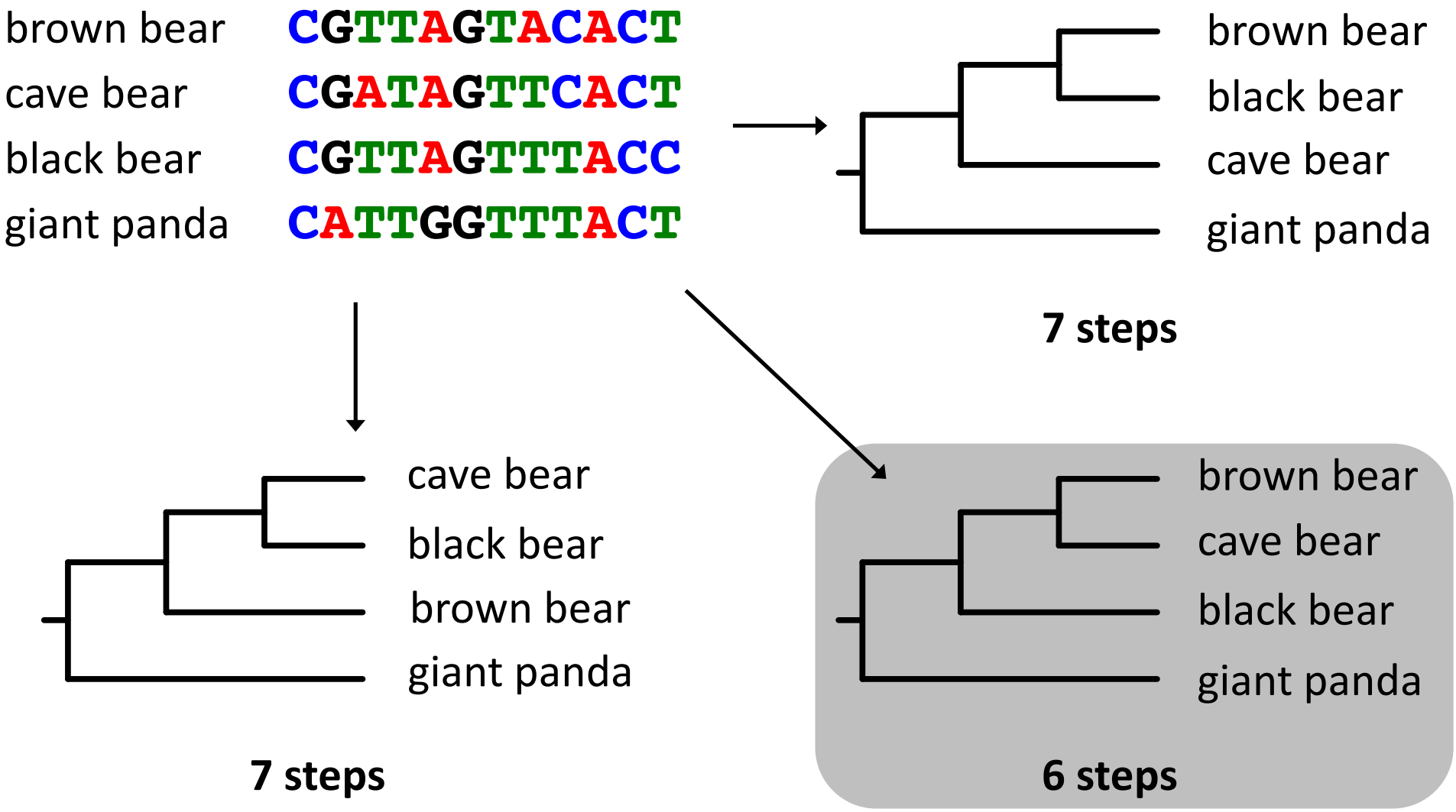
Lecture 1.4

Phylogenetic Methods

Maximum parsimony



Popular phylogenetic methods

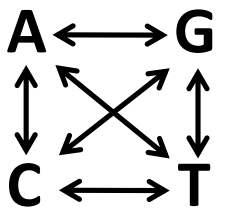
1. Maximum parsimony
2. Distance-based methods
3. Maximum likelihood
4. Bayesian inference

Model-based methods

Distance-Based Methods

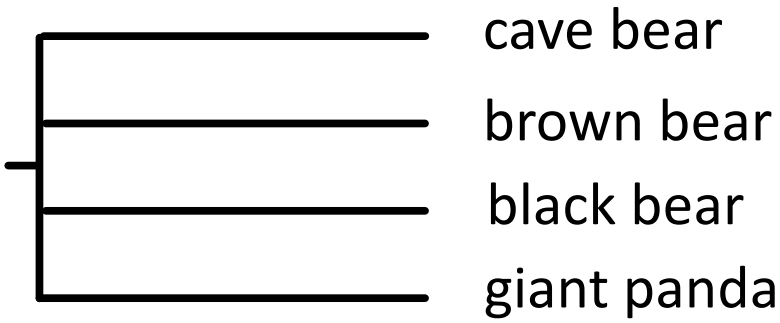
Neighbour joining

brown bear	CGTTAGTACACT
cave bear	CGATAGTTCACT
black bear	CGTTAGTTTACC
giant panda	CATTGGTTTACT



	brown bear	cave bear	black bear	giant panda
brown bear	–			
cave bear	.1	–		
black bear	.3	.3	–	
giant panda	.4	.5	.4	–

Clustering algorithm



Neighbour joining

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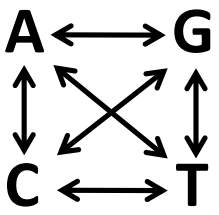

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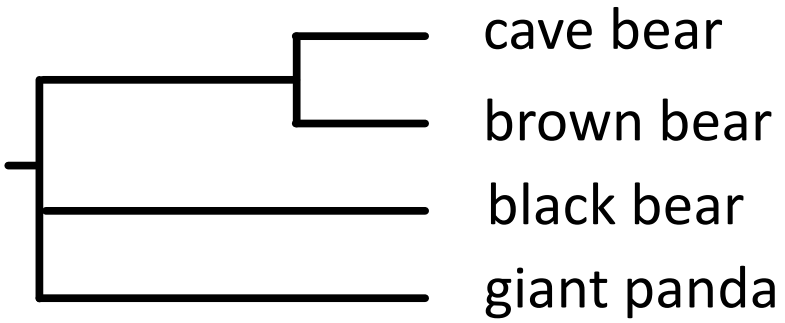
Clustering algorithm



Neighbour joining

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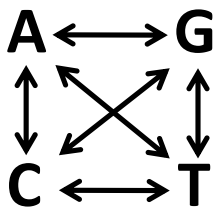

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brown bear	–			
cave bear	.1	–		
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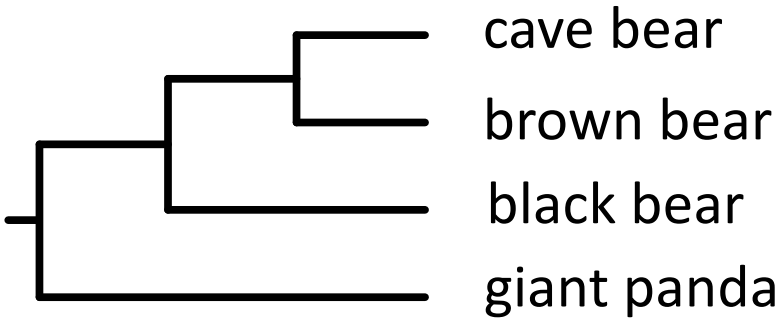
Clustering algorithm



Distance-based methods

- **Clustering algorithms**
  - Unweighted Pair Group Method with Arithmetic Mean (UPGMA)
  - Neighbour joining

- **Tree searching using optimality criteria**
  - Minimum evolution
  - Least-squares inference

Strengths and weaknesses

- **Strengths**
  - Very quick method
  - Deals with multiple substitutions and long-branch attraction

- **Weaknesses**
  - Does not use all information in alignment
  - Loss of information in pairwise comparisons
  - Unable to implement sophisticated evolutionary models

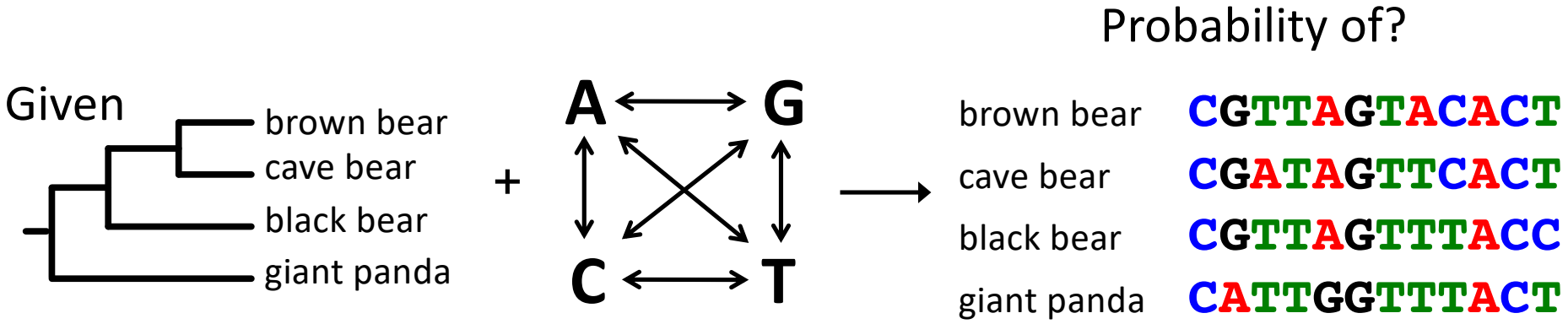
Maximum Likelihood

Maximum likelihood

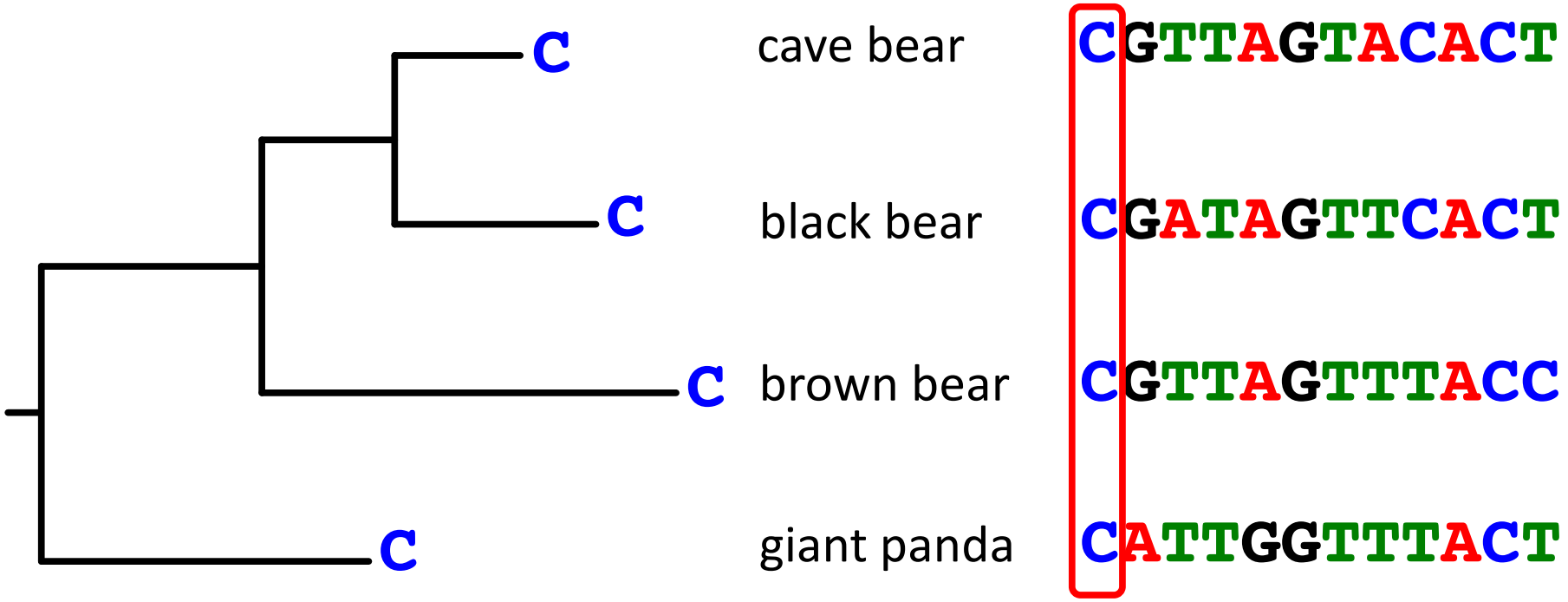
Likelihood of hypothesis *H* =

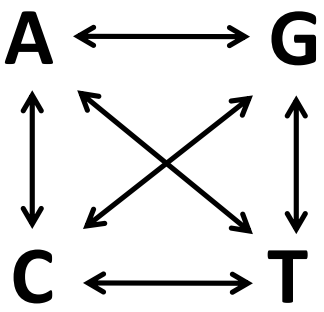
$$P(D|H)$$

Probability of the data, given the hypothesis

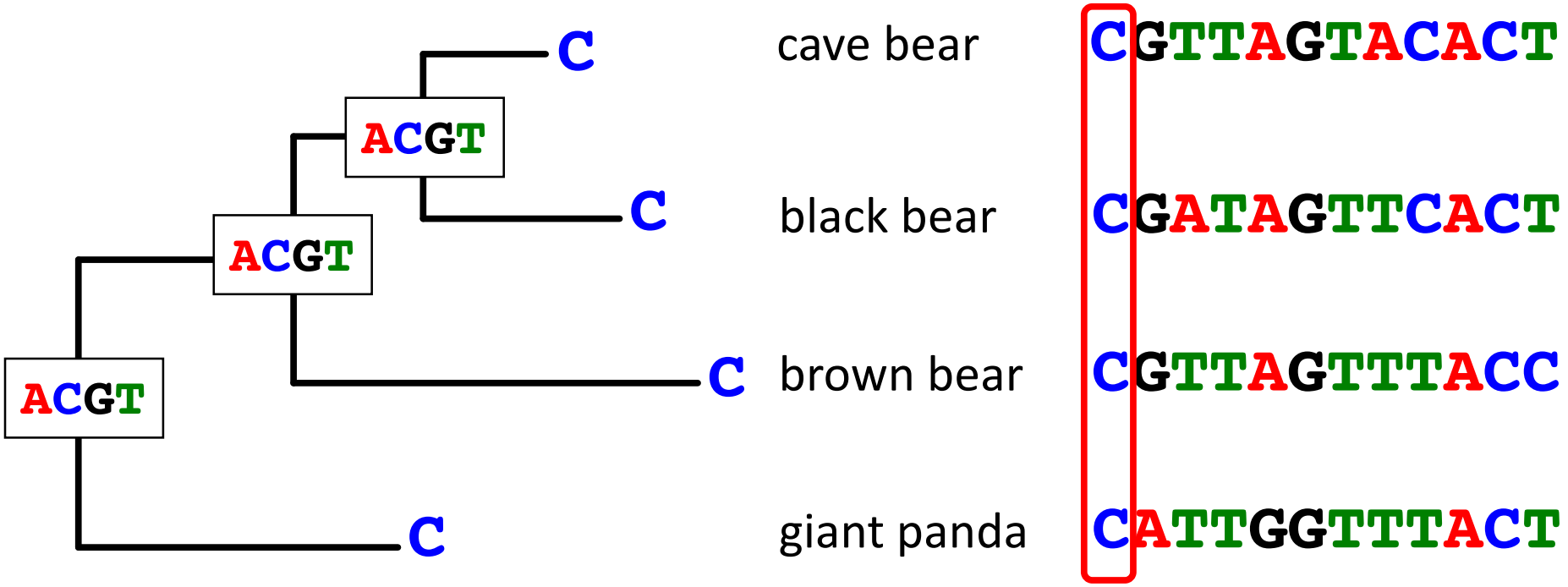


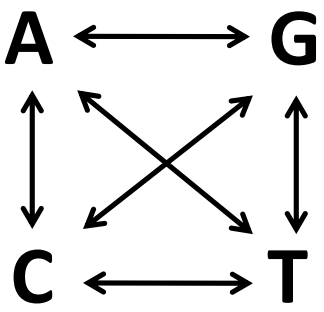
Maximum likelihood



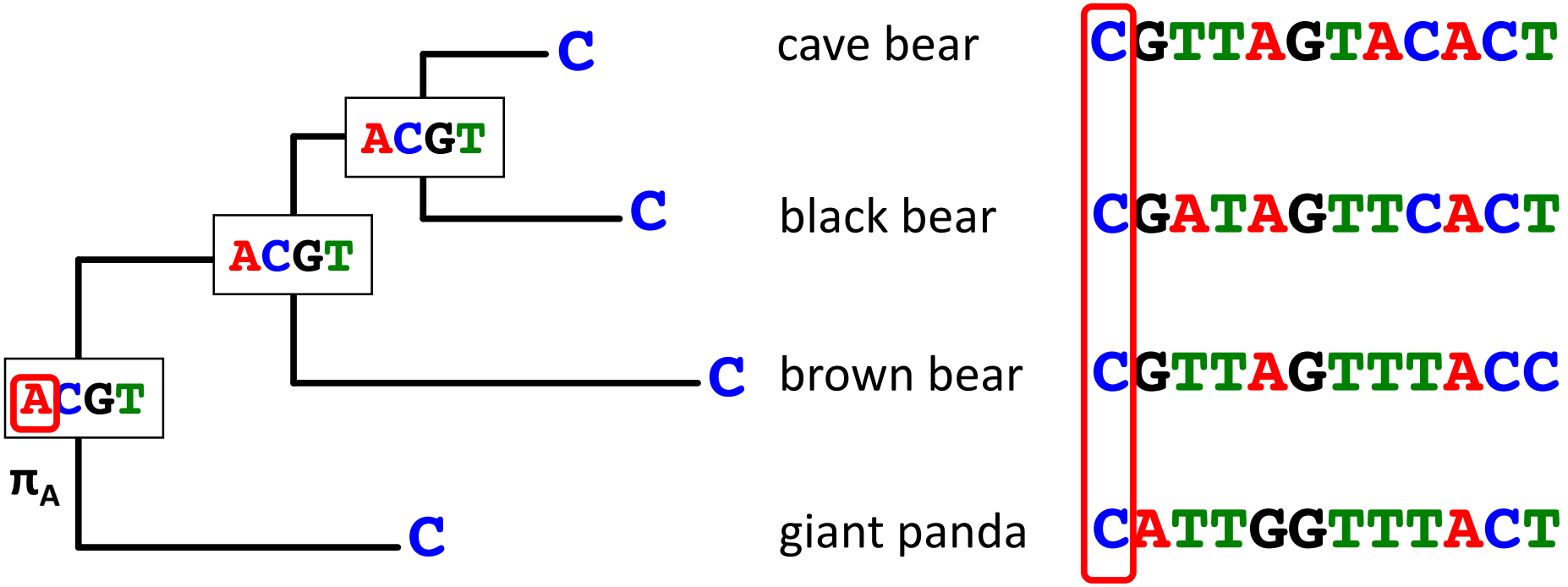


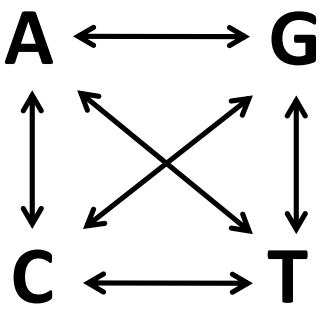
Maximum likelihood



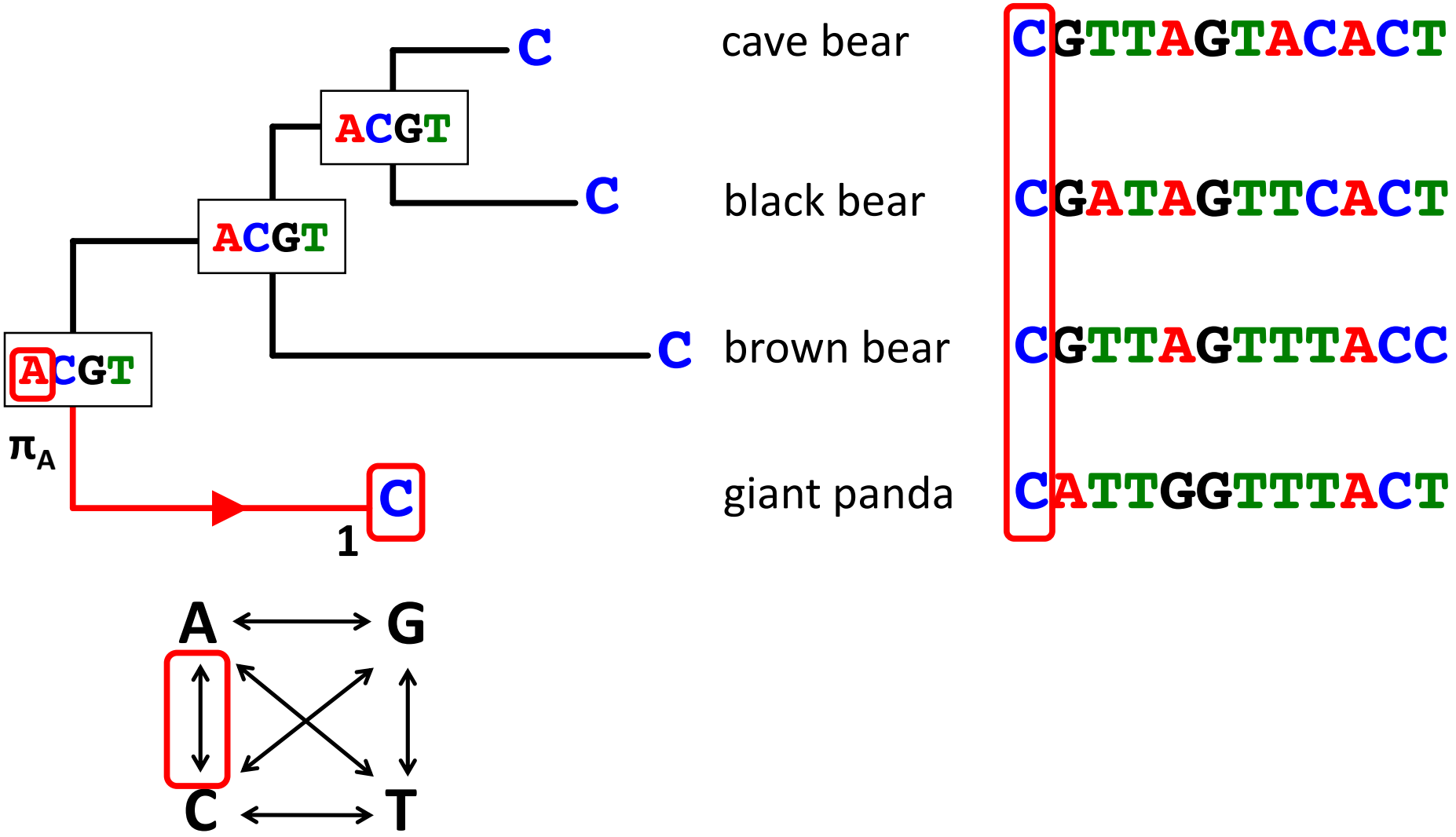


Maximum likelihood

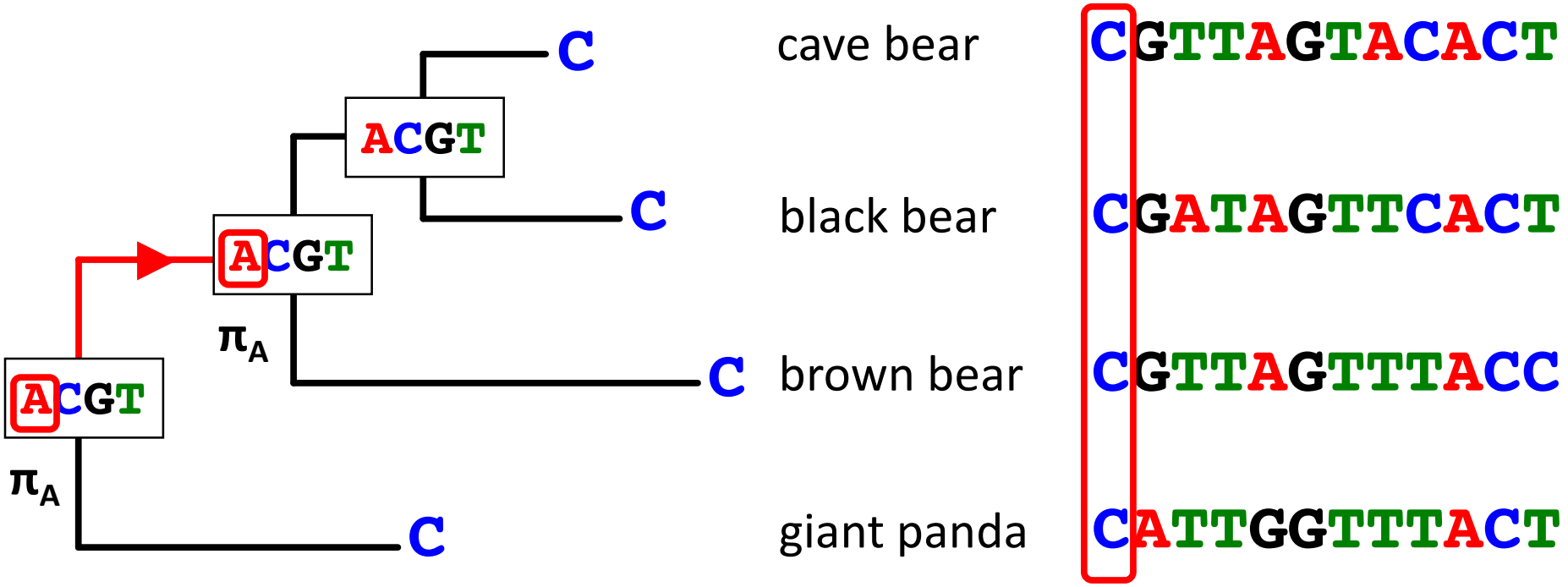


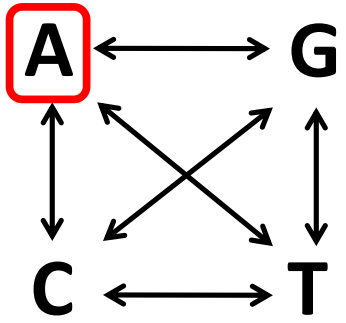


Maximum likelihood

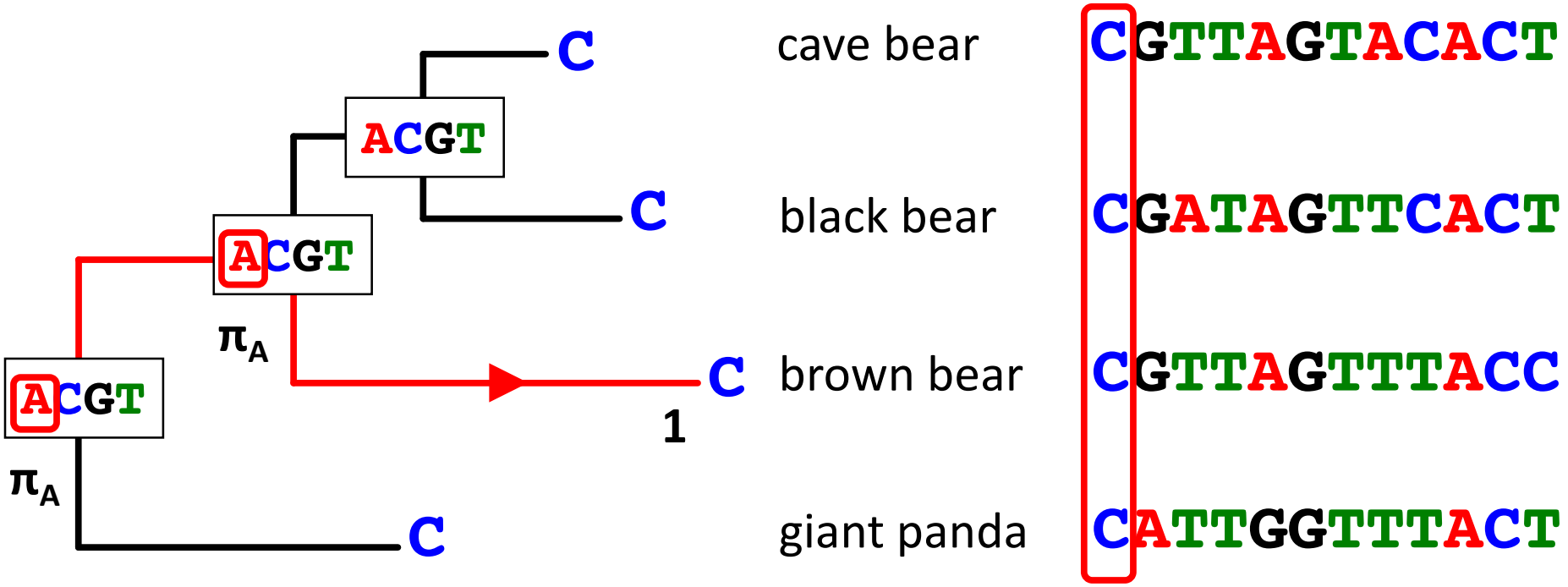


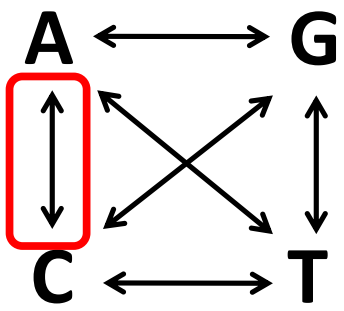
Maximum likelihood



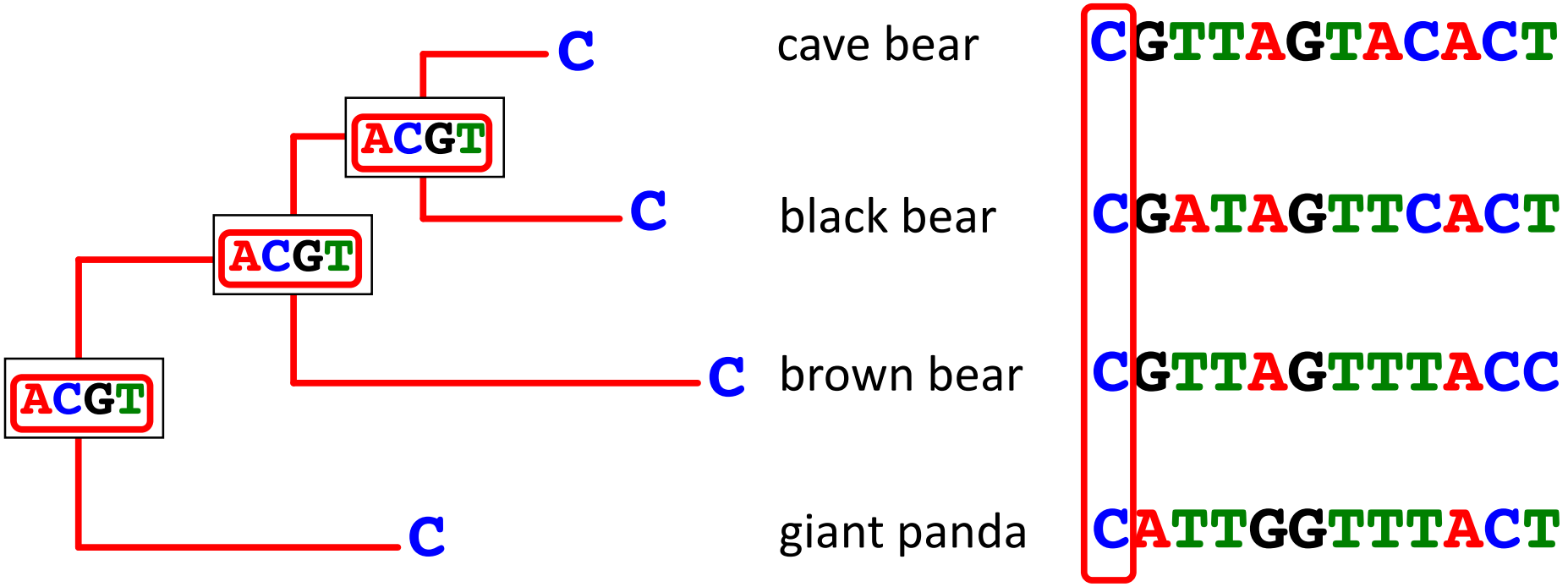


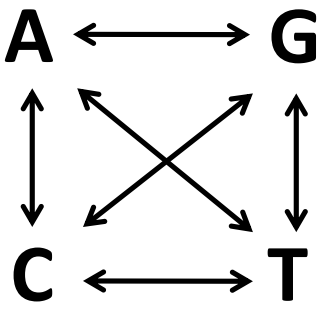
Maximum likelihood





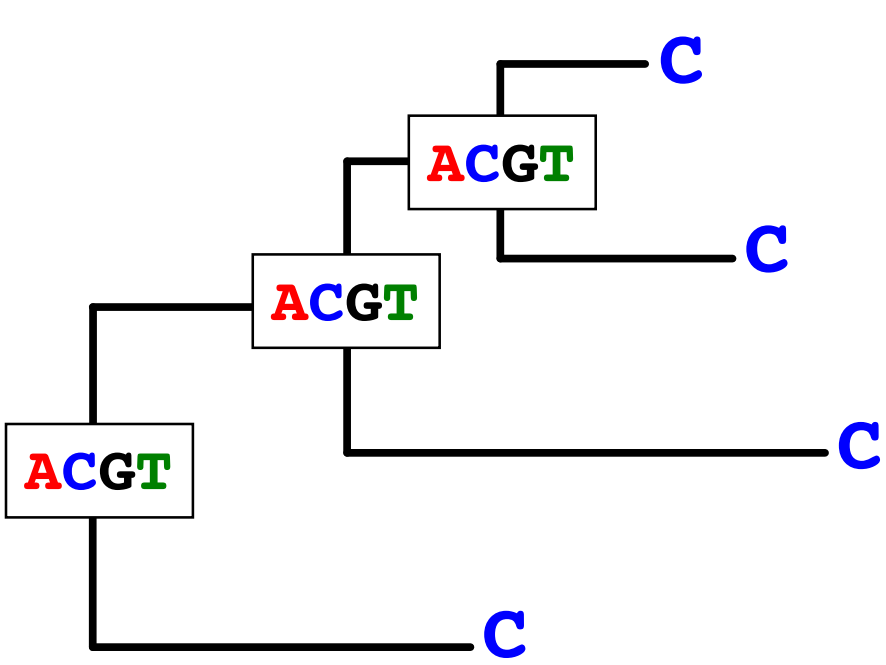
Maximum likelihood





Likelihood is summed over all possibilities

Maximum likelihood



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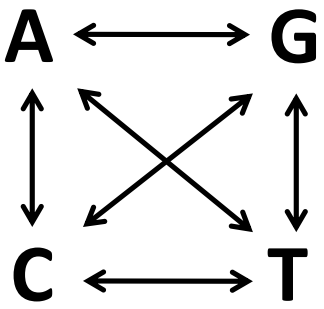
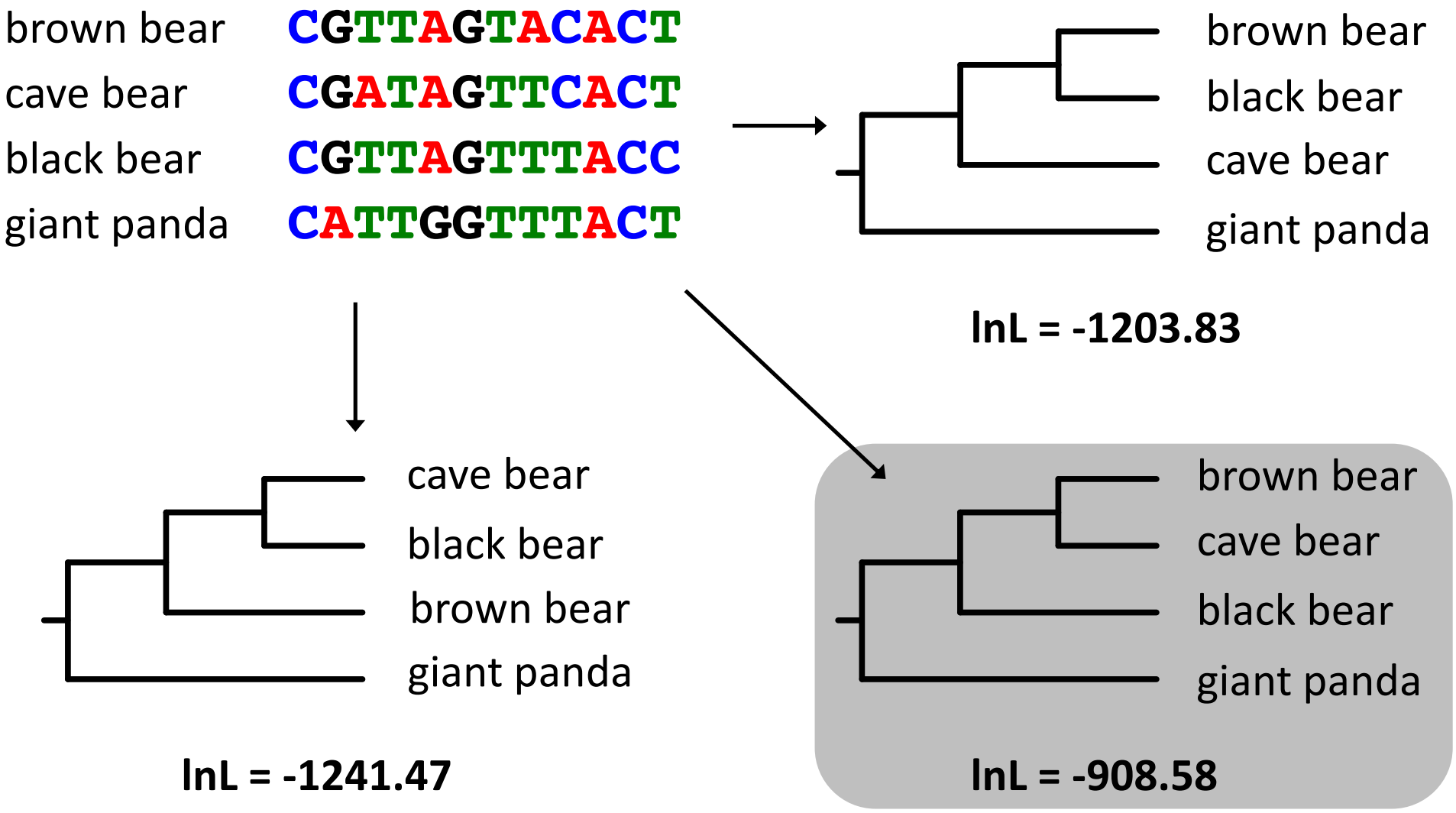


Likelihood is multiplied across all sites

Very low probability of observing any particular alignment

Maximum likelihood



Likelihood optimisation

- Search through the space of possible trees and parameter values
- Calculate the likelihood for these
- Find best tree and model parameter values
- Multivariate optimisation

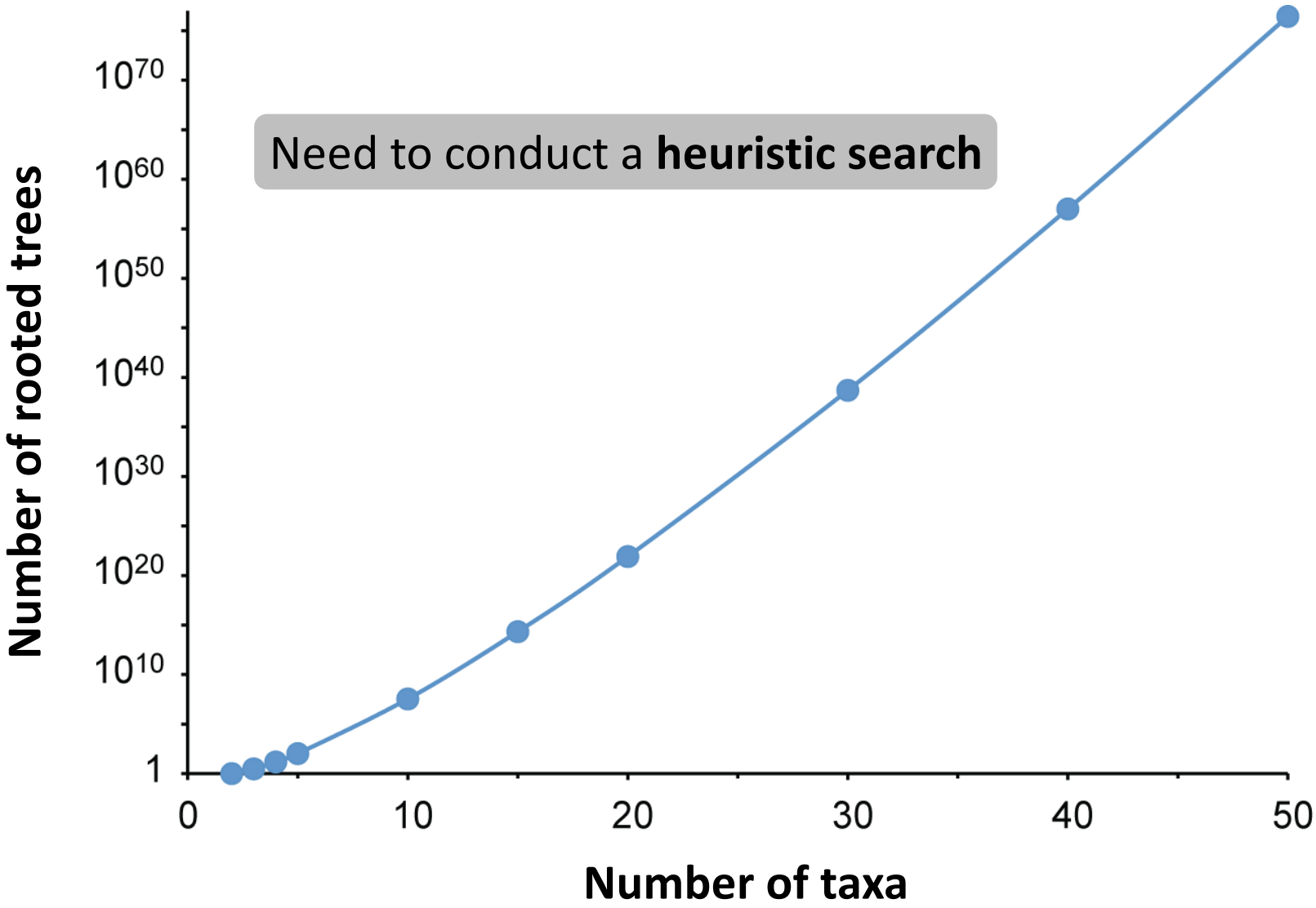
Finding the best tree

- For *n* taxa, the number of possible unrooted trees (B_n) is:

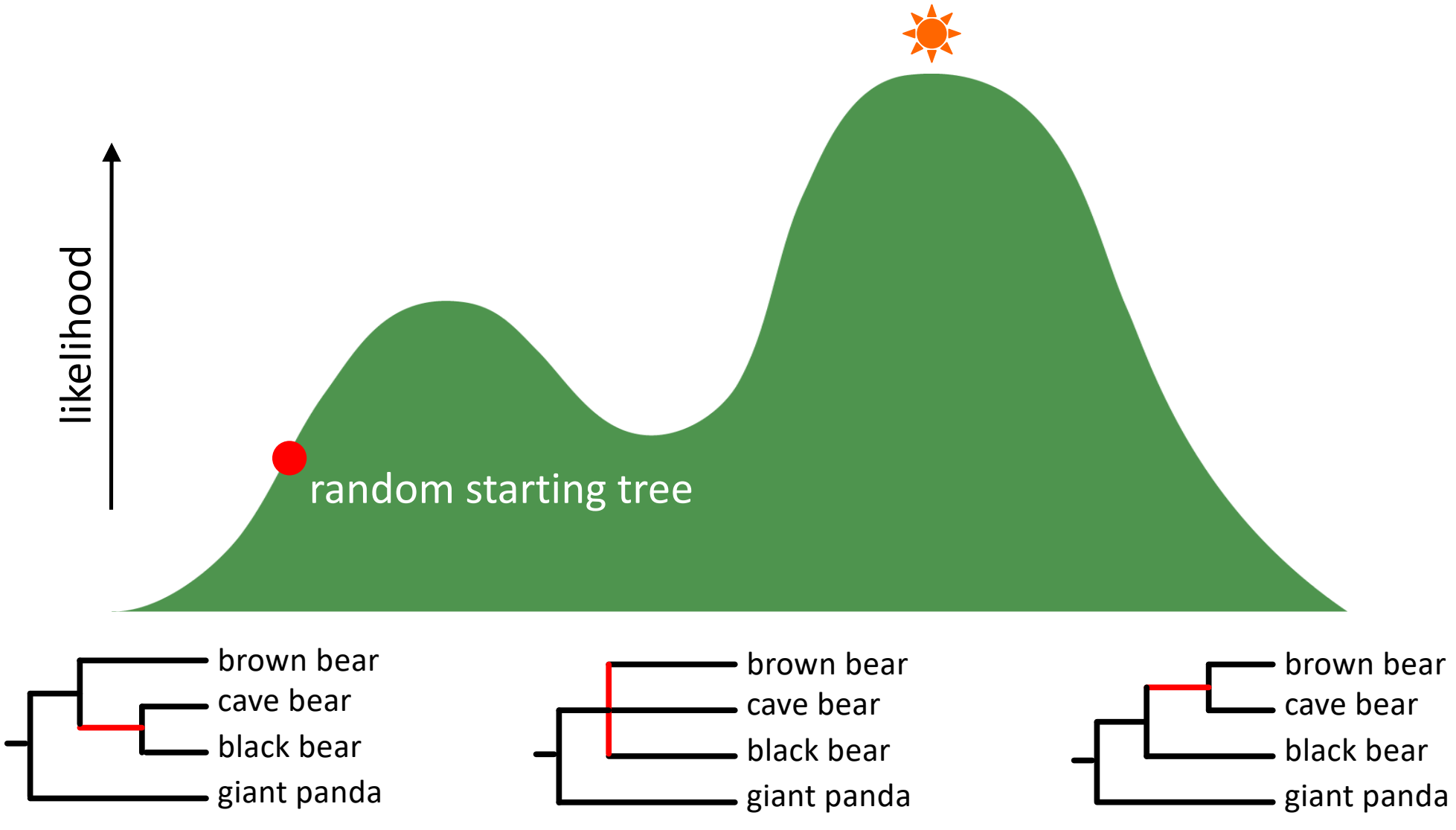
$$B_n = 1 \times 3 \times 5 \times \ldots \times (2n-5) = \prod_{i=3}^{n} (2i-5)$$

- For example:
  - 4 taxa → 3 trees
  - 5 taxa → 15 trees
  - 10 taxa → 2,027,025 trees

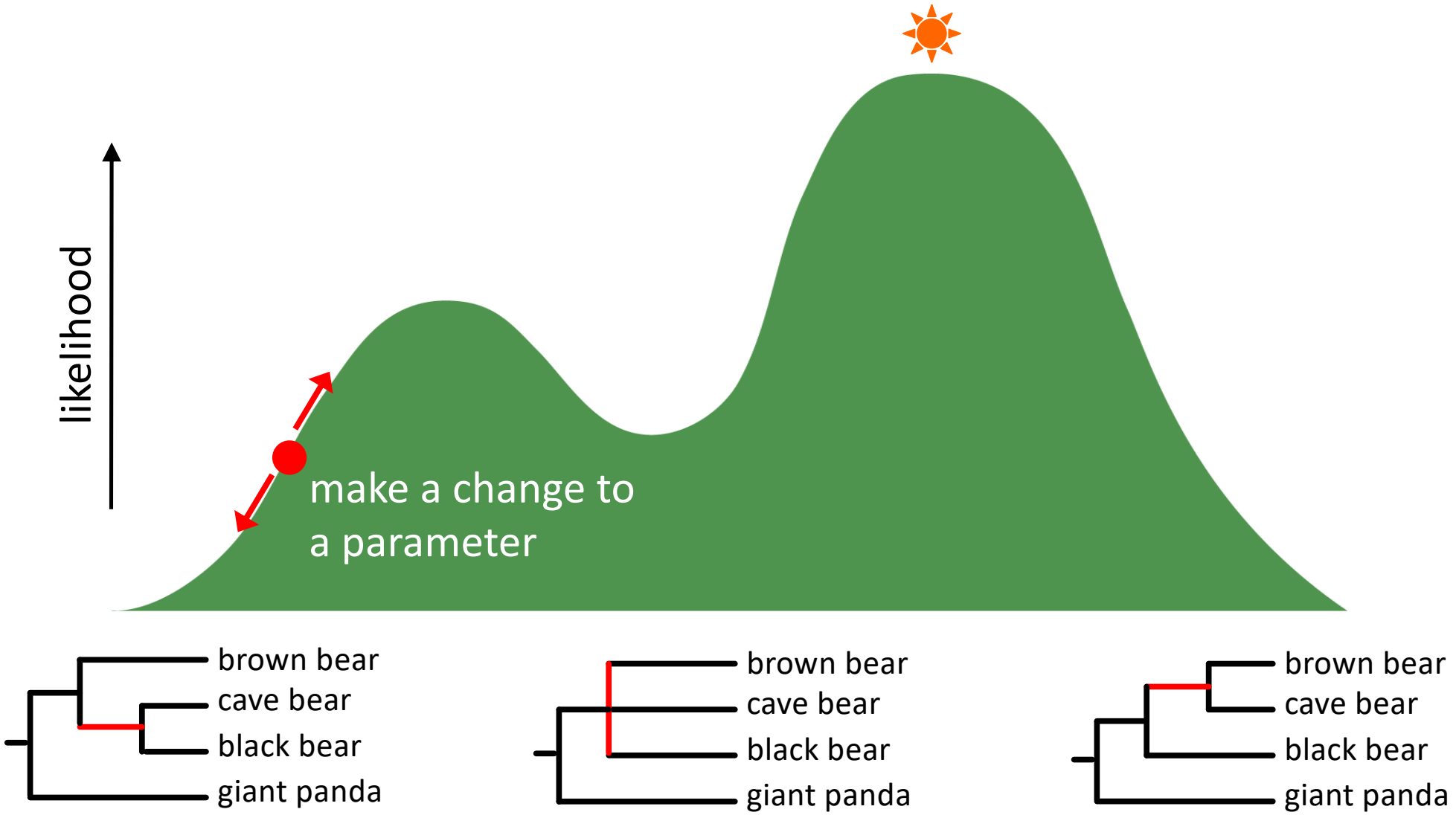
Finding the best tree



Heuristic search



Heuristic search



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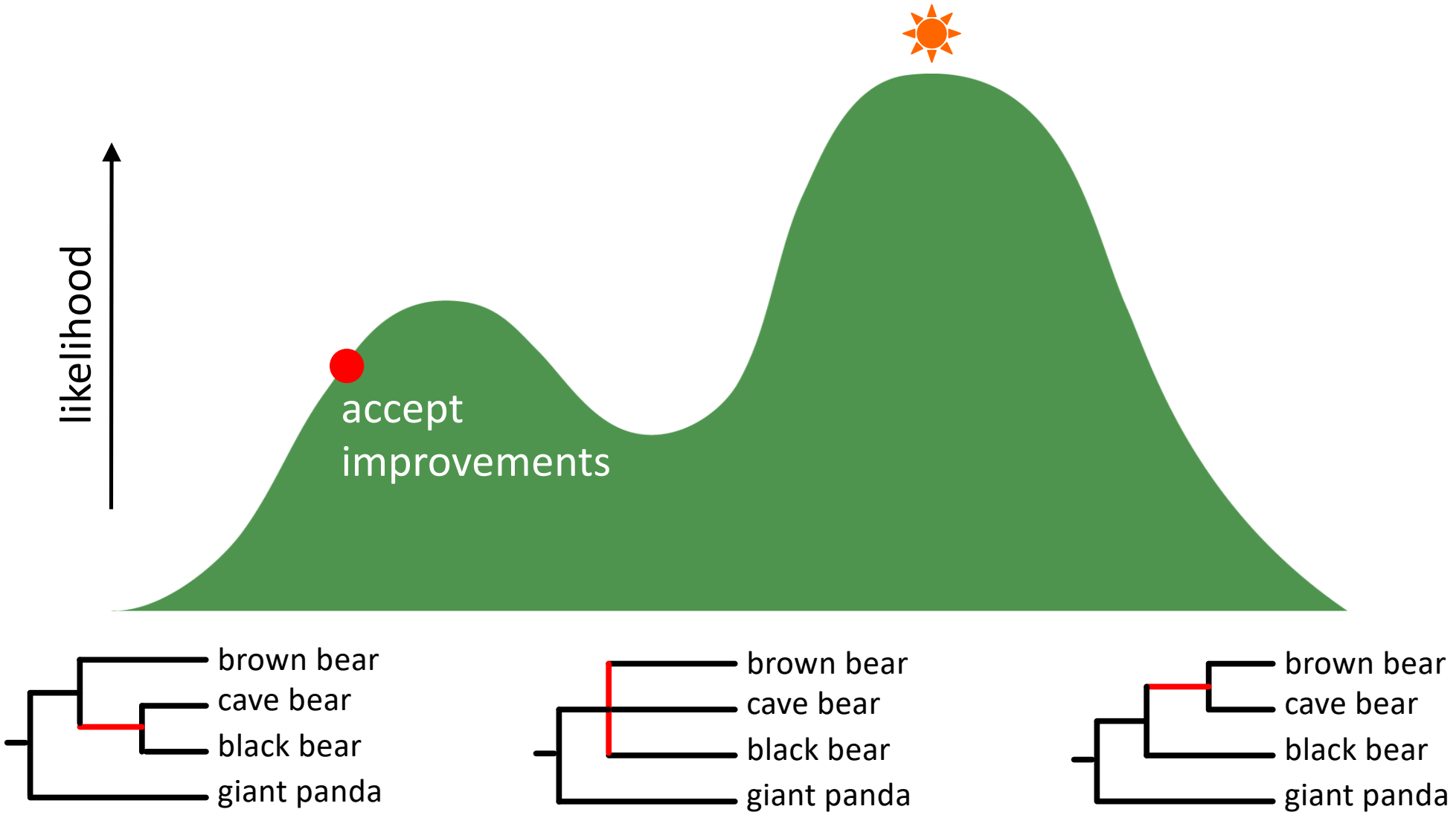

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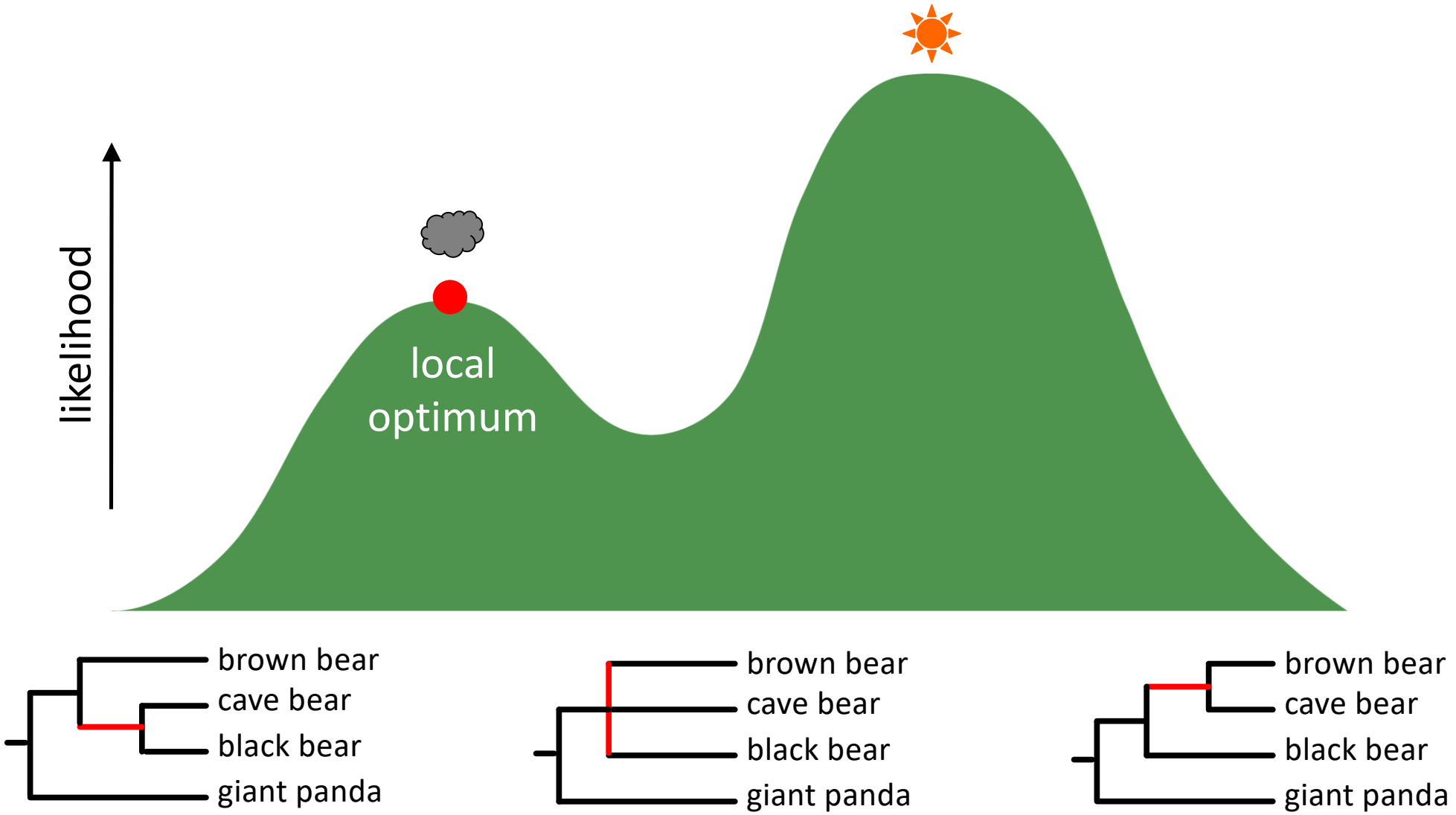

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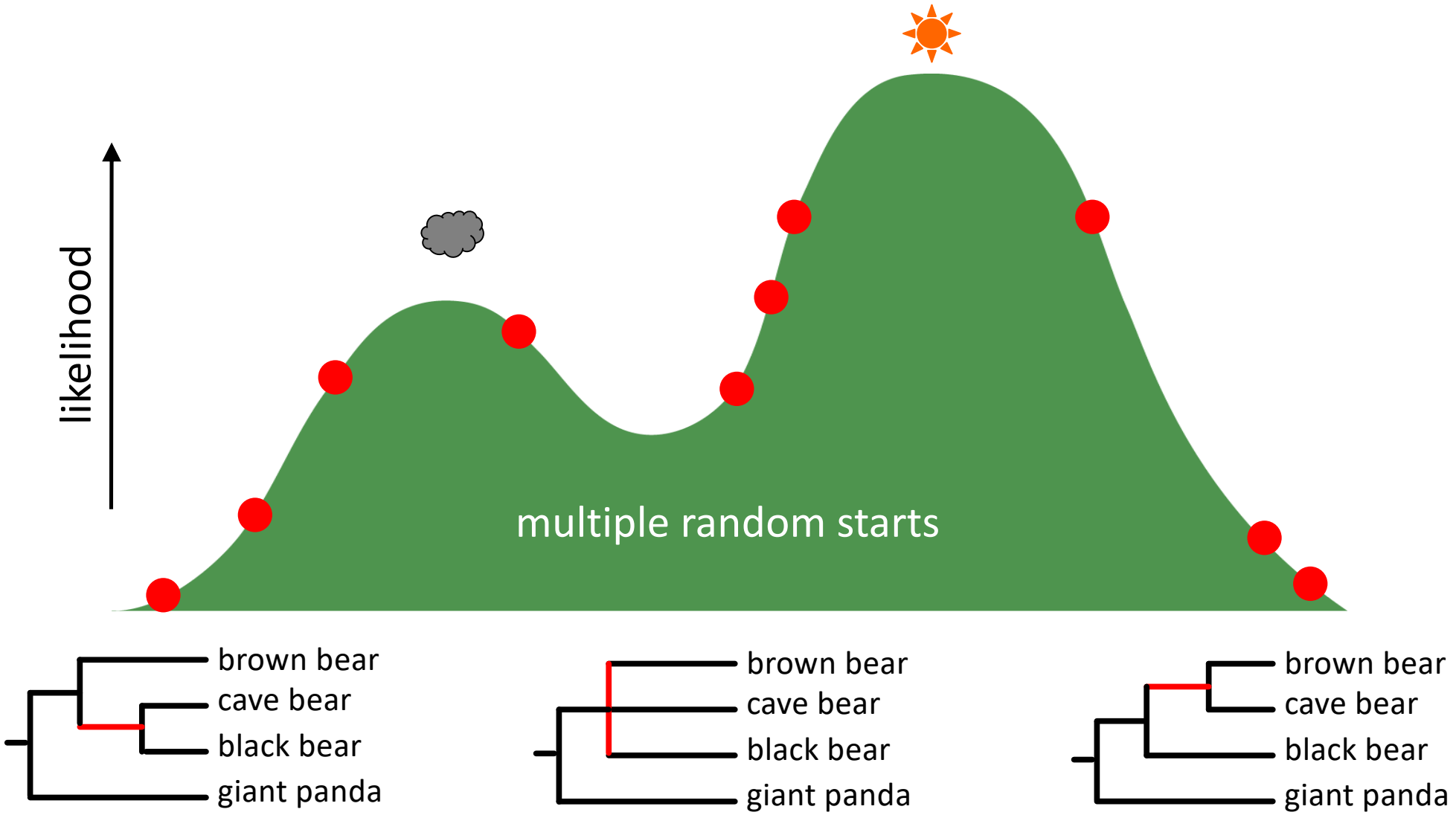
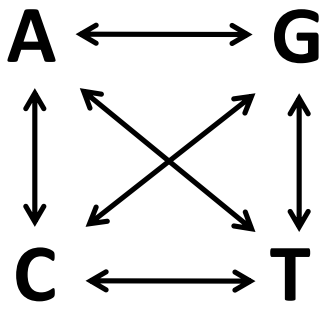
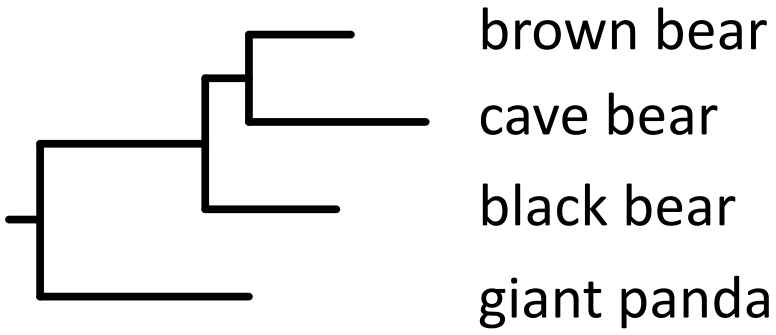


Maximum-likelihood estimates

A single set of maximum-likelihood estimates of model parameters



A single maximum-likelihood tree



Strengths and weaknesses

- **Strengths**
  - Rigorous statistical method
  - Deals with multiple substitutions and long-branch attraction
  - Highly robust to violations of assumptions

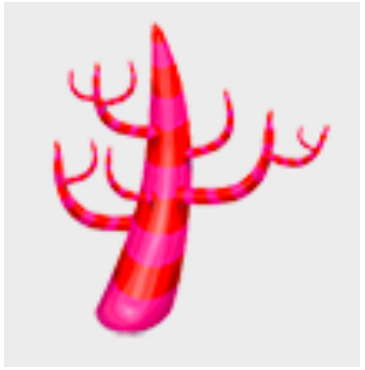
- **Weaknesses**
  - Not feasible to implement very parameter-rich models
  - Searching tree space can be difficult

Software

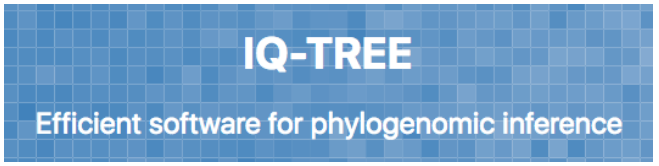
RAxML

PhyML

MEGA



PAML



IQ-TREE

RAxML

- **R**andomized **Ax**elerated **M**aximum **L**ikelihood
- Compile to suit your processor architecture
- Can run sequentially or in parallel
- Rapid bootstrapping (Stamatakis *et al*. 2008)

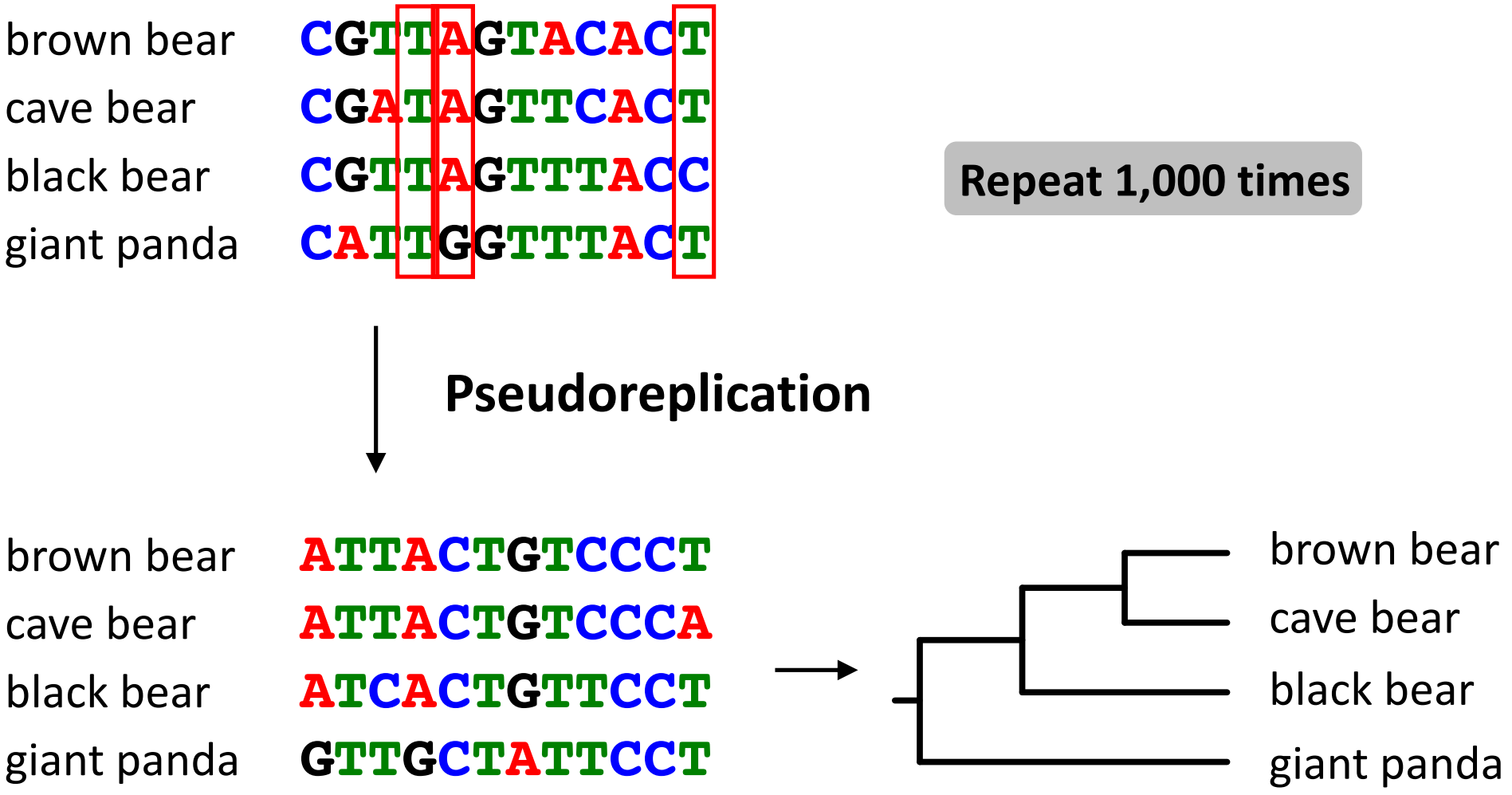
Bootstrapping

Nonparametric bootstrap

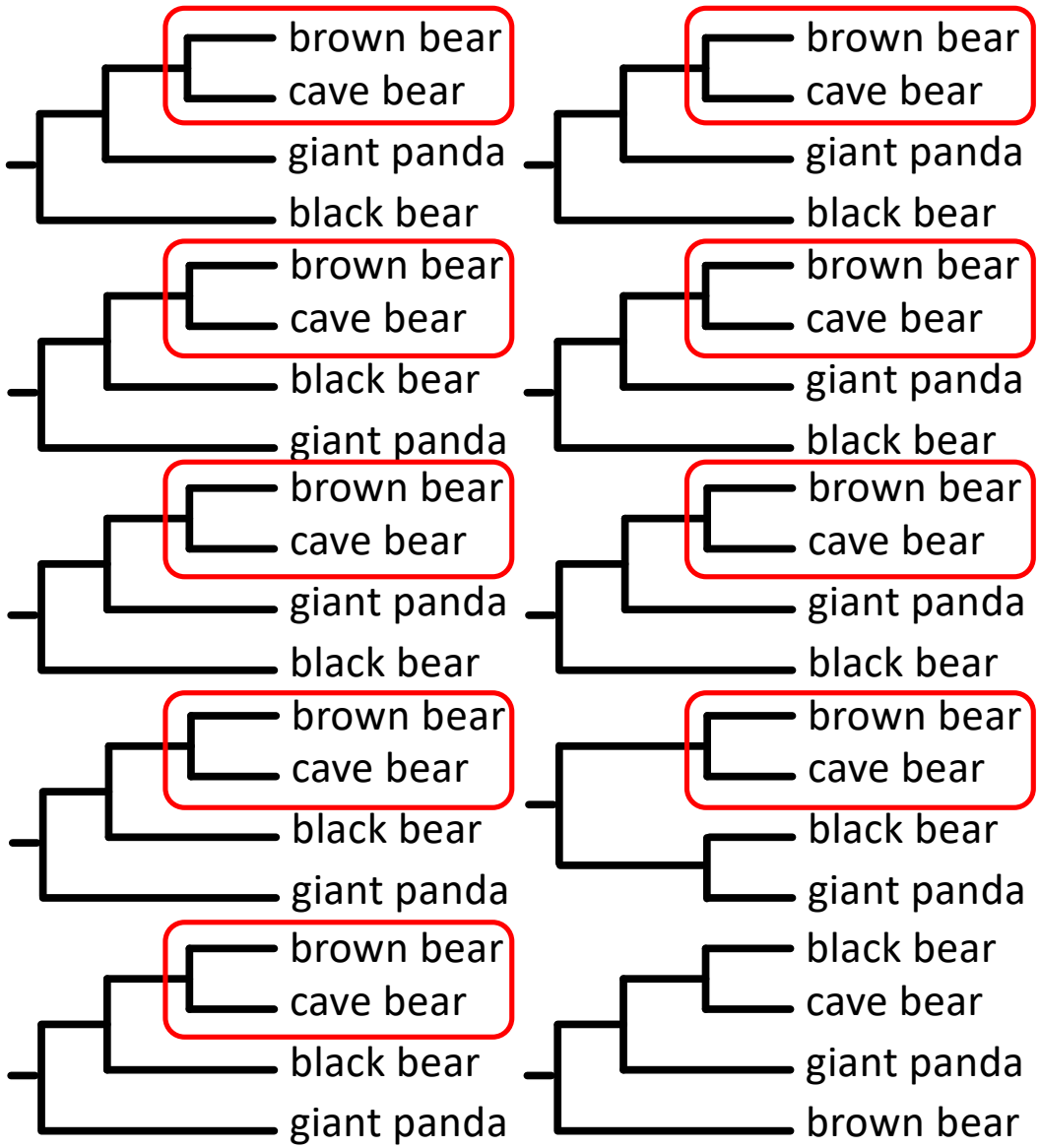
- Uncertainty in the estimate of the tree is inferred indirectly using **bootstrapping analysis**
- “pull oneself up by one's bootstraps”

  - Bootstrapping analysis can be used in various phylogenetic methods:
    - Maximum parsimony
    - Distance-based methods
    - Maximum likelihood

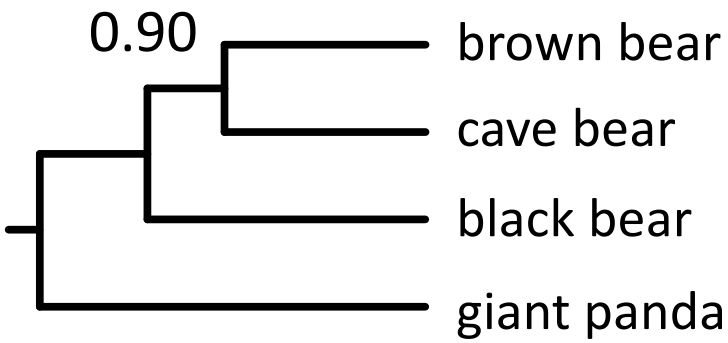
Bootstrapping



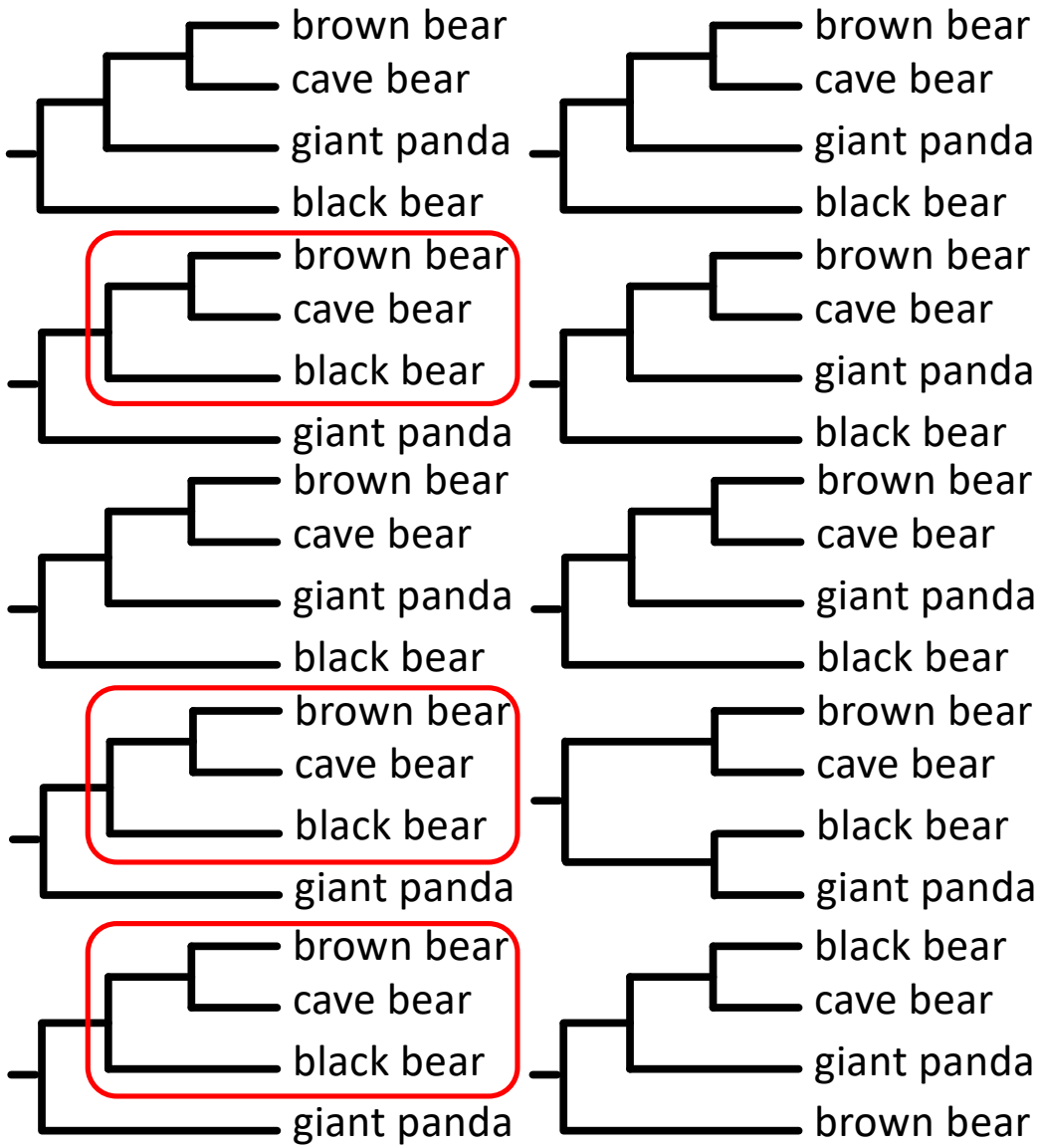
Bootstrapping



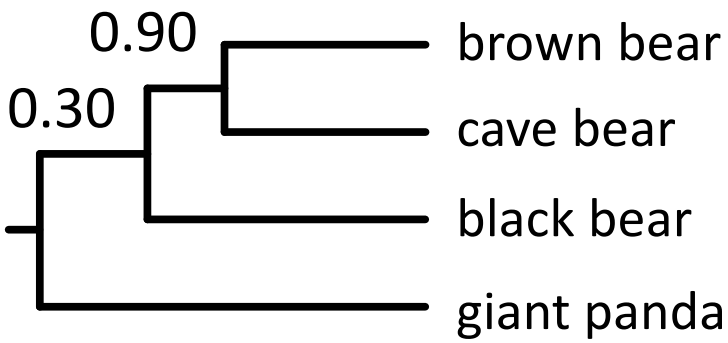
ML tree



Bootstrapping



ML tree



Interpreting bootstrap values

- **Felsenstein (1985)**
  bootstrapping provides a confidence interval that contains the *phylogeny that would be estimated from repeated sampling of many characters from the underlying set of all characters*

- Bootstrap values are **measures of repeatability**
  - High when the data set is large
  - Not meaningful when analysing genome-scale data

Soltis & Soltis (2003) *Stat Sci*

Methods in practice

- **Maximum parsimony**
  - Commonly used to analyse morphological data
  - Rarely used to analyse molecular data
- **Distance-based methods**
  - Popular in some fields of research
  - Used to analyse very large data sets with many taxa
- **Maximum likelihood**
  - Widely used, but has been losing ground to Bayesian methods

Useful references

- **Molecular phylogenetics: principles and practice**
  Yang & Rannala (2012) *Nature Reviews Genetics* 13: 303–314.