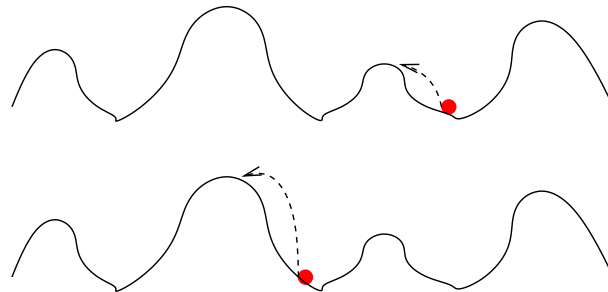


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- Repeat for different tree topologies S .



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- Heuristic search methods.

