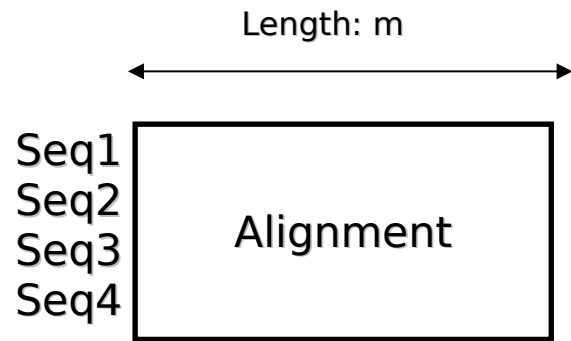


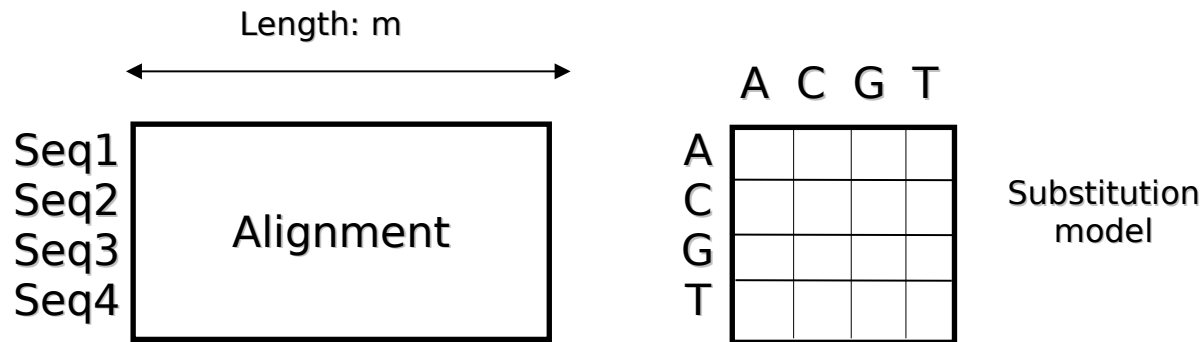
Introduction to Bioinformatics for Computer Scientists

Lecture 9c

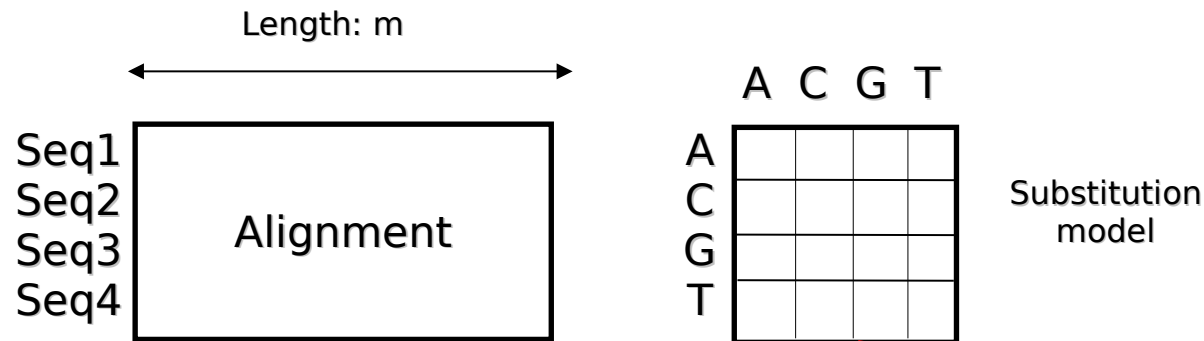
Maximum Likelihood



Maximum Likelihood

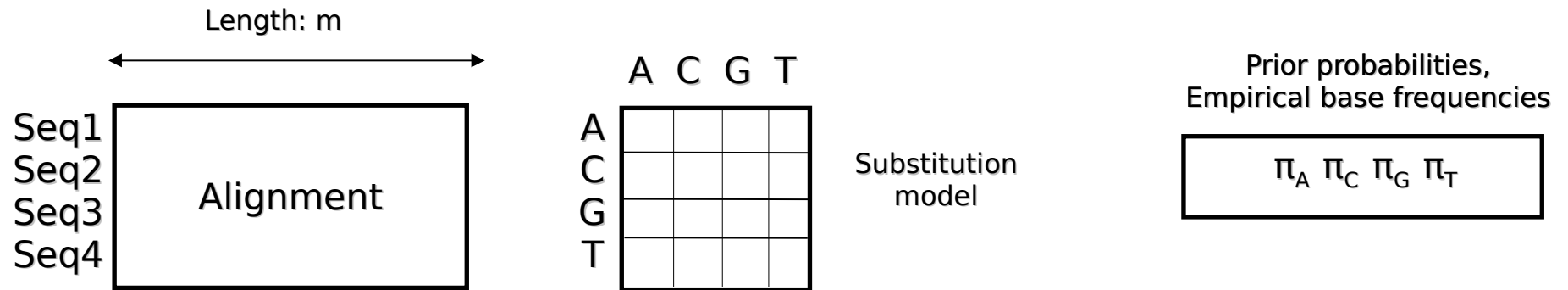


Maximum Likelihood

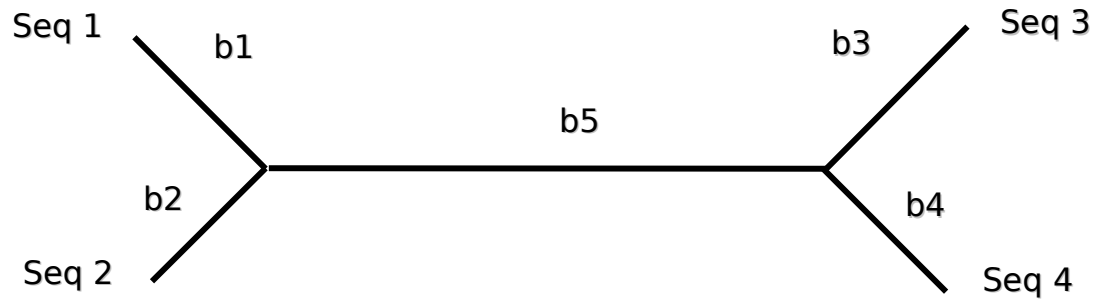
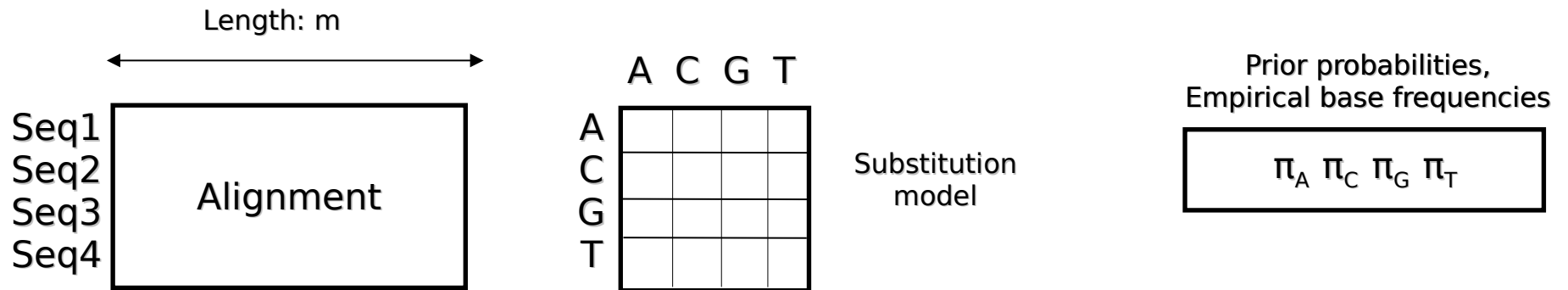


Commonly denoted as Q matrix:
transition probs for time dt , for time
 t : $P(t) = e^{Qt}$

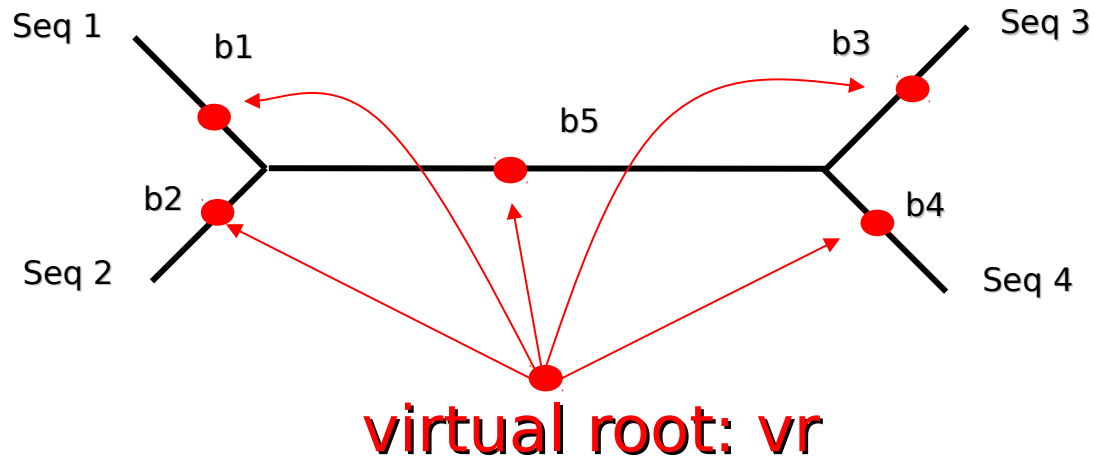
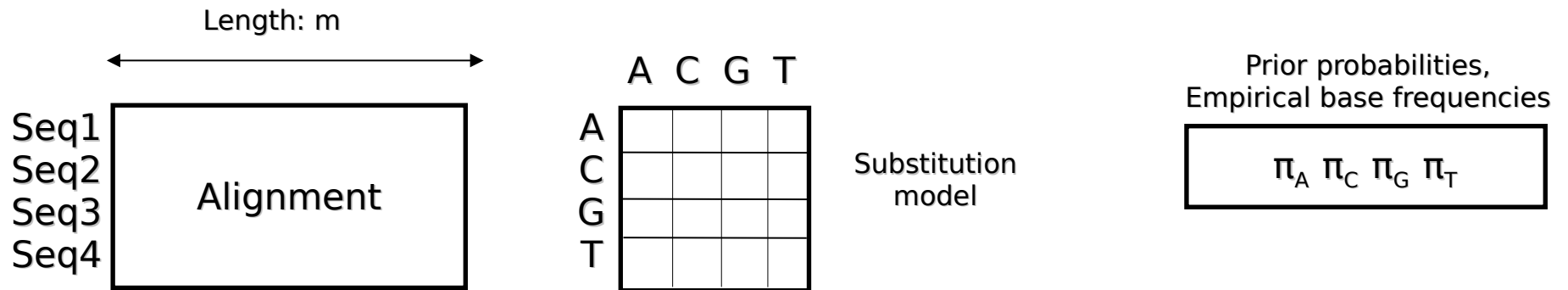
Maximum Likelihood



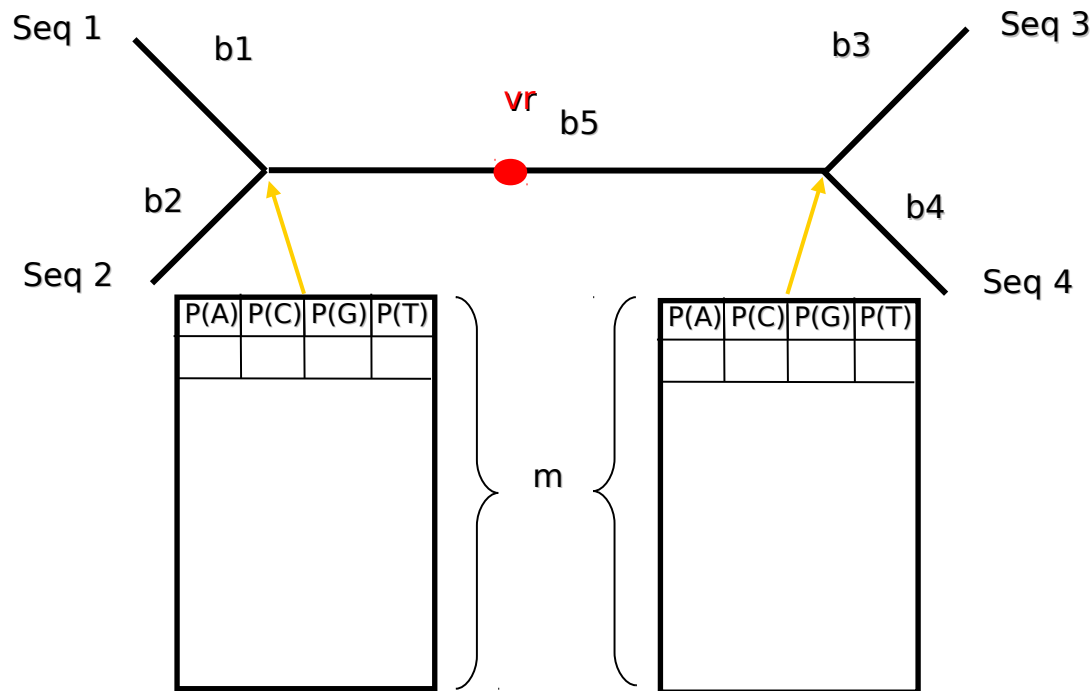
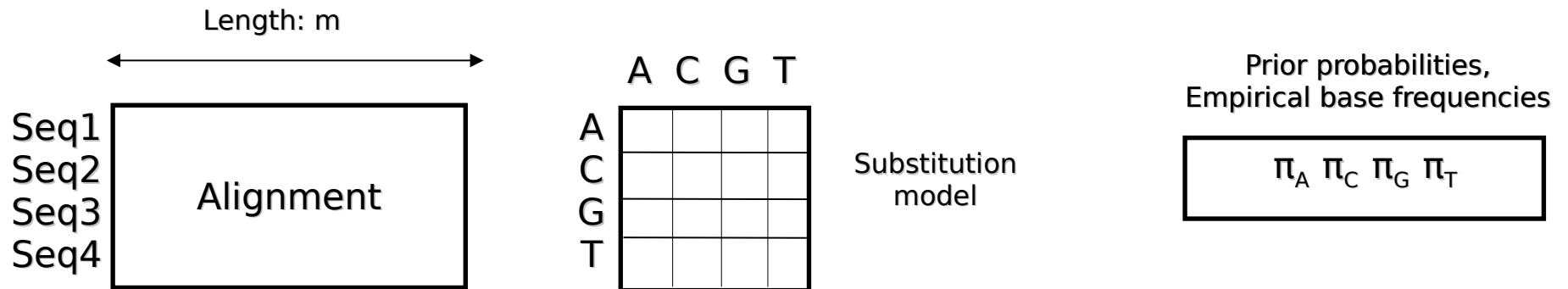
Maximum Likelihood



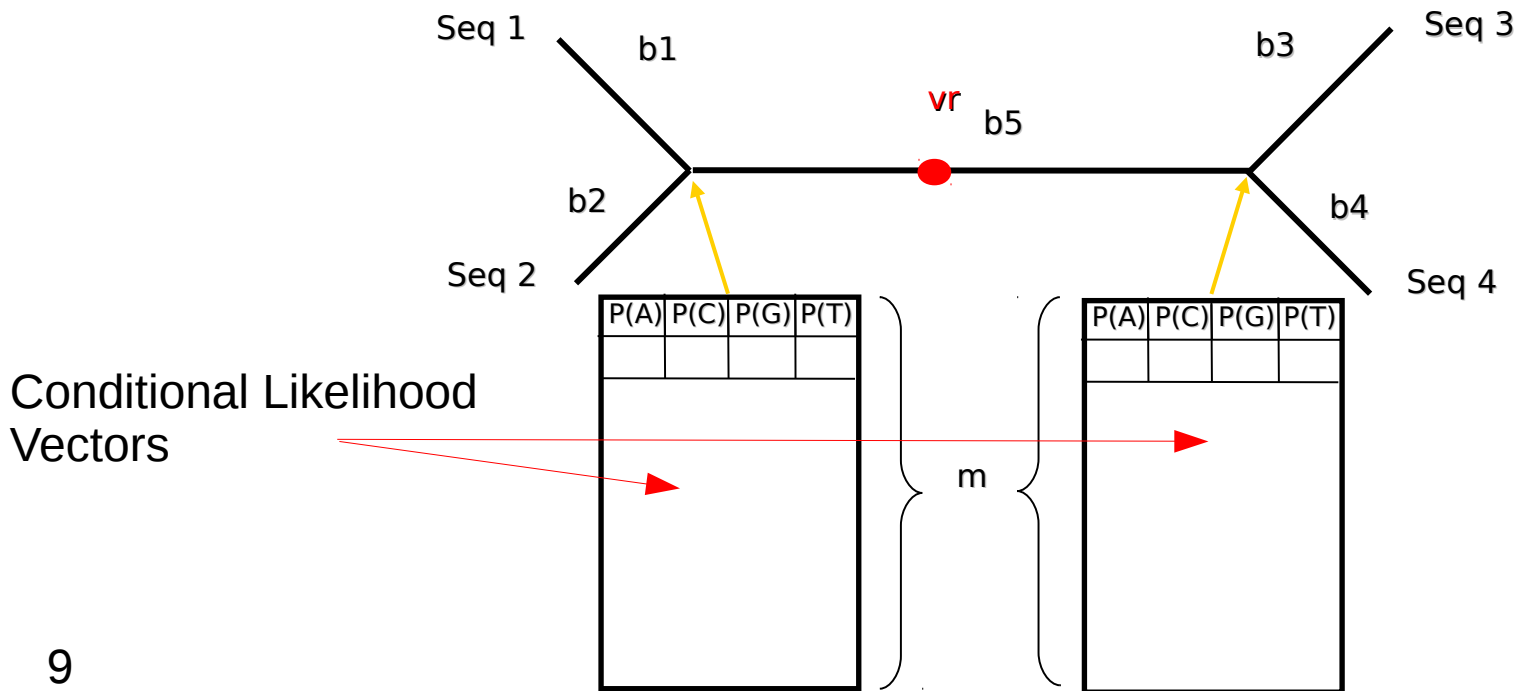
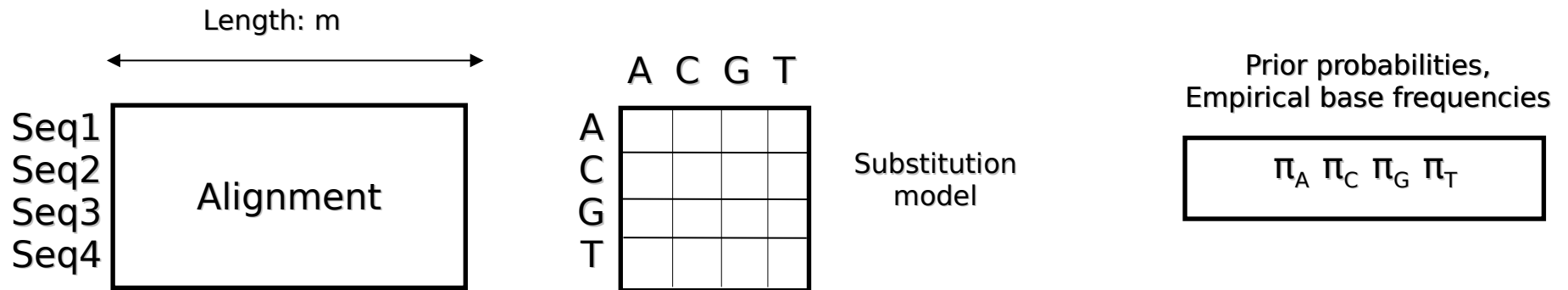
Maximum Likelihood



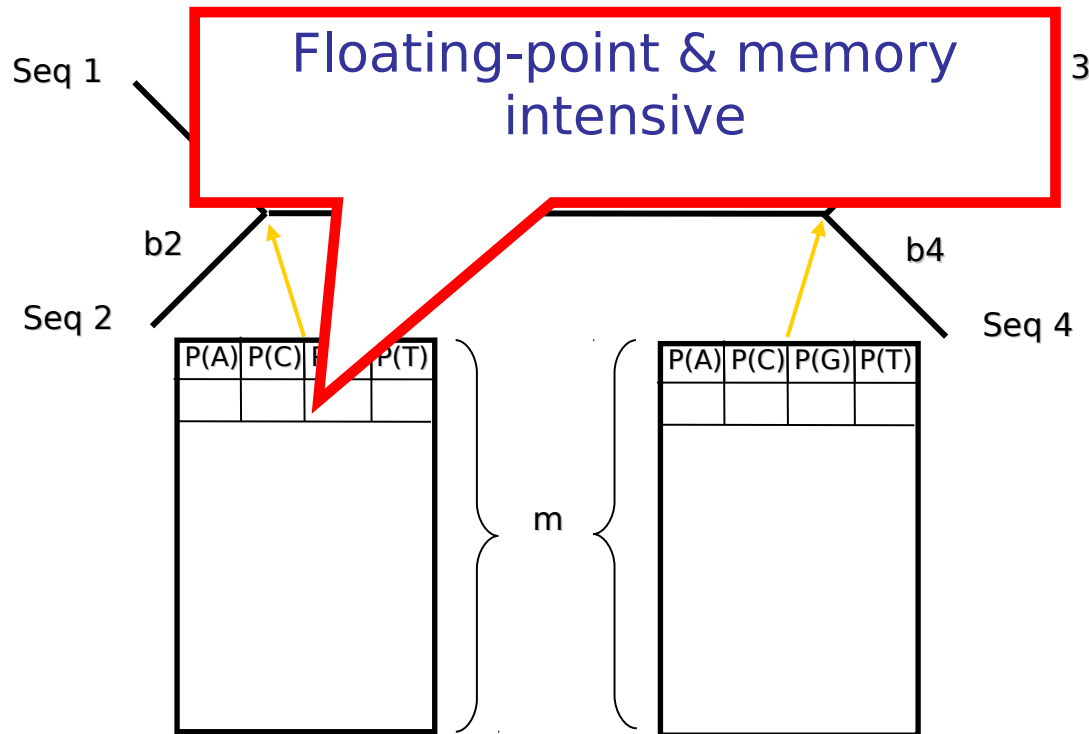
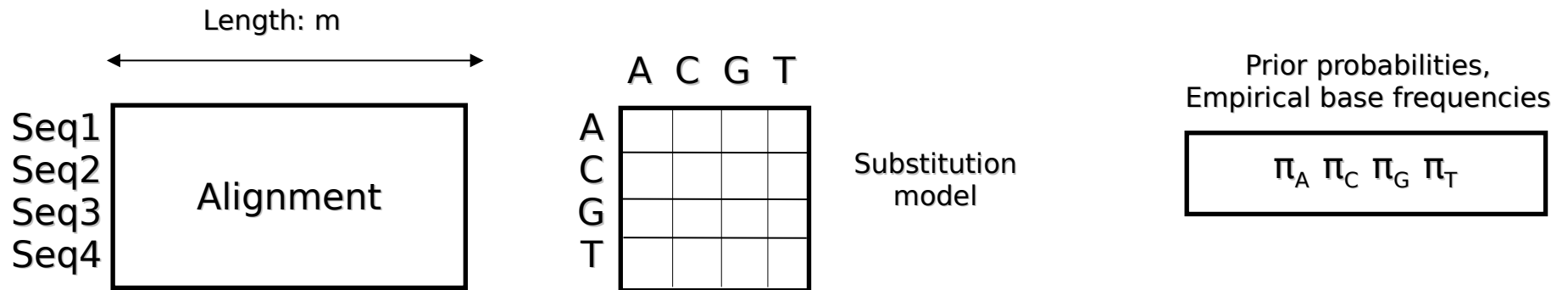
Maximum Likelihood



Maximum Likelihood

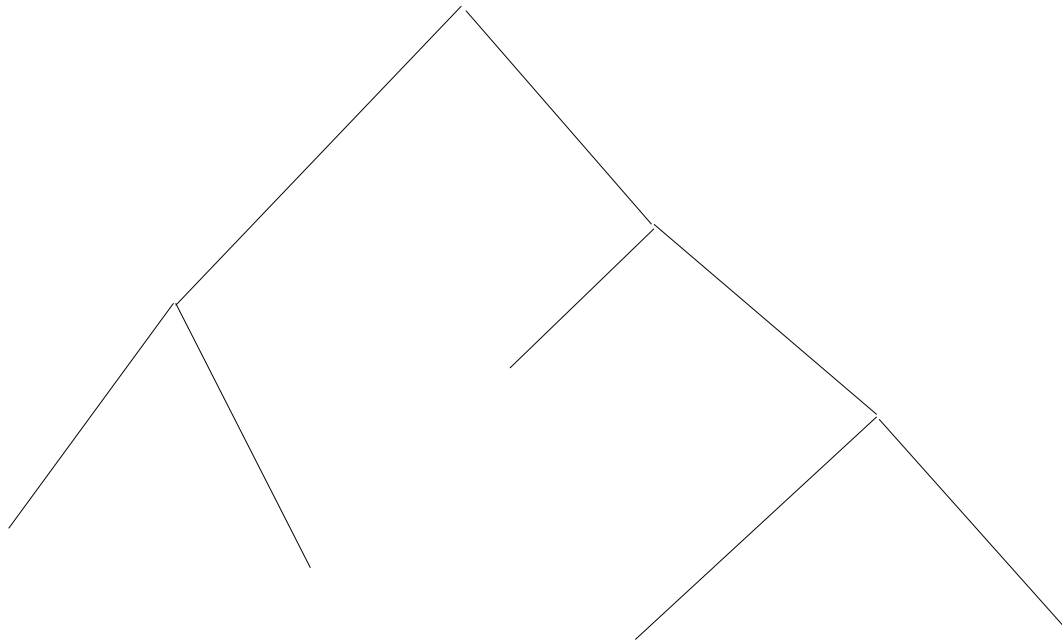


Maximum Likelihood

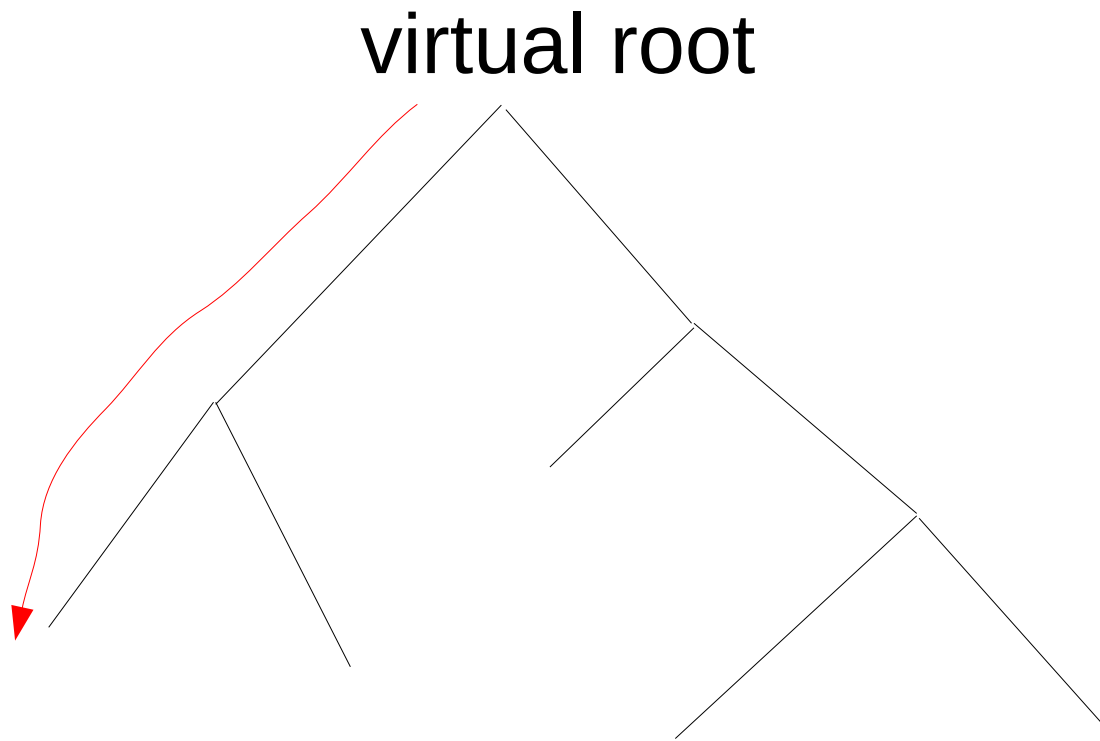


Post-order Traversal

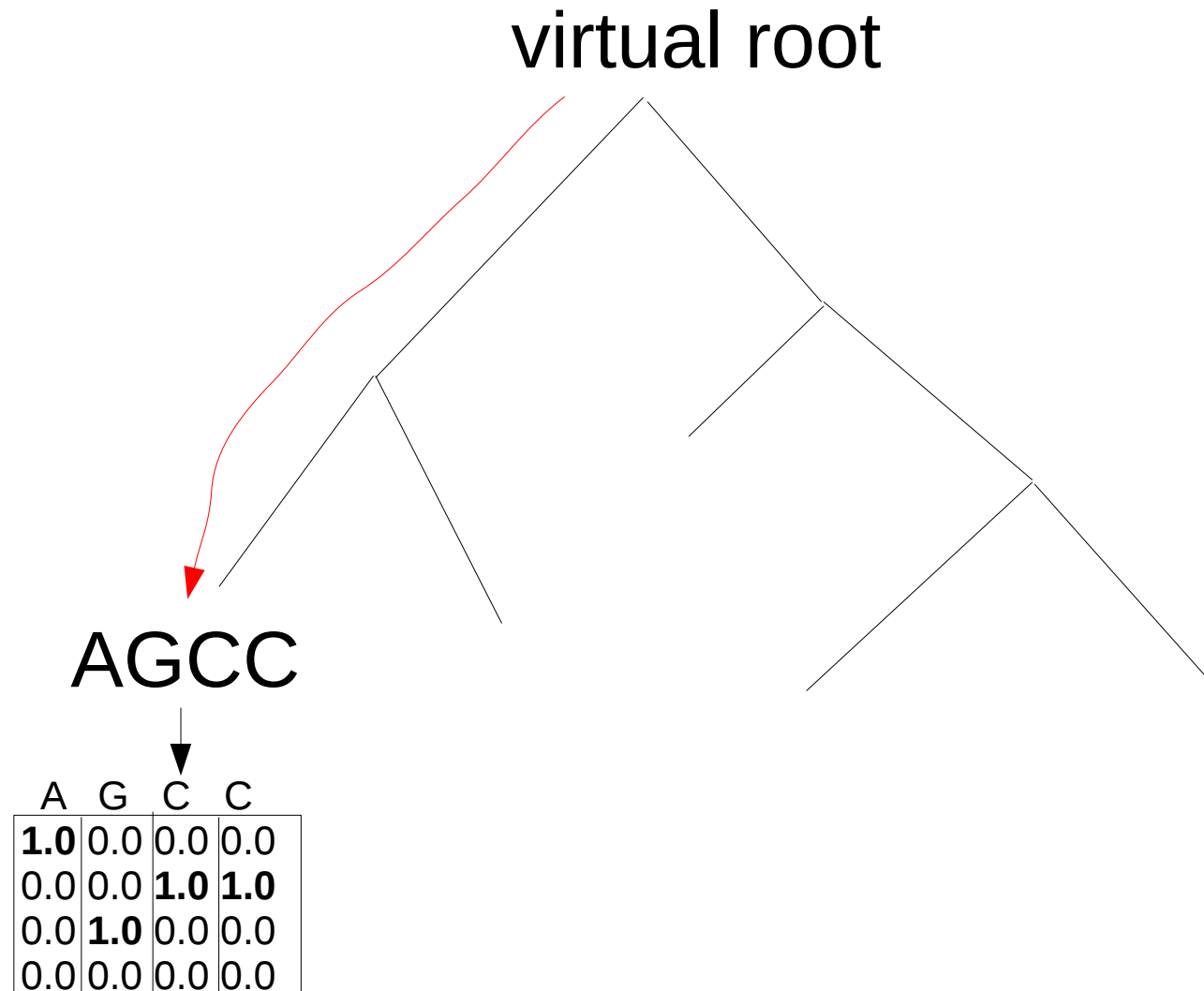
virtual root



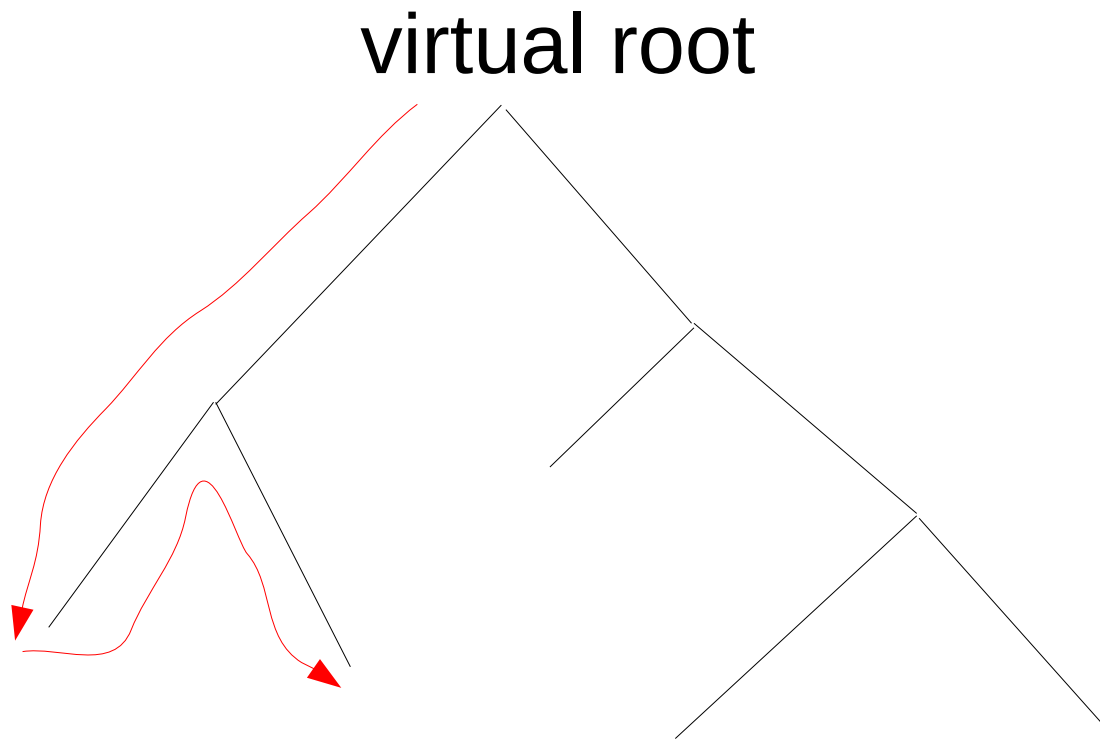
Post-order Traversal



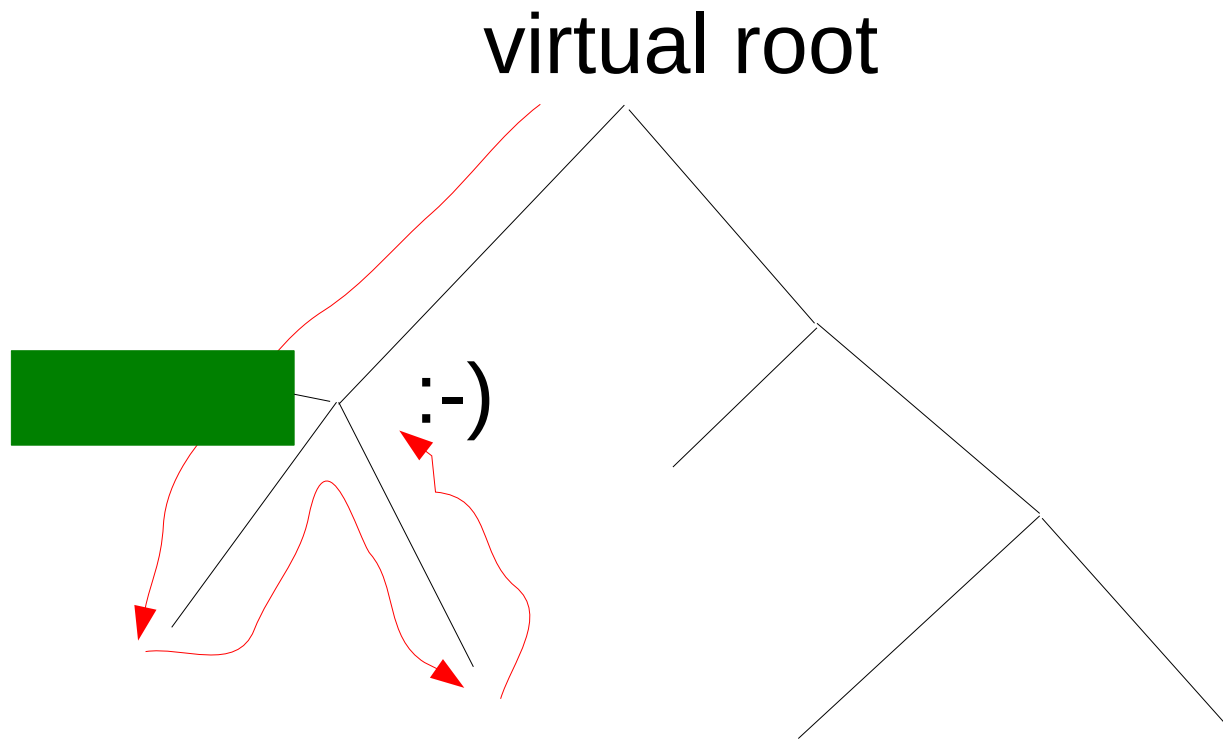
Post-order Traversal



Post-order Traversal

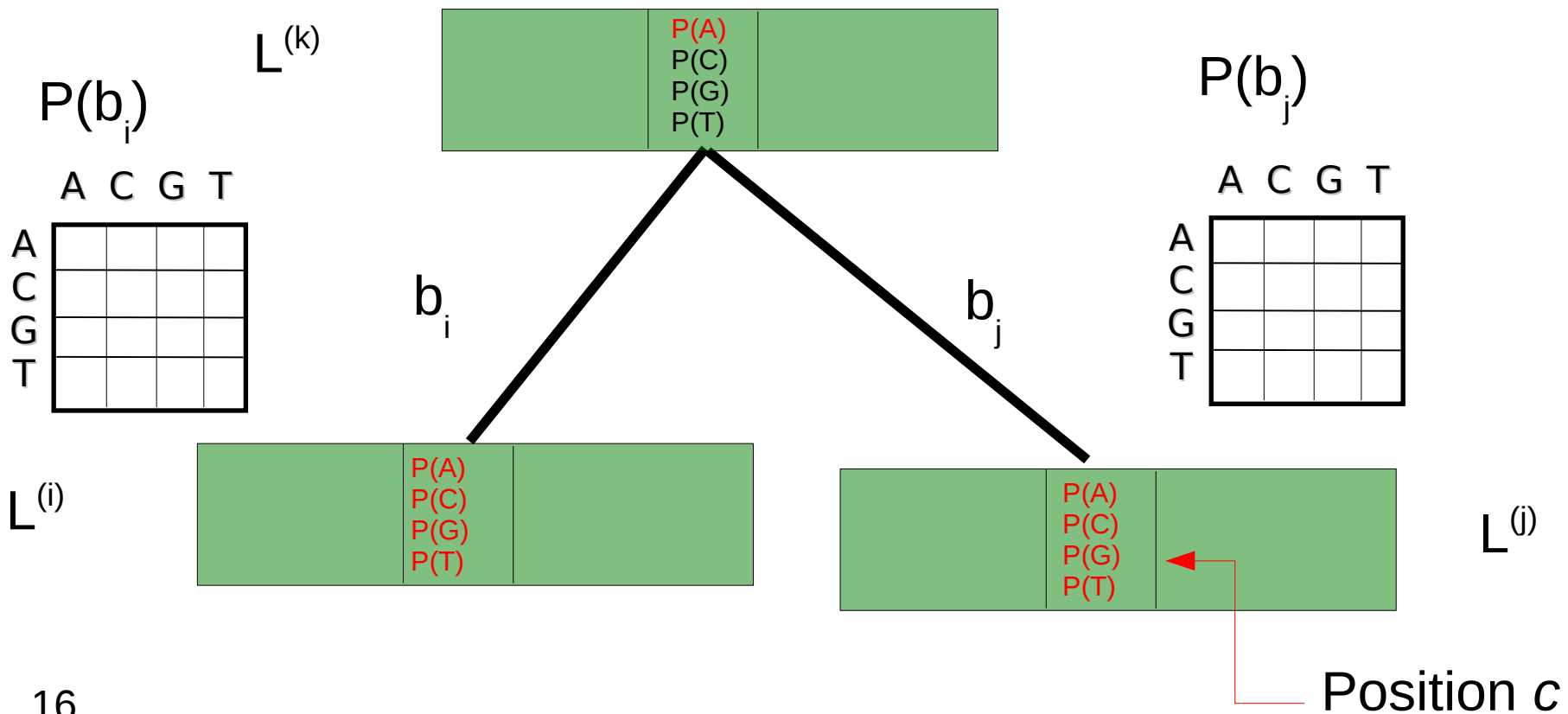


Post-order Traversal

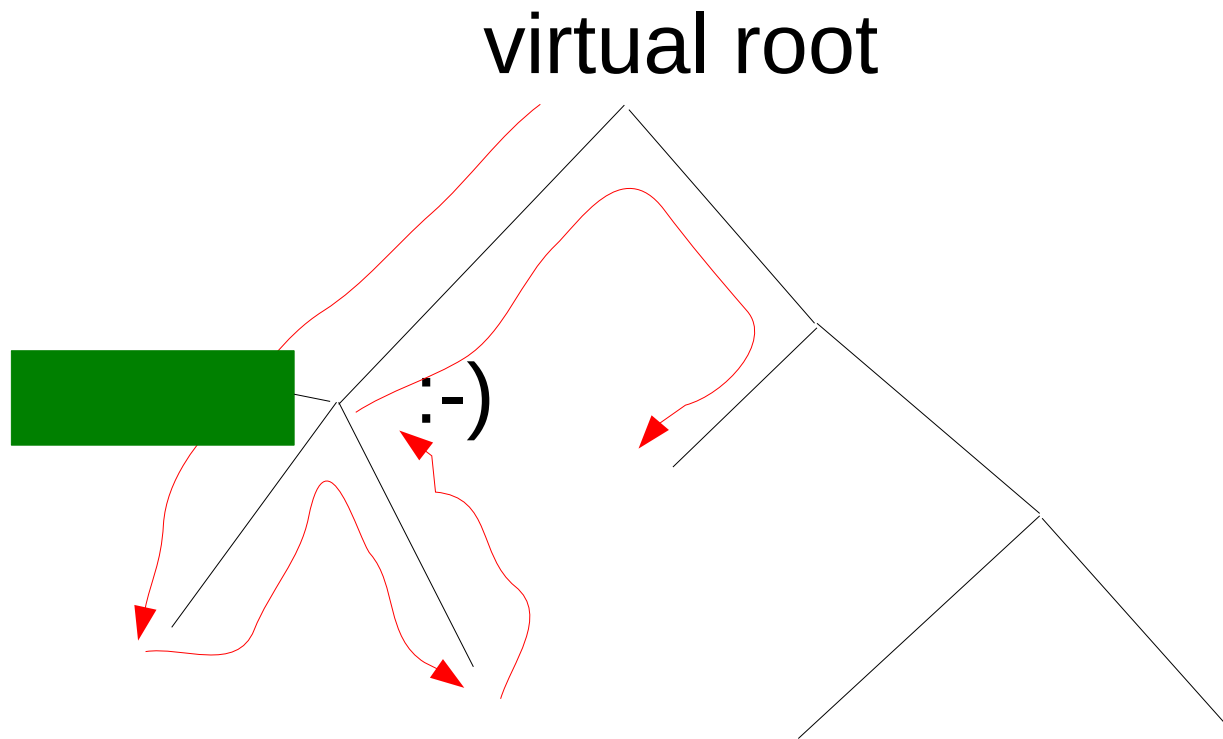


What happens when we compute this inner vector?

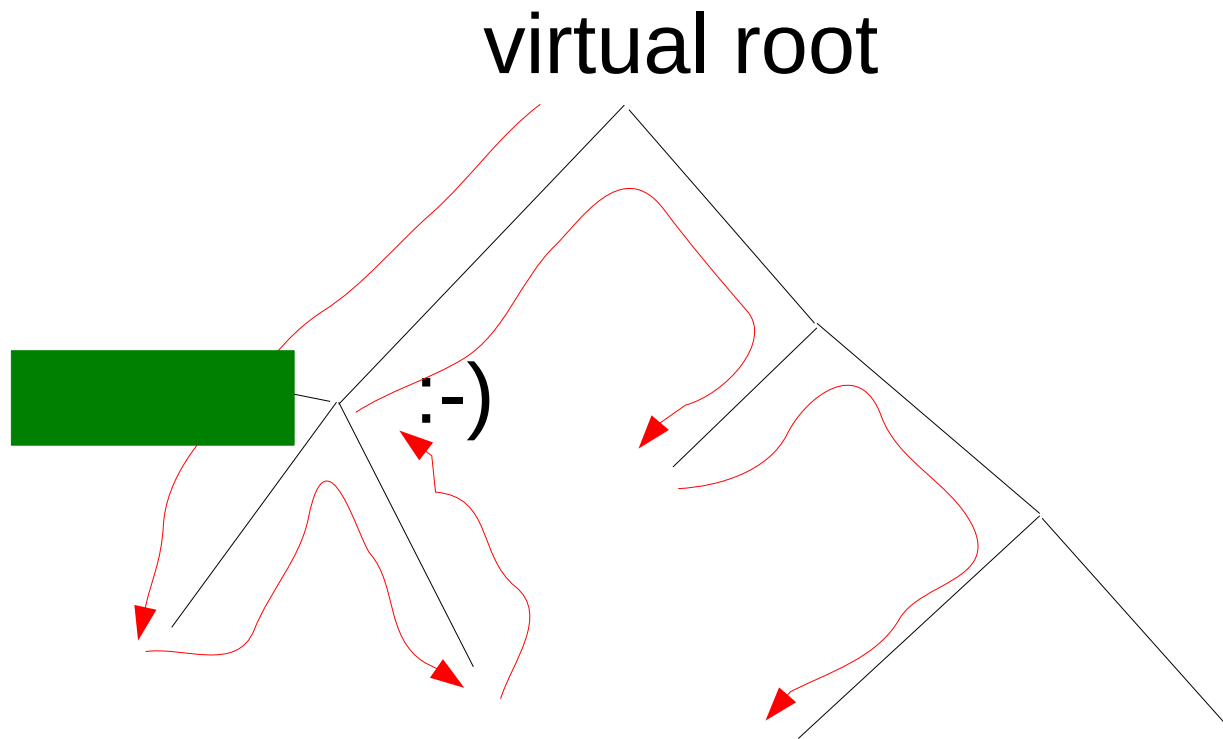
$$\vec{L}_A^{(k)}(c) = \left(\sum_{S=A}^T P_{AS}(b_i) \vec{L}_S^{(i)}(c) \right) \left(\sum_{S=A}^T P_{AS}(b_j) \vec{L}_S^{(j)}(c) \right)$$



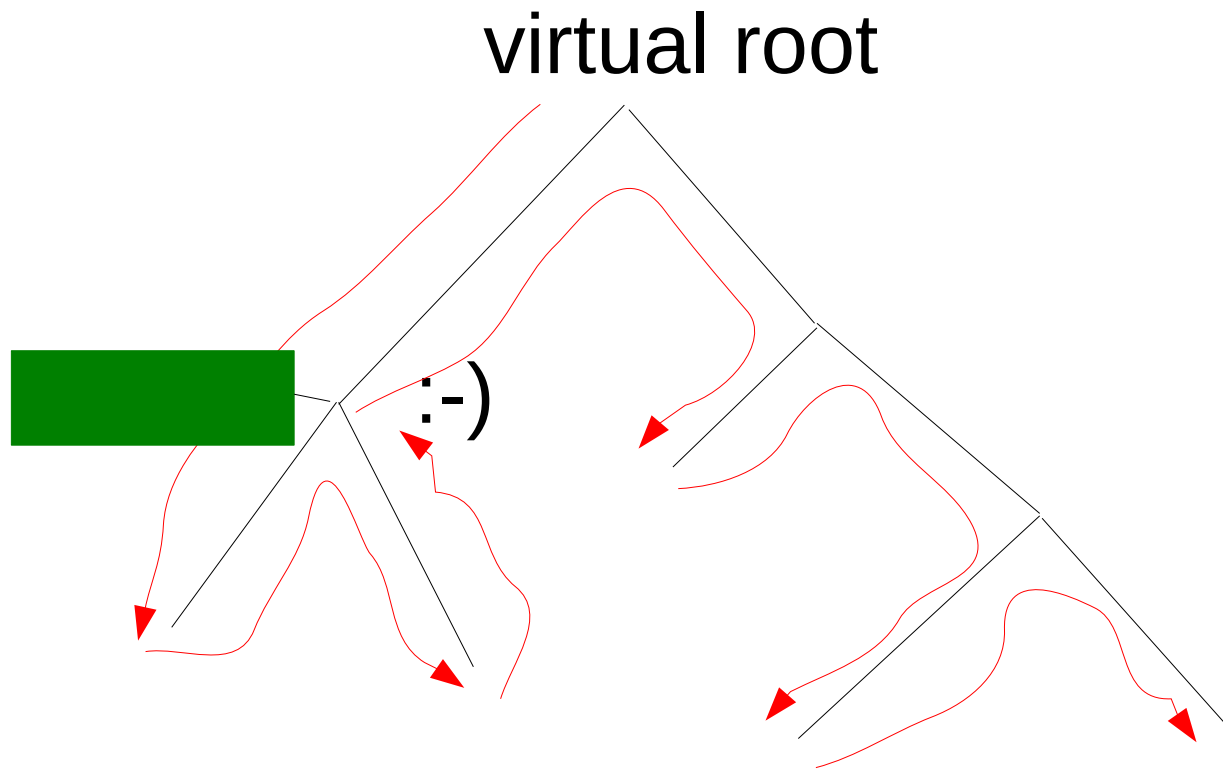
Post-order Traversal



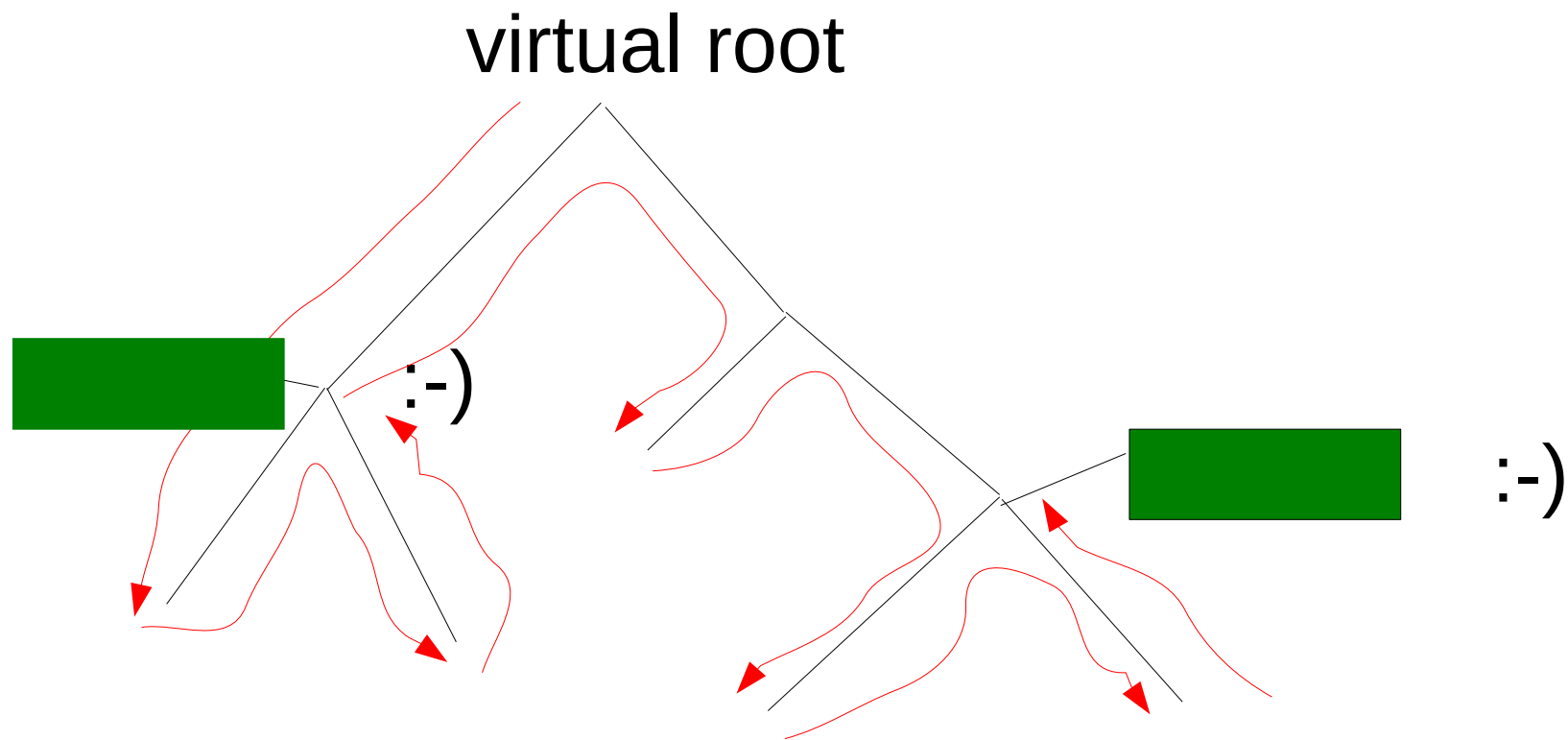
Post-order Traversal



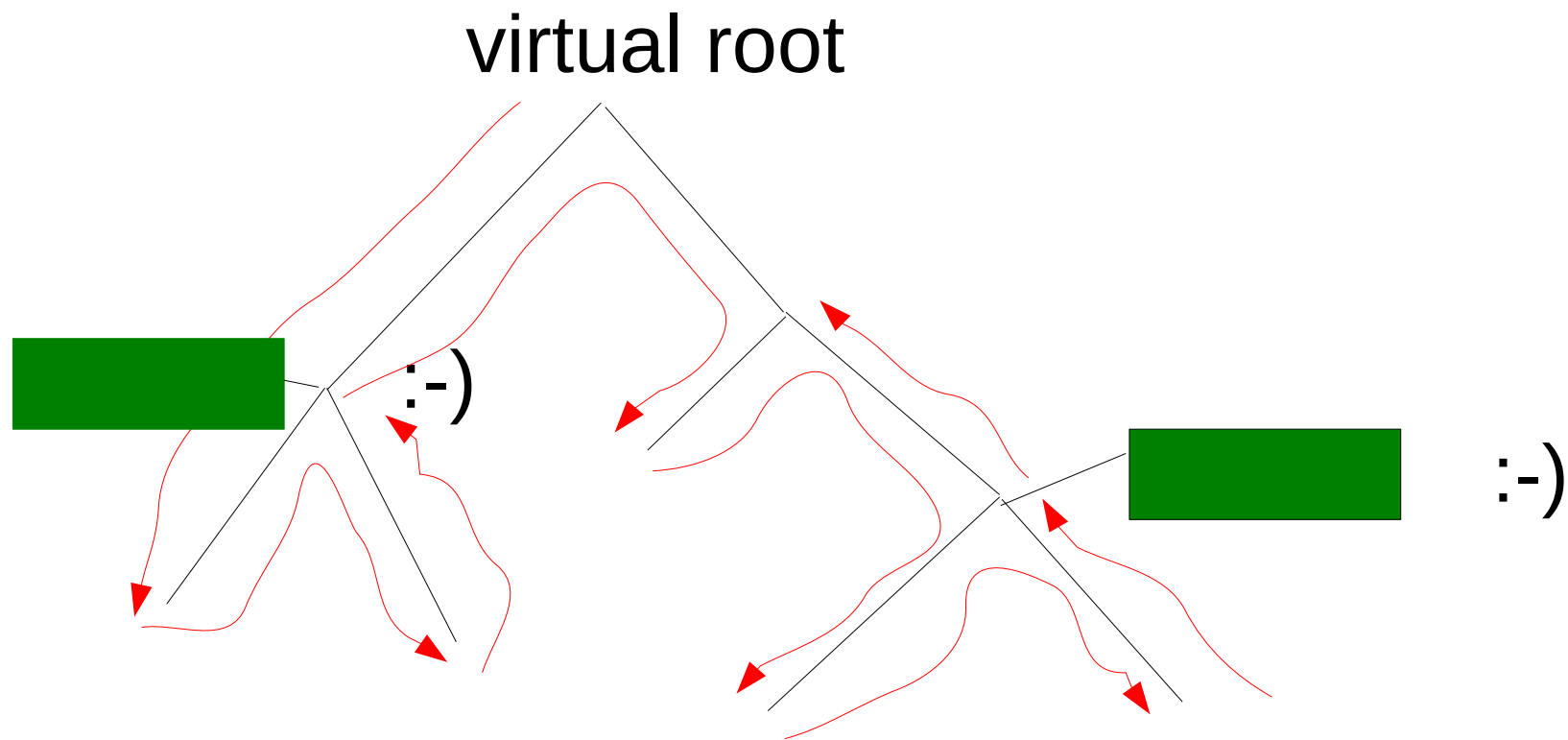
Post-order Traversal



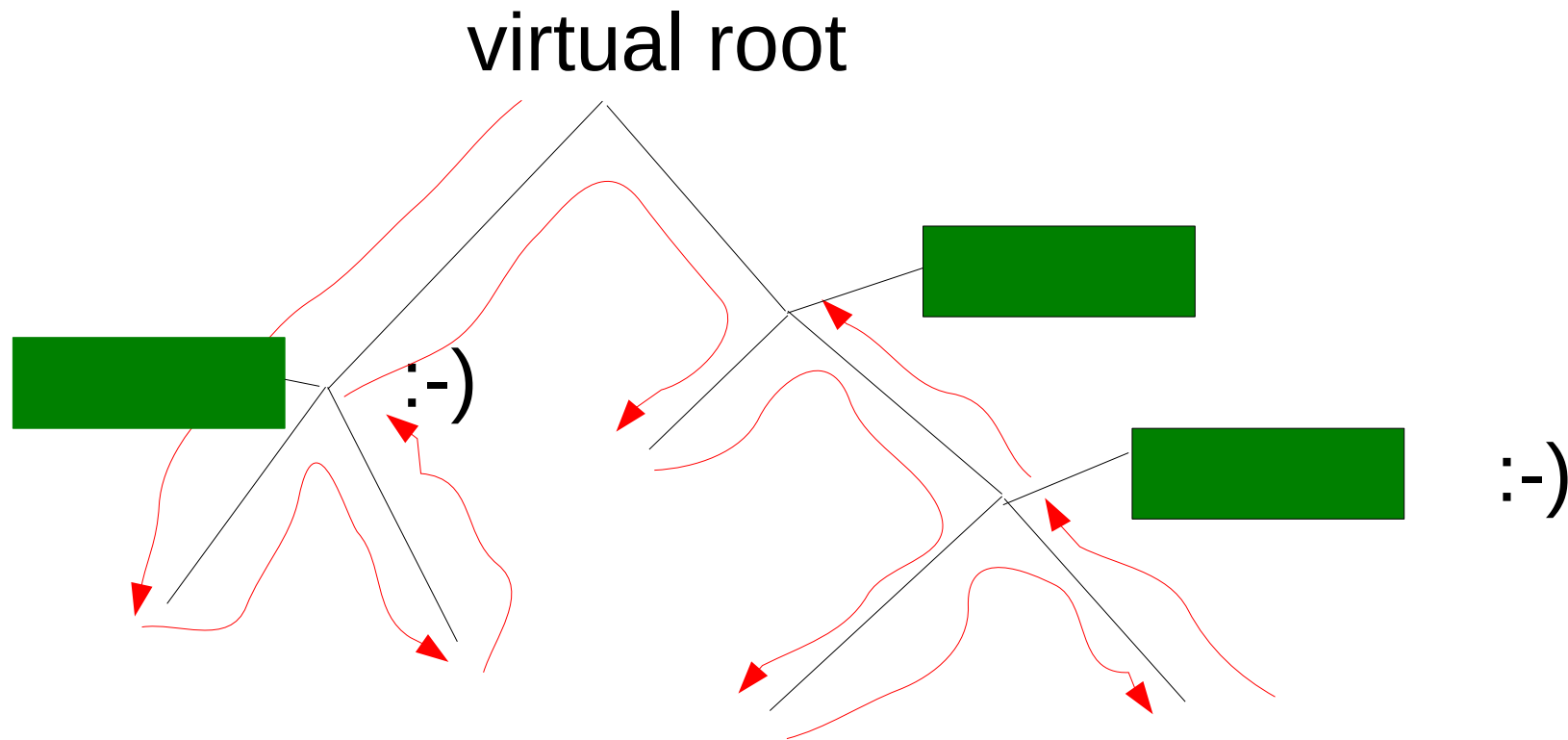
Post-order Traversal



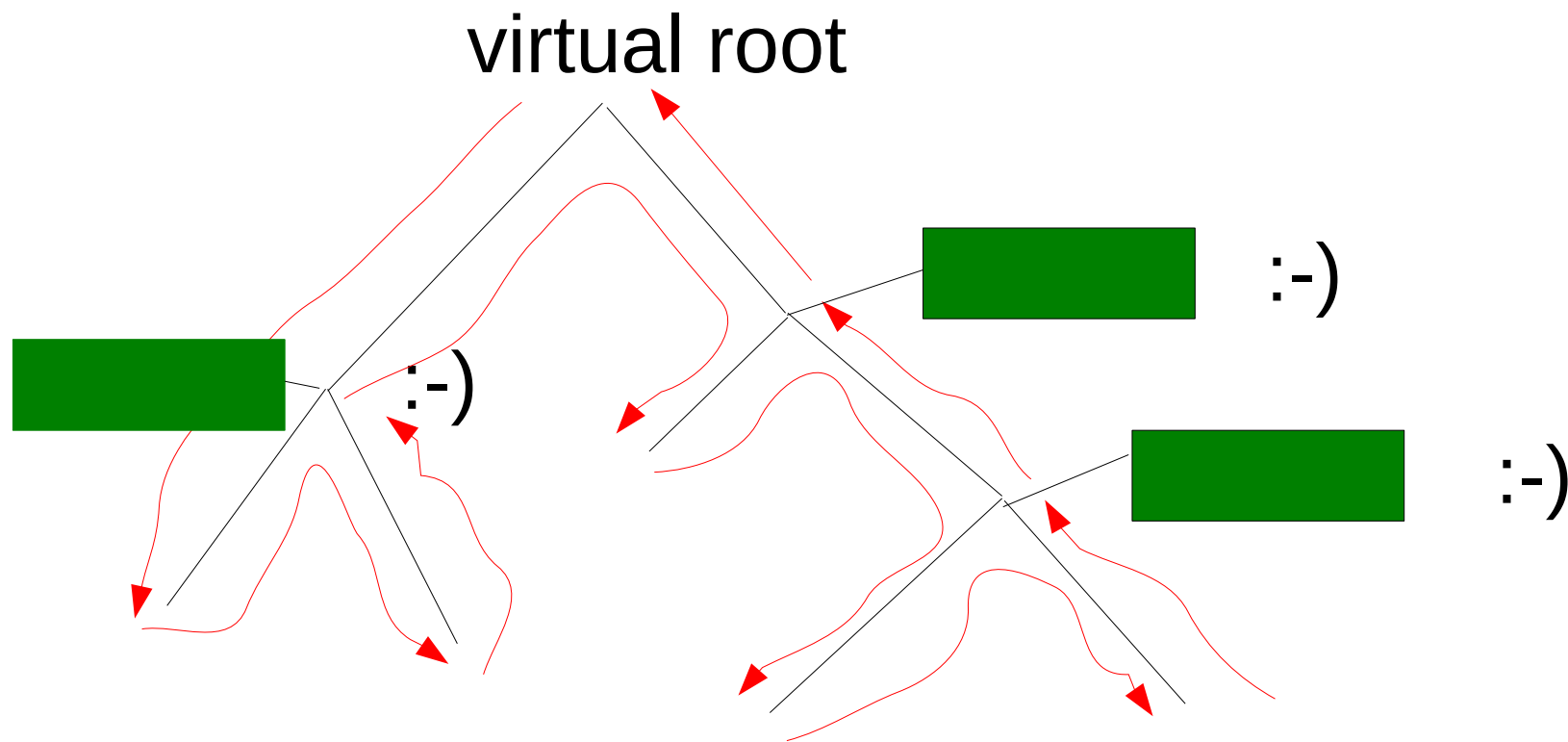
Post-order Traversal



Post-order Traversal

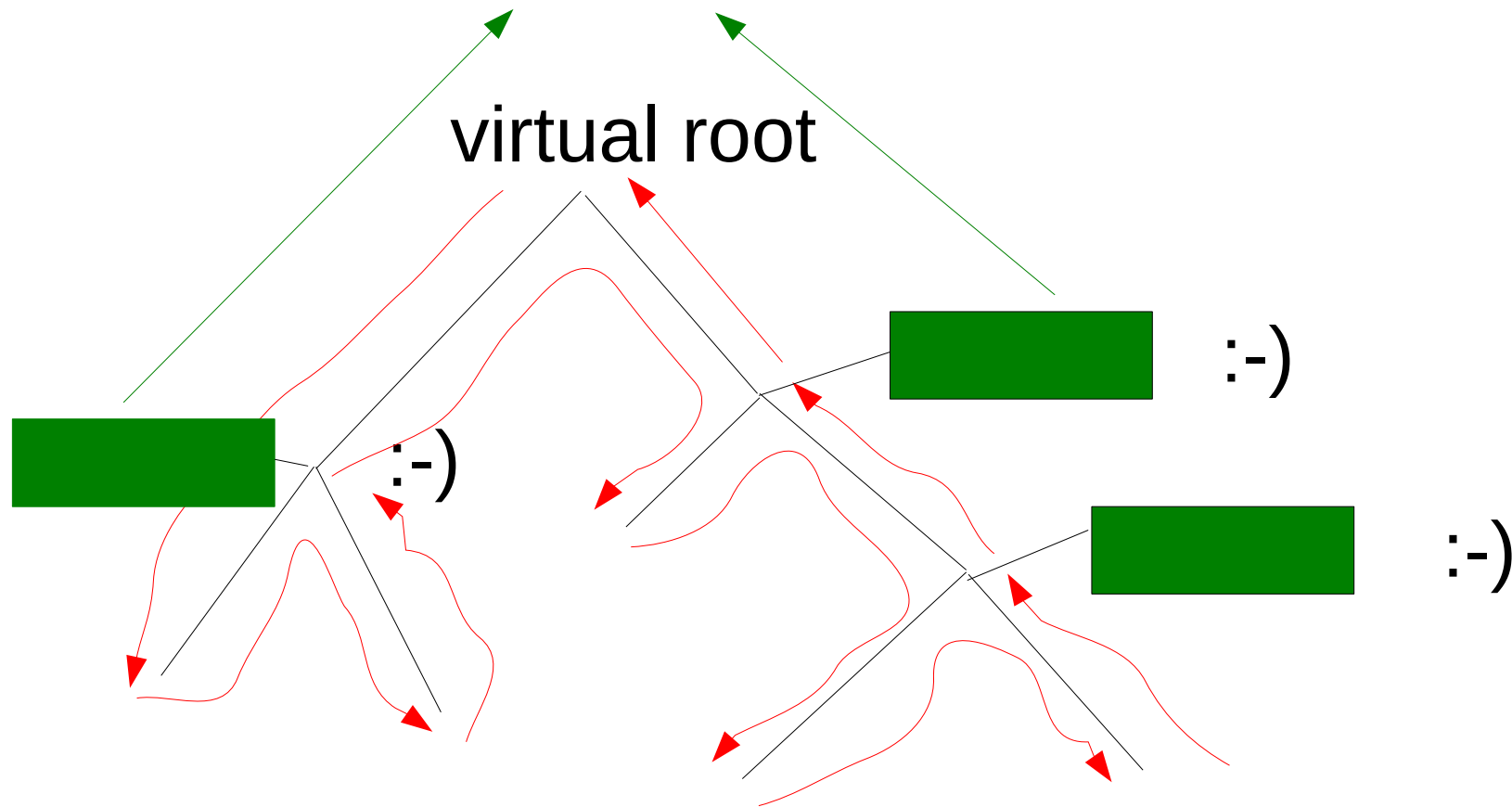


Post-order Traversal



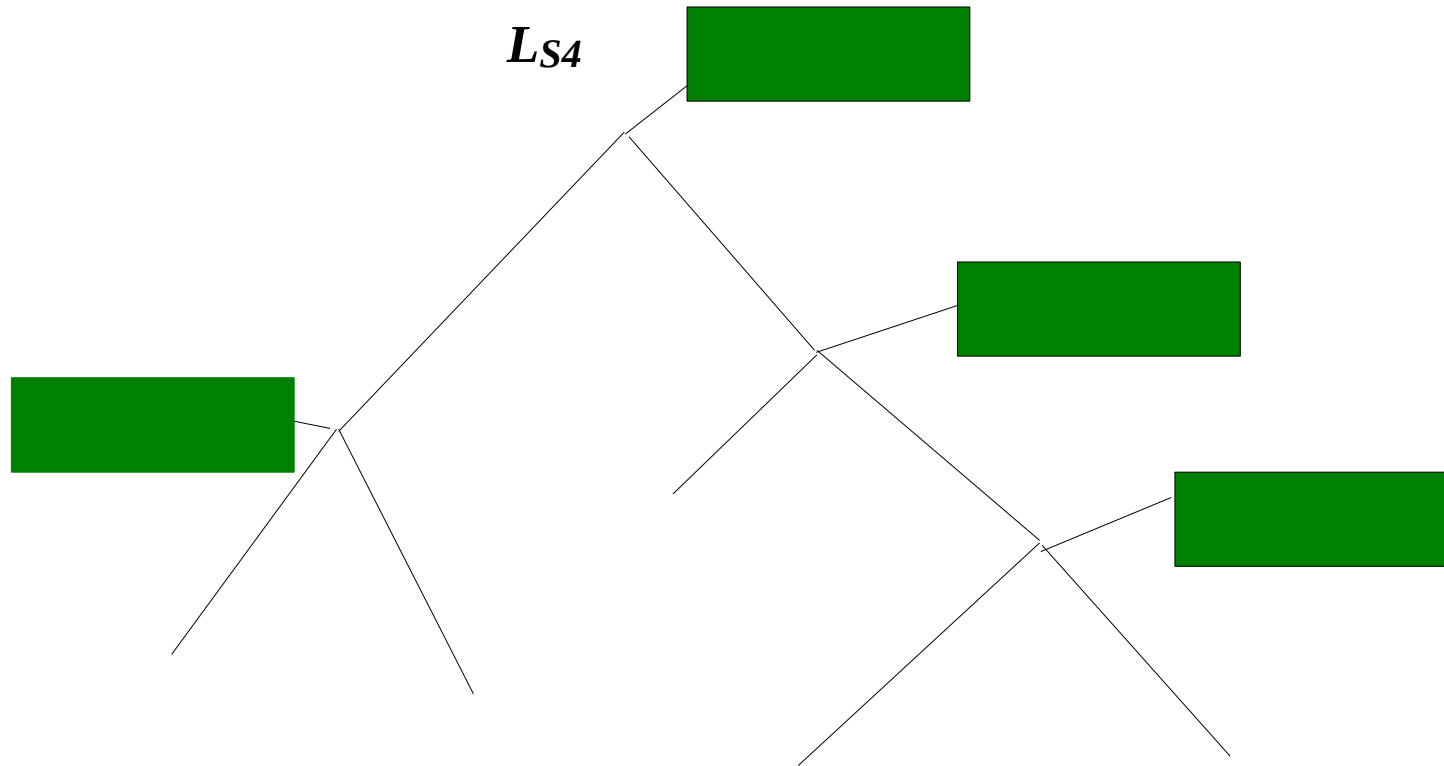
Post-order Traversal

Overall likelihood: sum over logarithms of per-site likelihoods

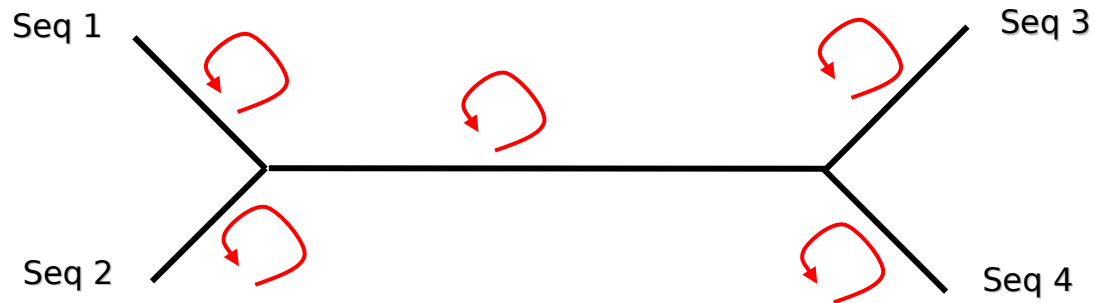
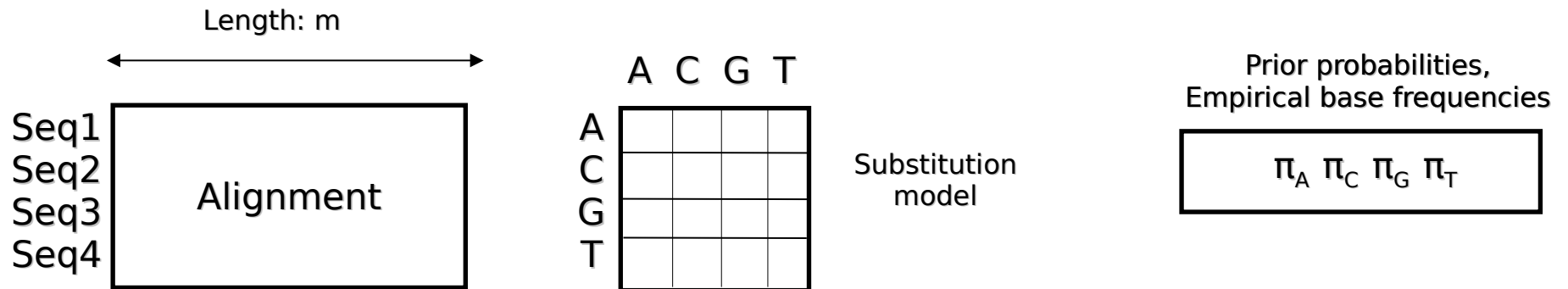


Post-order Traversal

$$L = \sum_{S_4=A}^T \pi_{S_4} L_{S_4}$$

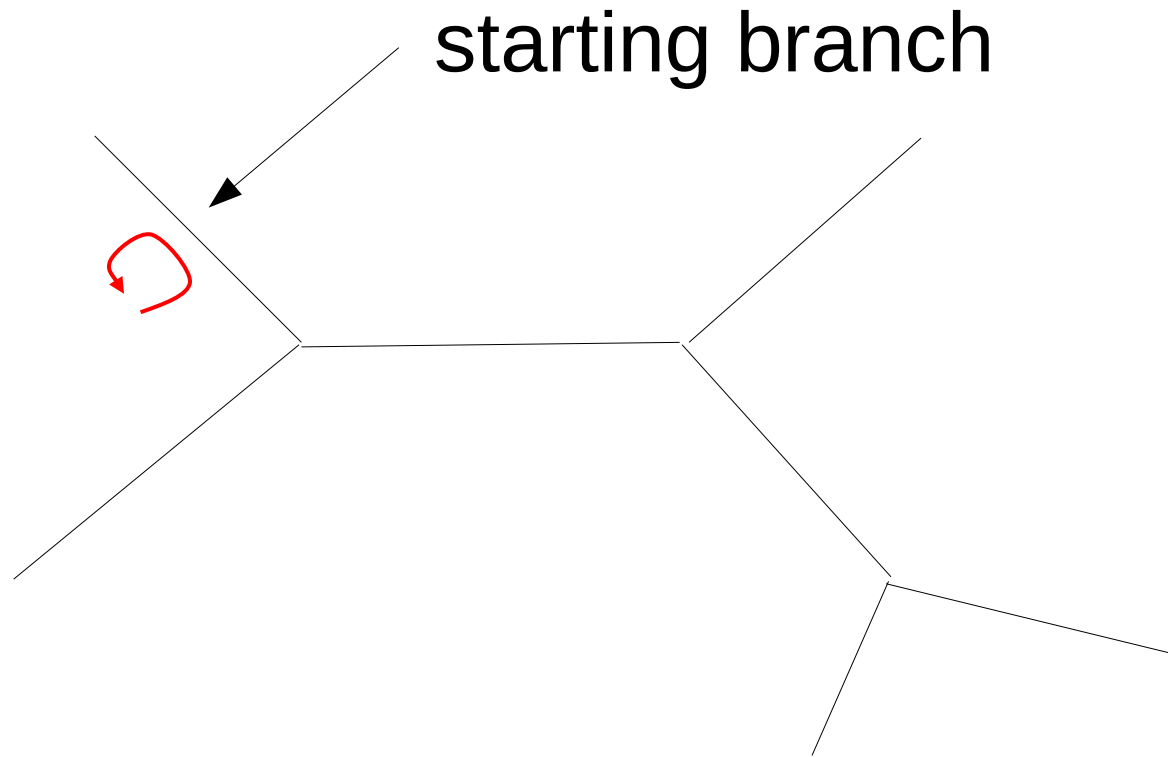


Maximum Likelihood

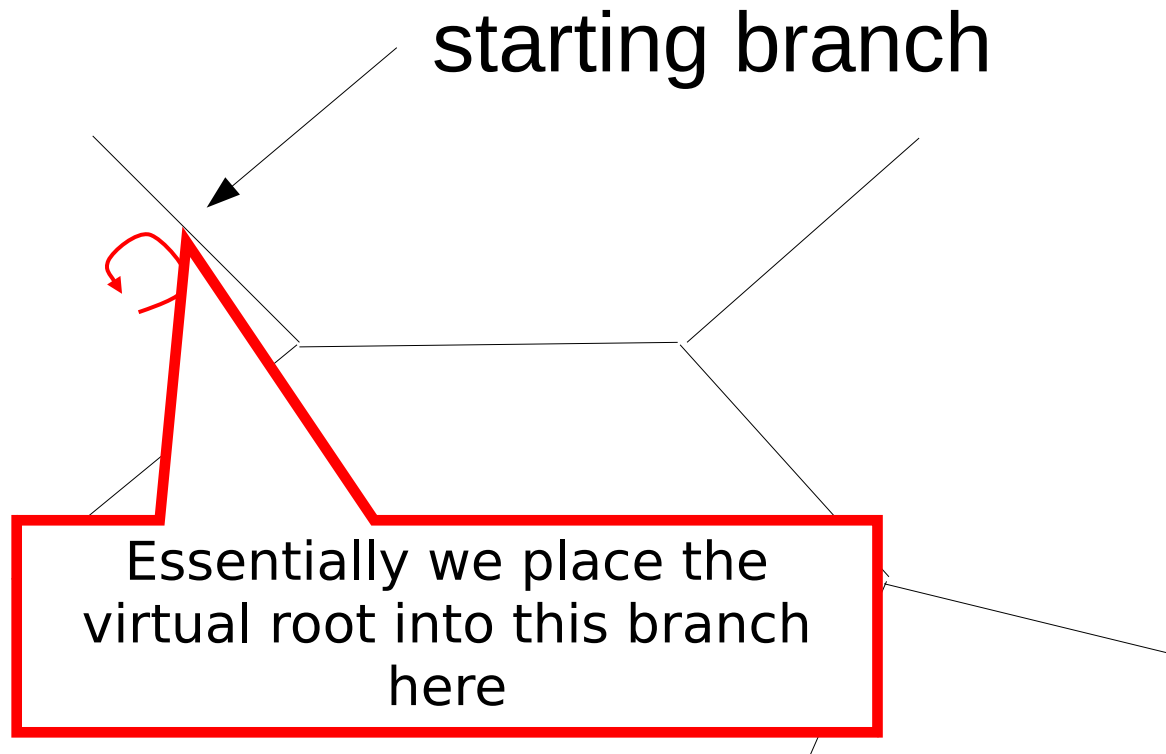


optimize branch lengths

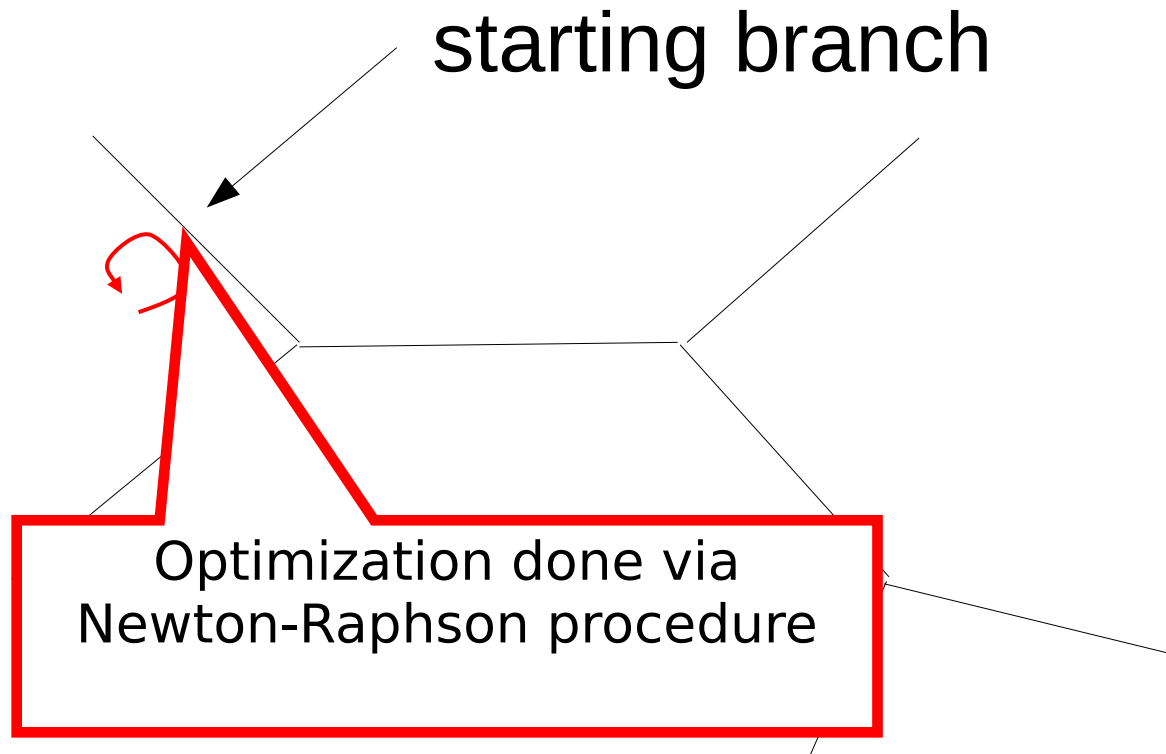
Branch Length Optimization



Branch Length Optimization



Branch Length Optimization



Newton Raphson

- We want to find the branch length b that maximizes the likelihood $L(b)$ of the tree
- For this, we want to know where the *first* derivative of $L(b)$ is 0
- To achieve this numerically we use the Newton-Raphson procedure for root finding deploying the first and second derivative of the likelihood $L'(b)$ and $L''(b)$
- Note that, the likelihood only depends on branch b , all other model parameters (Q matrix, base frequencies, tree topology) remain fixed

Derivatives of $L(b)$

- To compute the derivatives of $L(b)$, we essentially need to be able to compute the derivatives of $P(b)$ since the rest is just sums and does not depend on b

- Recall

$$P(b) = e^{Qb} = Ue^{\Lambda b}U^{-1}$$

- thus

$$(P(b))' = U\Lambda e^{\Lambda b}U^{-1}$$

- and

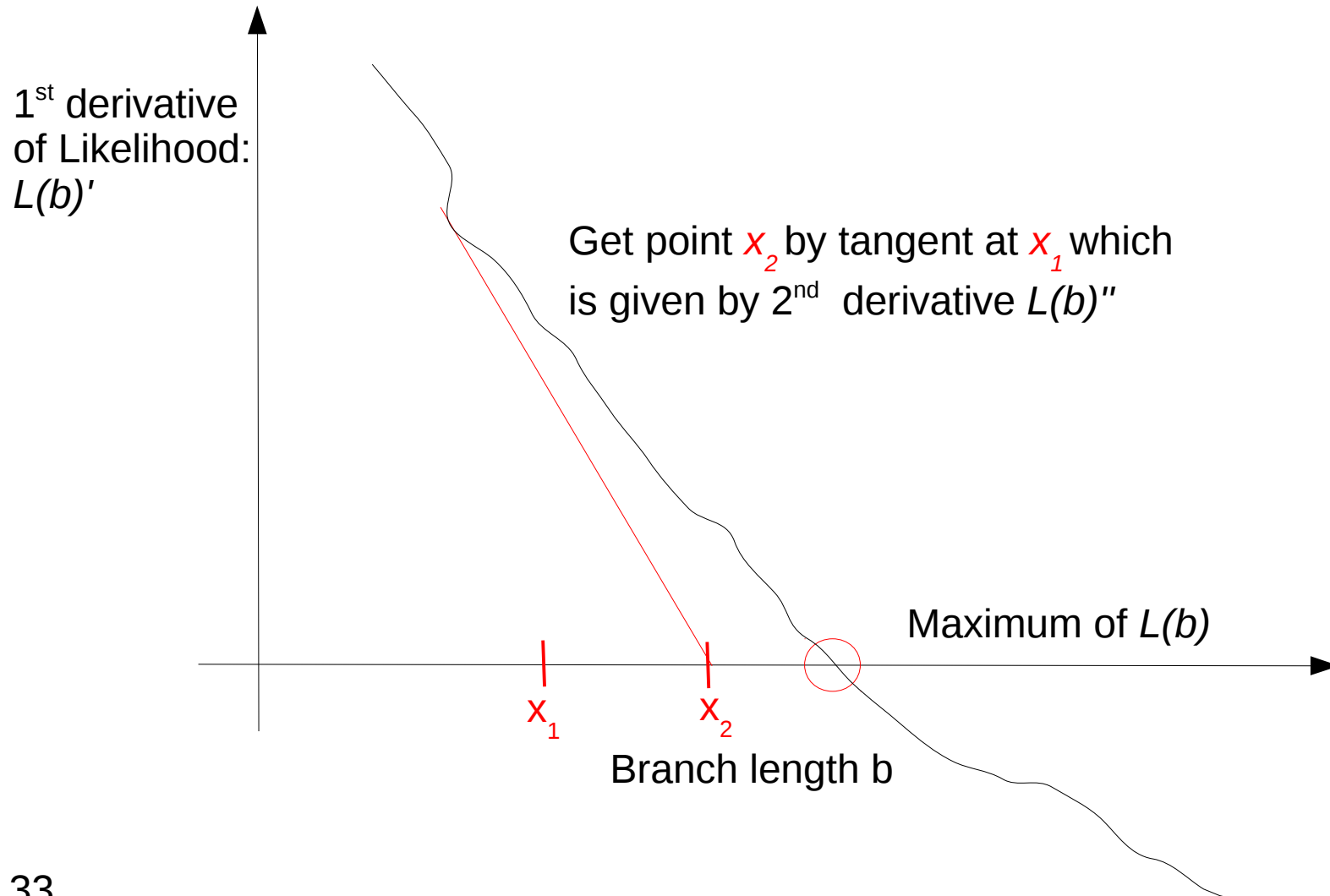
$$(P(b))'' = U\Lambda^2 e^{\Lambda b}U^{-1}$$

- In practice we compute the derivatives of the log likelihood $\log(L(b))$, but it is essentially the same

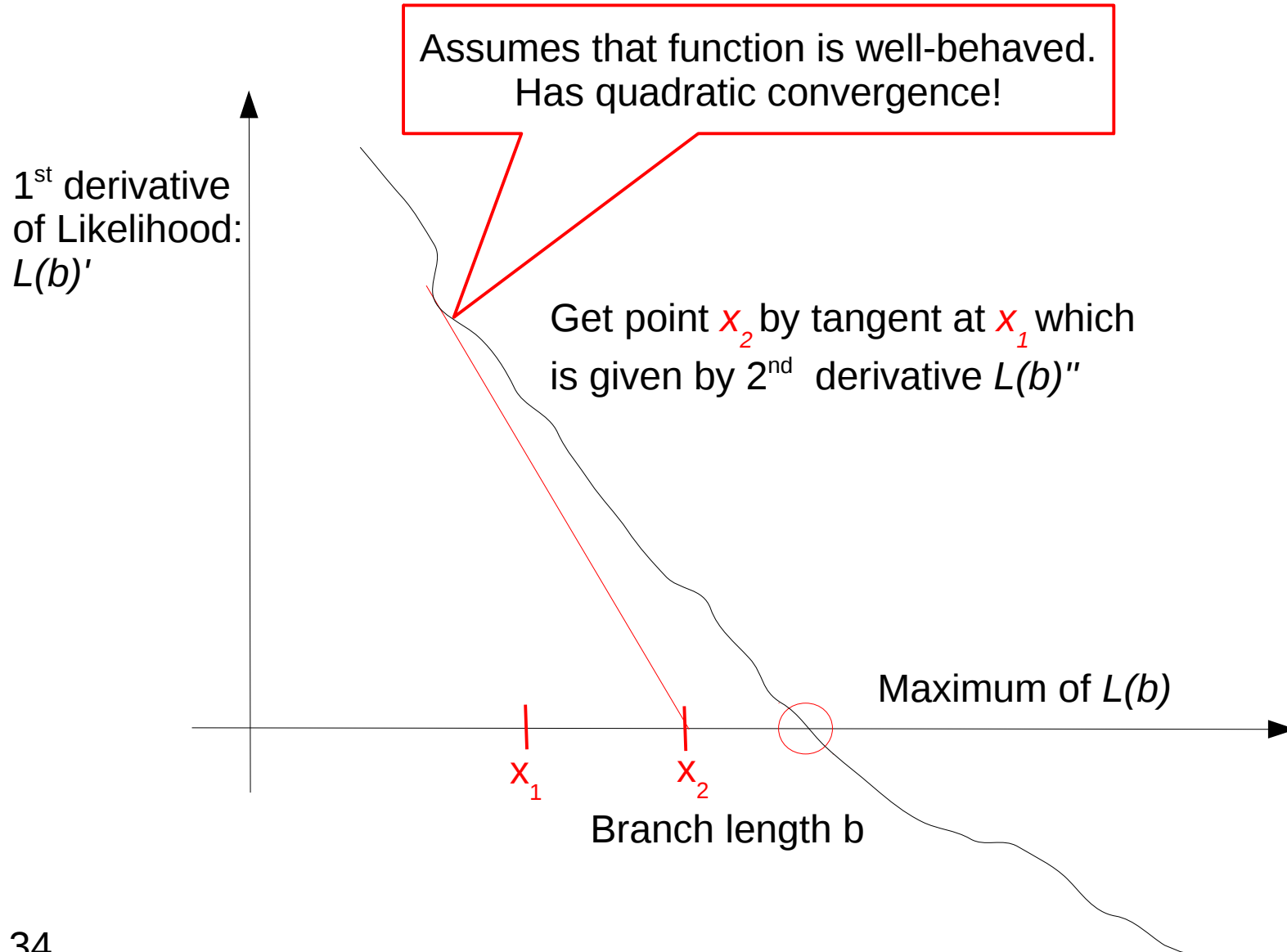
Derivatives of $\log(L(b))$

- 1st derivative: $L(b)' / L(b)$
- 2nd derivative: $(L(b) L(b)'' - (L(b)')^2) / L(b)^2$

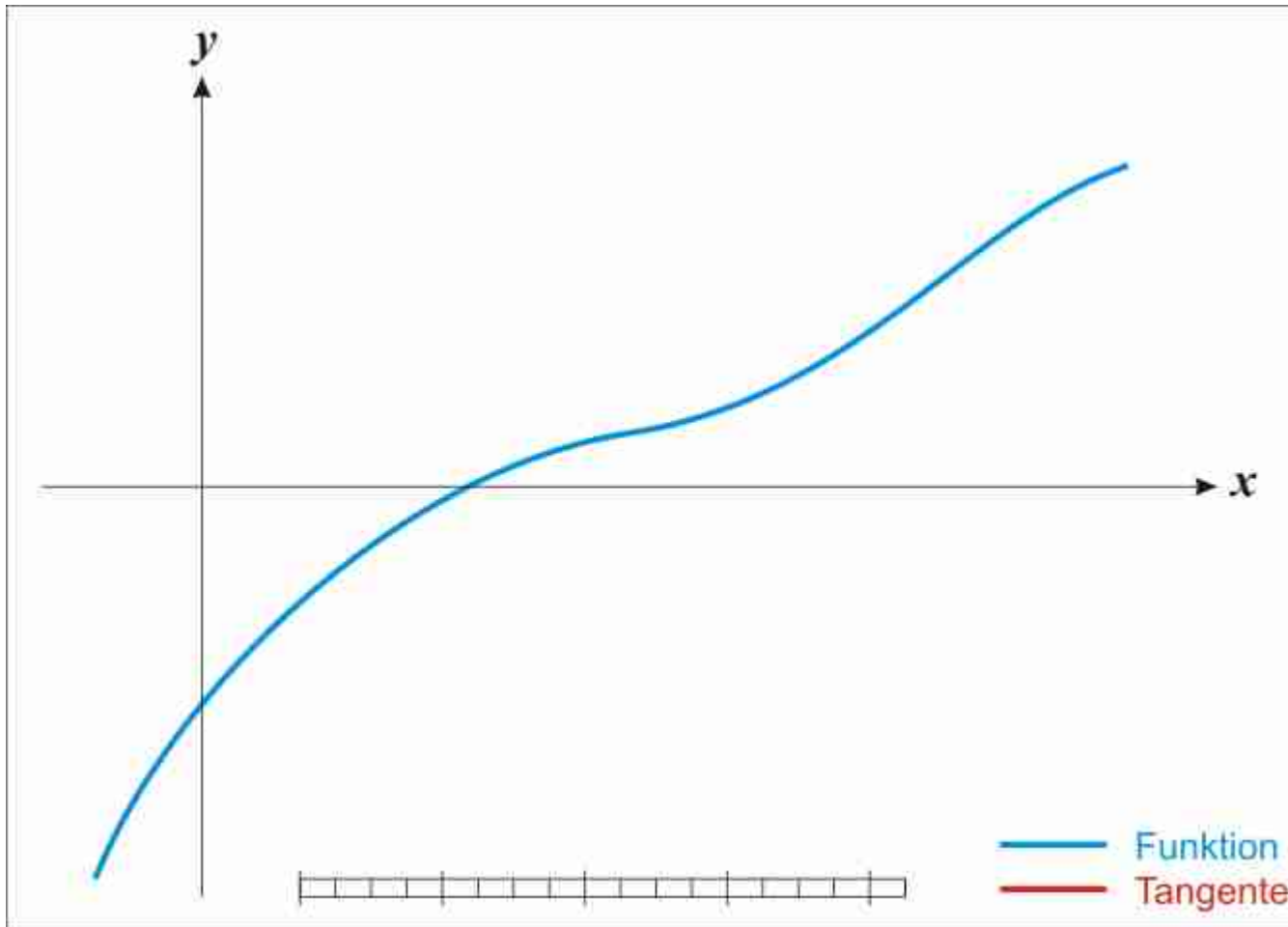
Newton Raphson



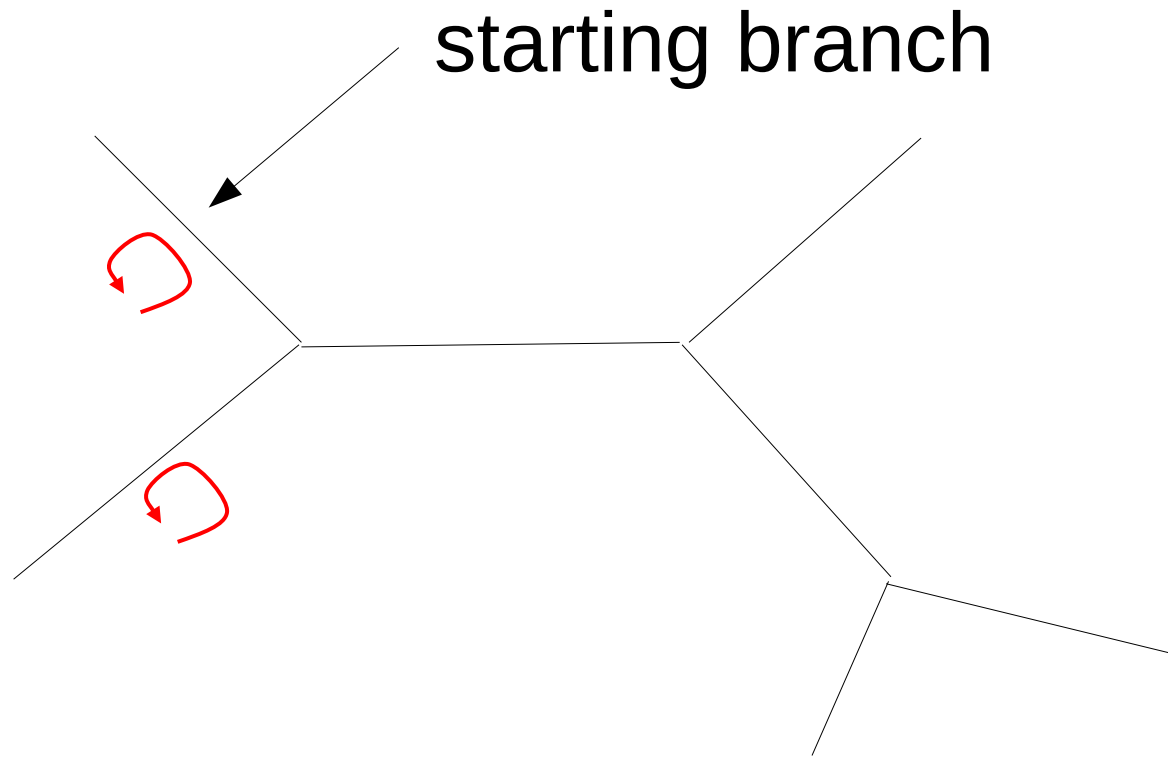
Newton Raphson



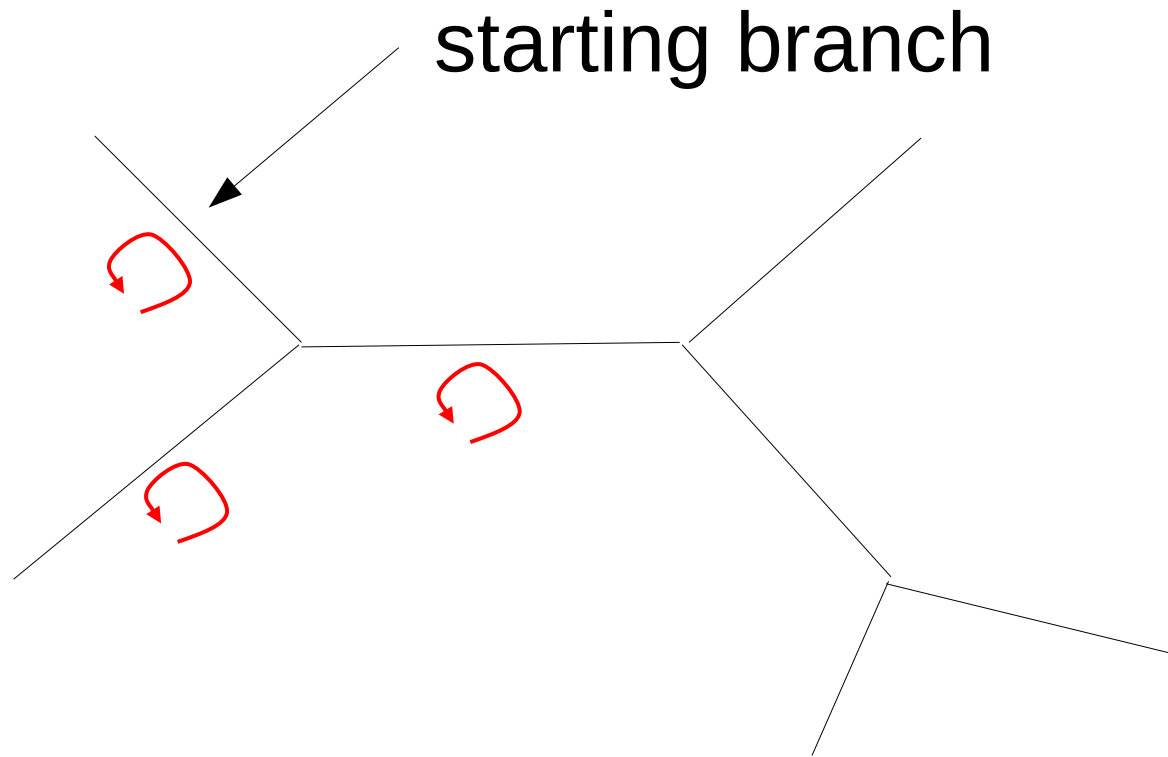
An animation



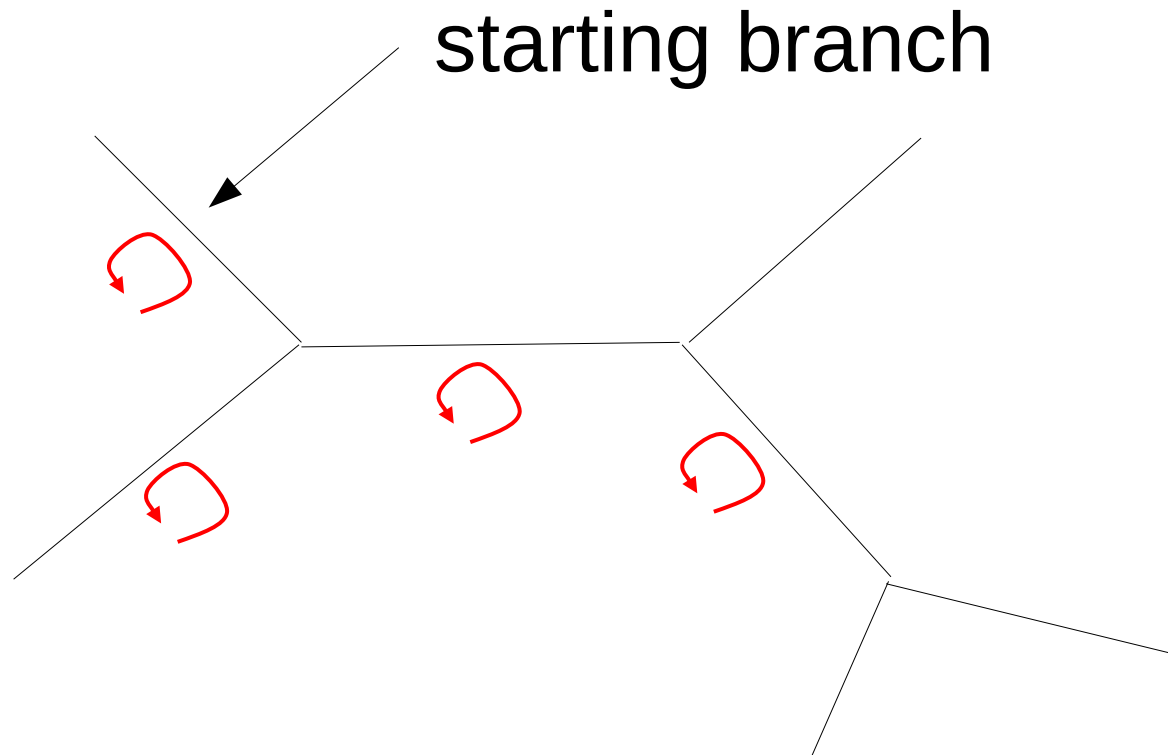
Branch Length Optimization



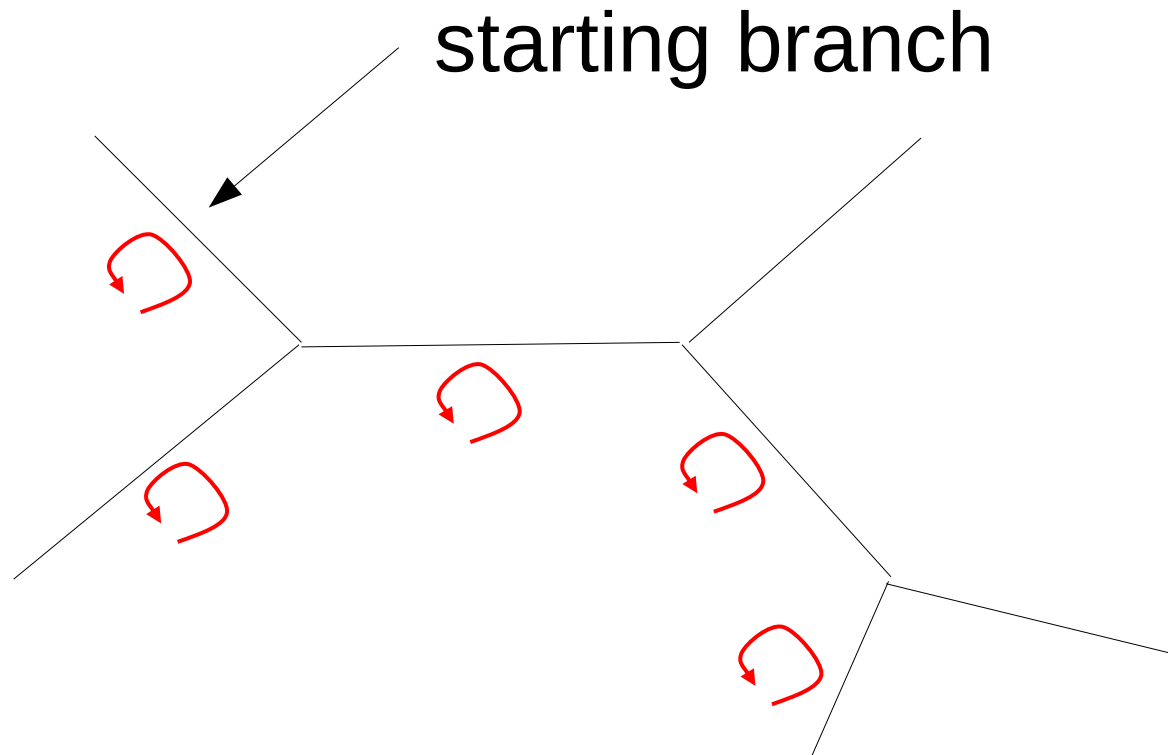
Branch Length Optimization



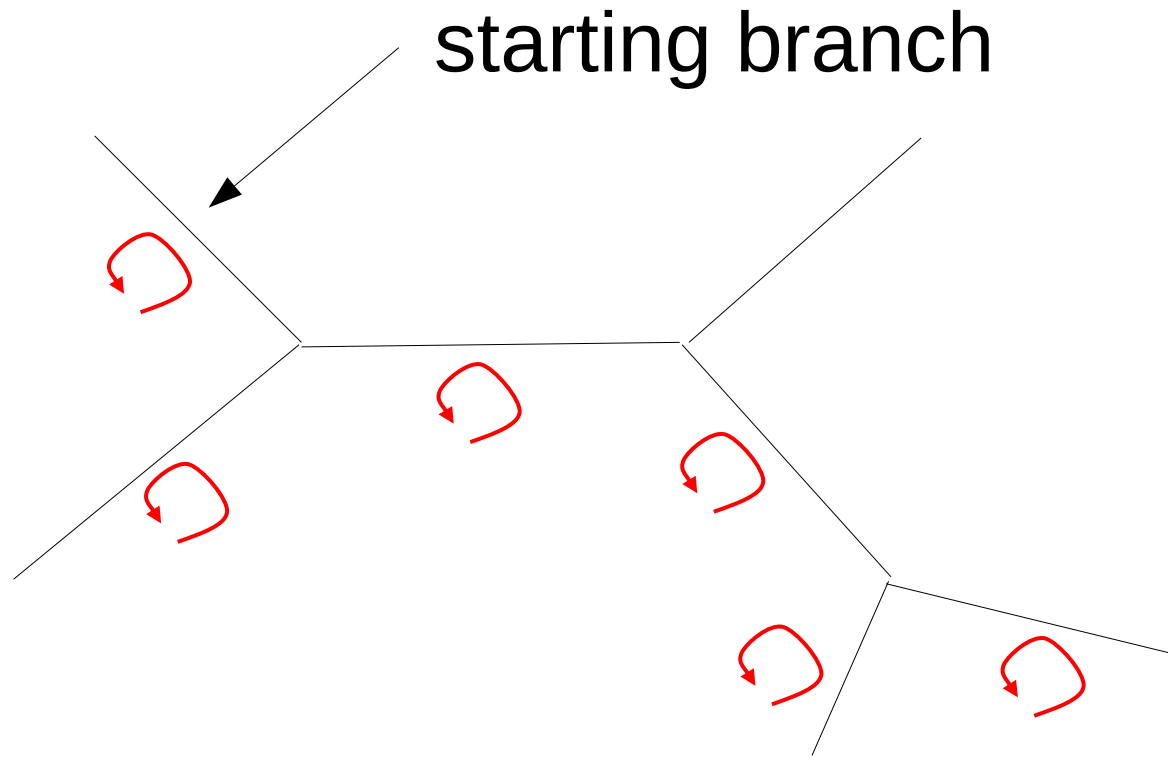
Branch Length Optimization



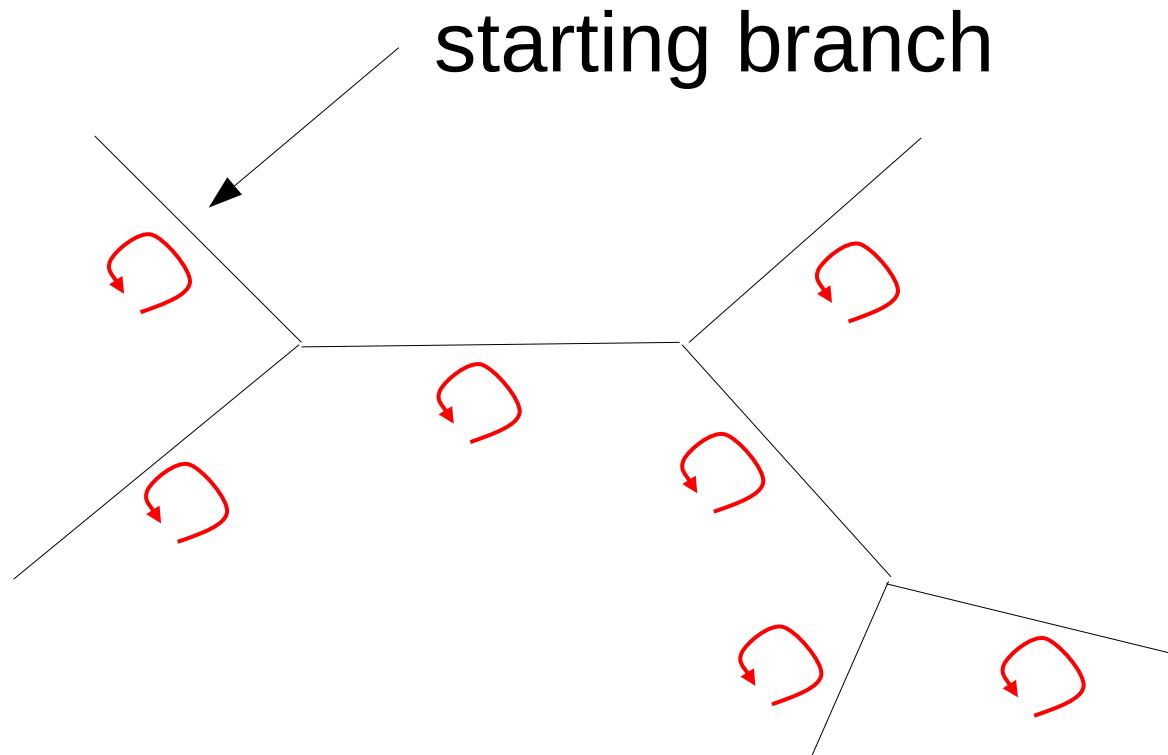
Branch Length Optimization



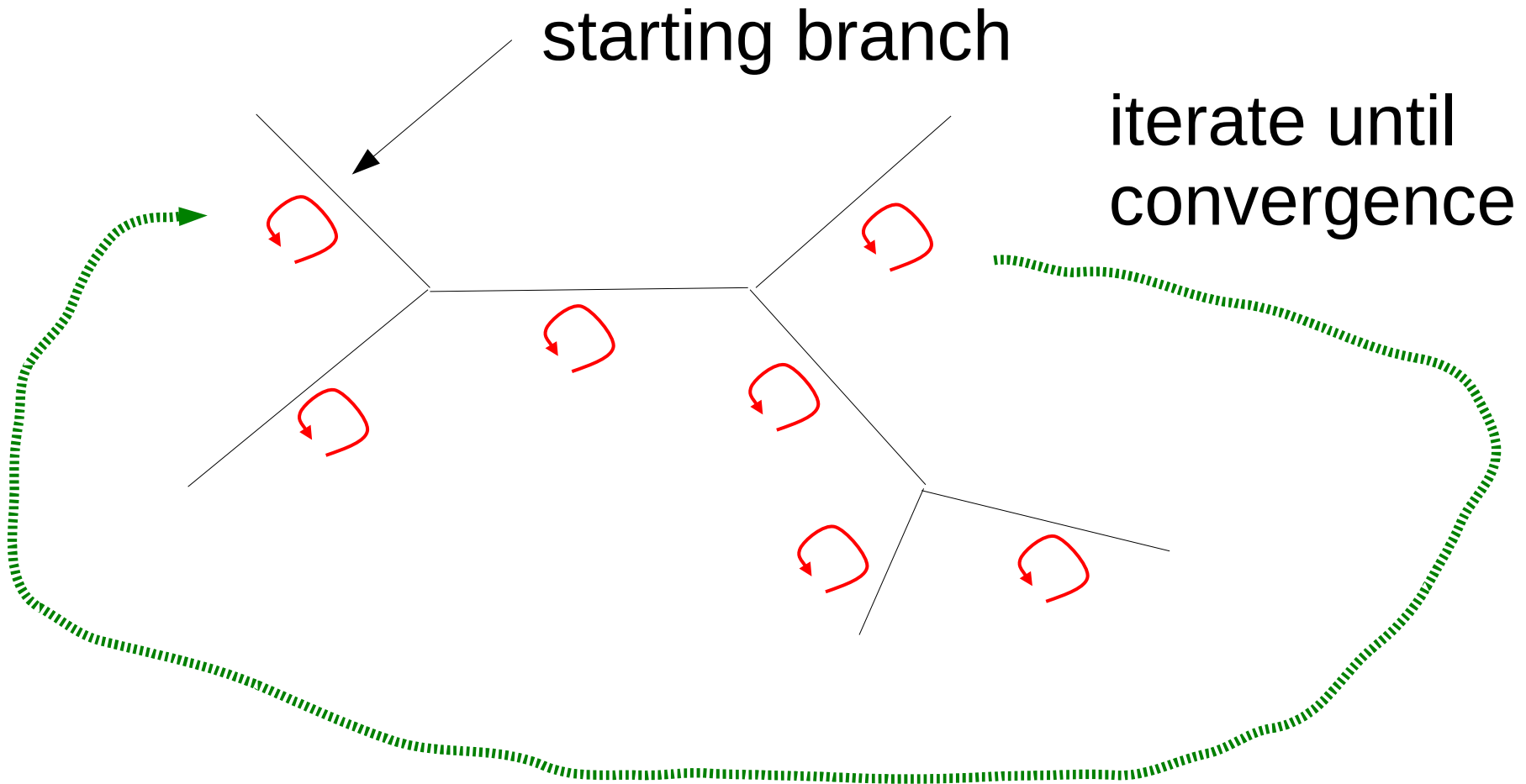
Branch Length Optimization



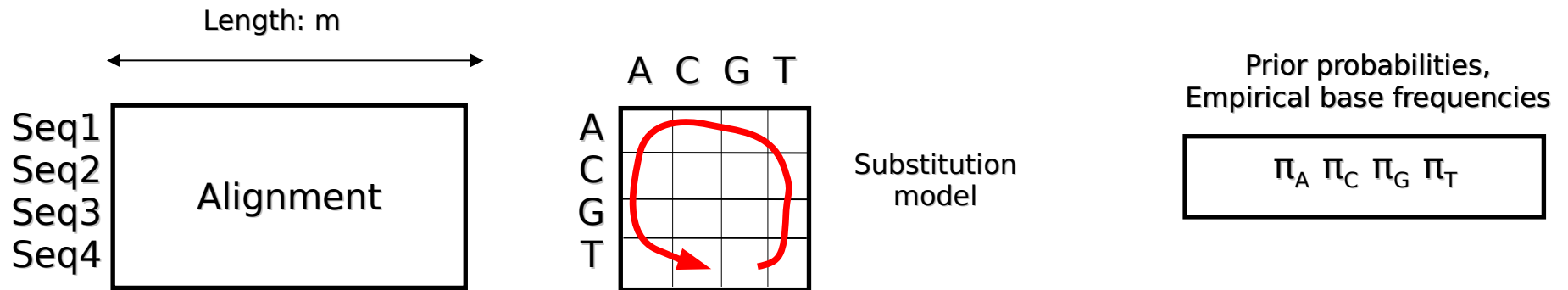
Branch Length Optimization



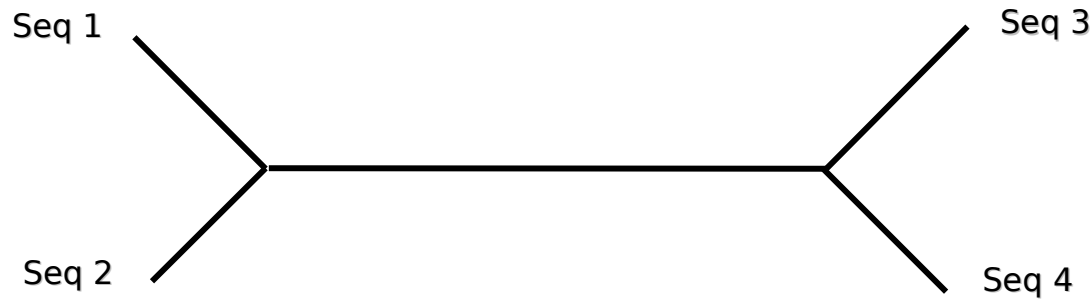
Branch Length Optimization



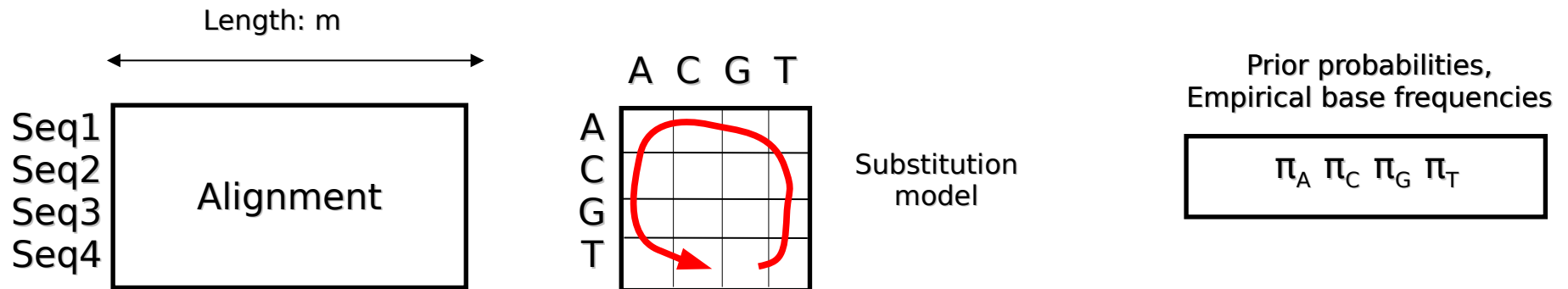
Maximum Likelihood



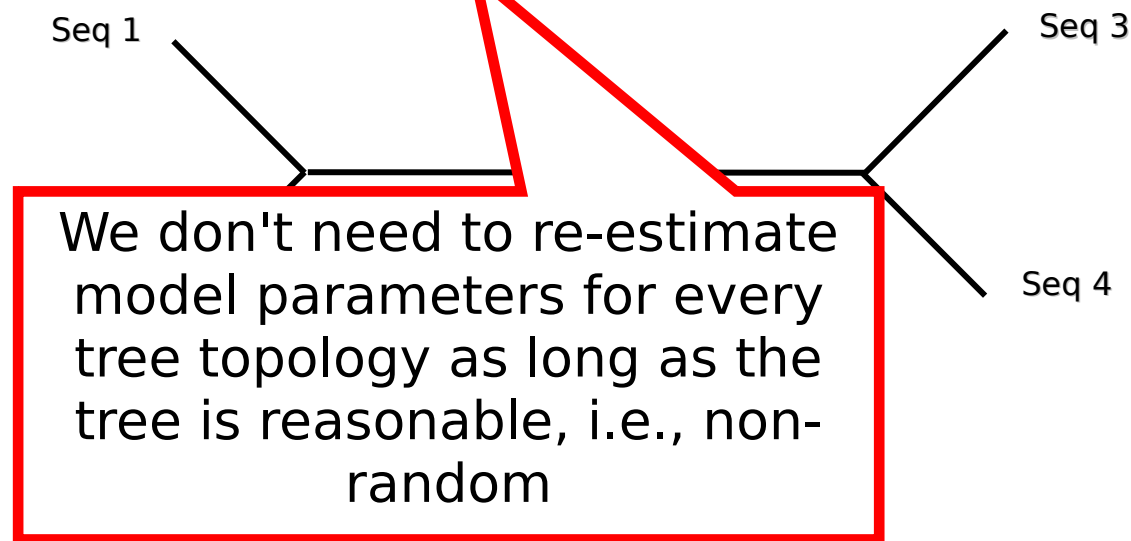
optimize model parameters



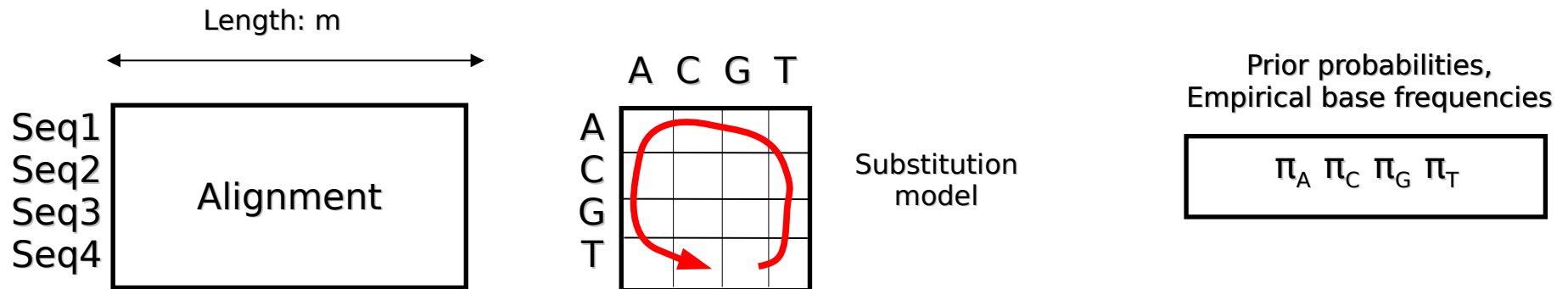
Maximum Likelihood



optimize model parameters



Maximum Likelihood



optimize model parameters

Seq 1

Seq 3

Methods used for model parameter optimization (other than branch lengths)

1. BFGS
2. Brent's method
3. Expectation maximization approaches

Numerical Optimization Procedures

- See chapters 9 & 10 of: *Numerical Recipes in C – The Art of Scientific Computing*

Basic Operations

Maximum Likelihood

- Compute Conditional Likelihood Vector at an inner node
- Compute Likelihood at Virtual Root
- Optimize a Branch Length for a given Branch
- Optimize all Branch Lengths
- Optimize other Model Parameters

Basic Operations

Maximum Likelihood

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The optimizers are the tricky routines!