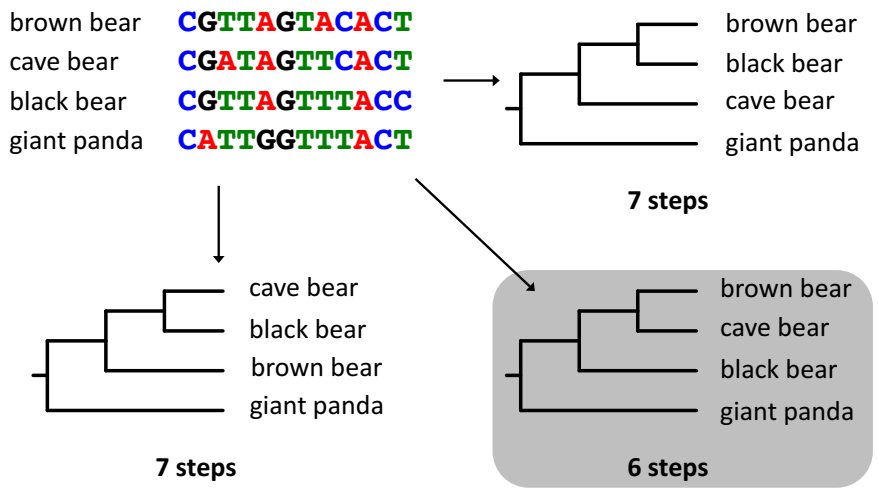
Lecture 1.4

Phylogenetic Methods

Simon Ho

Maximum parsimony



Popular phylogenetic methods

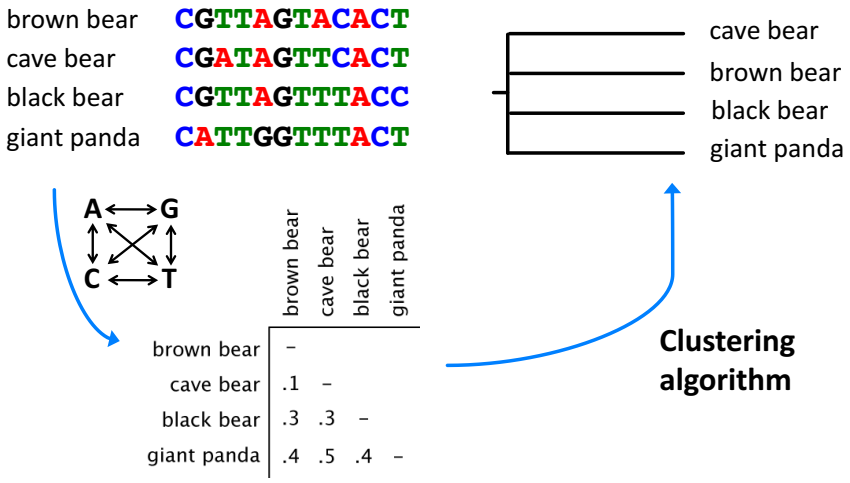
1. Maximum parsimony
2. Distance-based methods
3. Maximum likelihood
4. Bayesian inference

Model-based methods

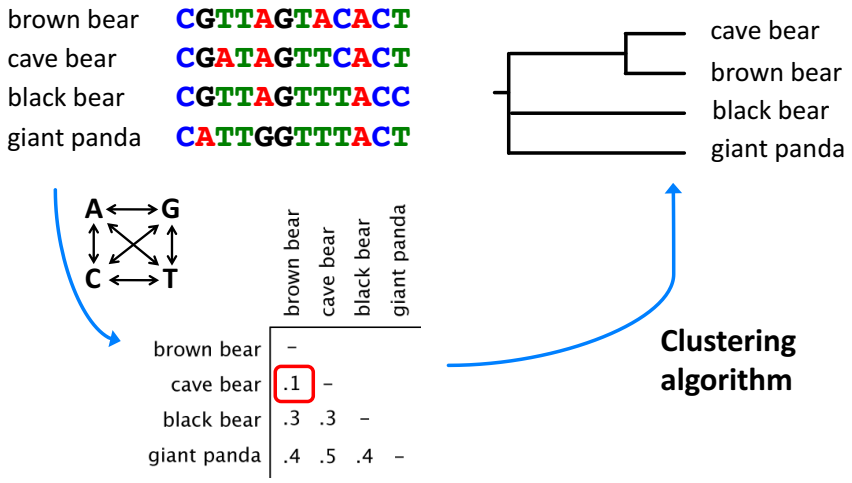



Distance-Based Methods

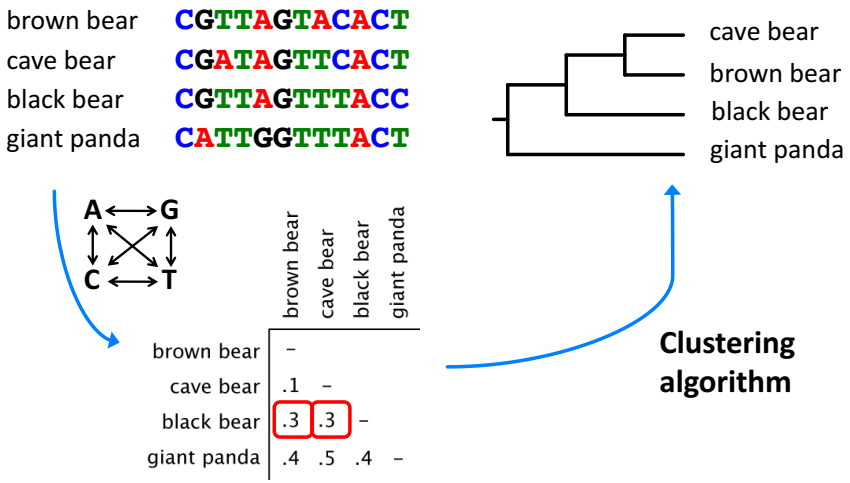
Neighbour joining



Neighbour joining



Neighbour joining



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

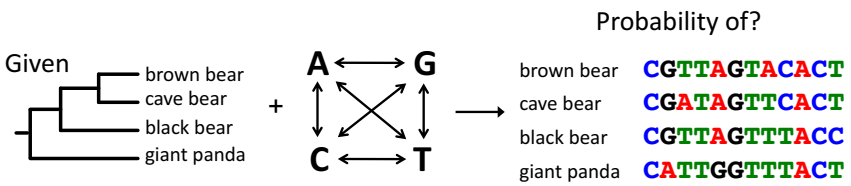
Maximum Likelihood

Maximum likelihood

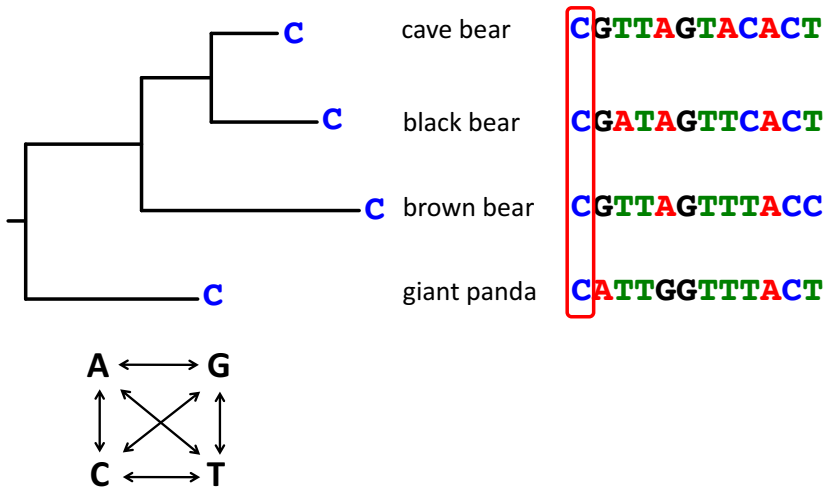
Likelihood of hypothesis *H* =

$P(D|H)$

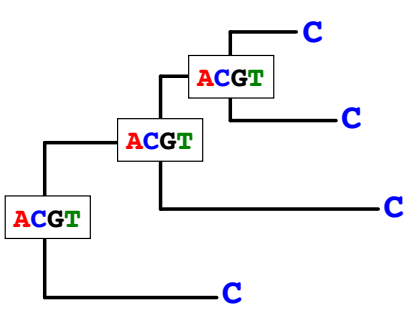
Probability of the data, given the hypothesis



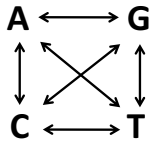
Maximum likelihood



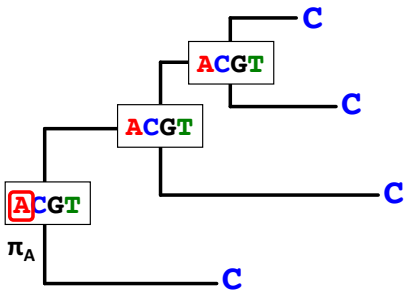
Maximum likelihood



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



Maximum likelihood



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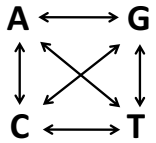
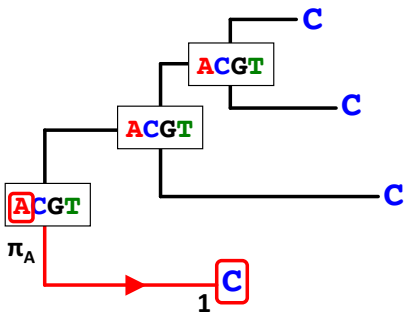


Maximum likelihood



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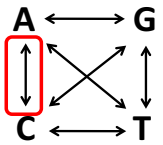
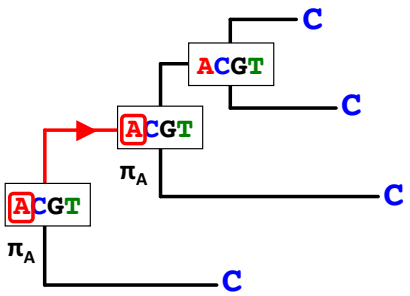


Maximum likelihood



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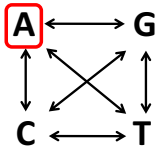
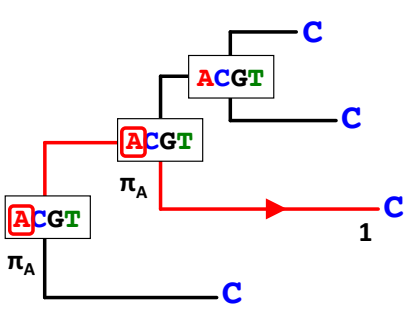


Maximum likelihood



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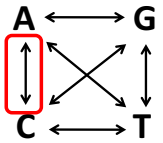
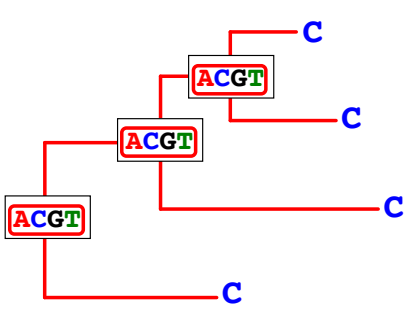


Maximum likelihood



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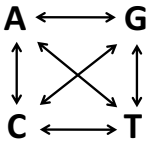
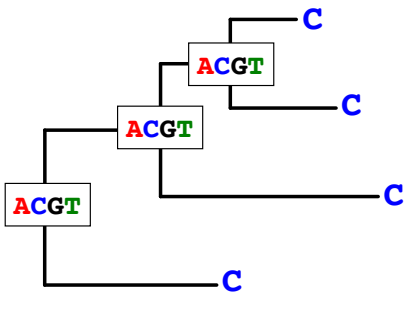


Likelihood is summed over all possibilities

Maximum likelihood



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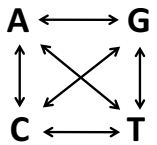
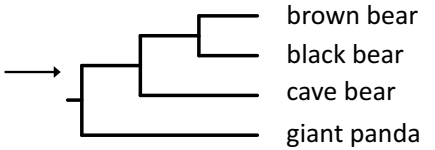


Likelihood is multiplied across all sites

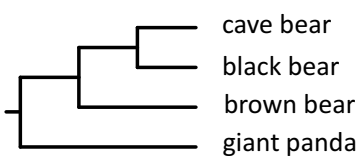
Very low probability of observing any particular alignment

Maximum likelihood

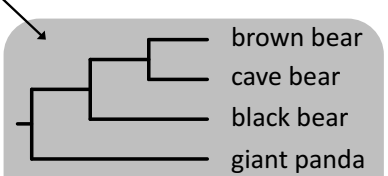
brown bear	CGTTAGTACACT
cave bear	CGATAGTTCACT
black bear	CGTTAGTTTACC
giant panda	CATTGGTTTACT



lnL = -1203.83



lnL = -1241.47

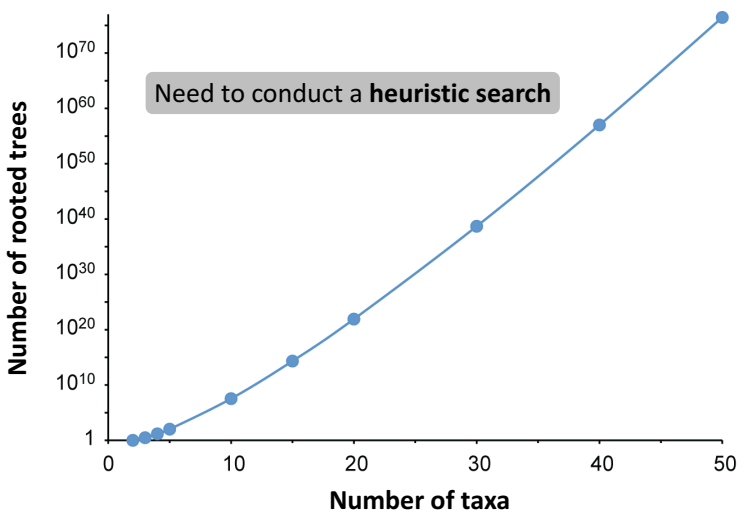


lnL = -908.58

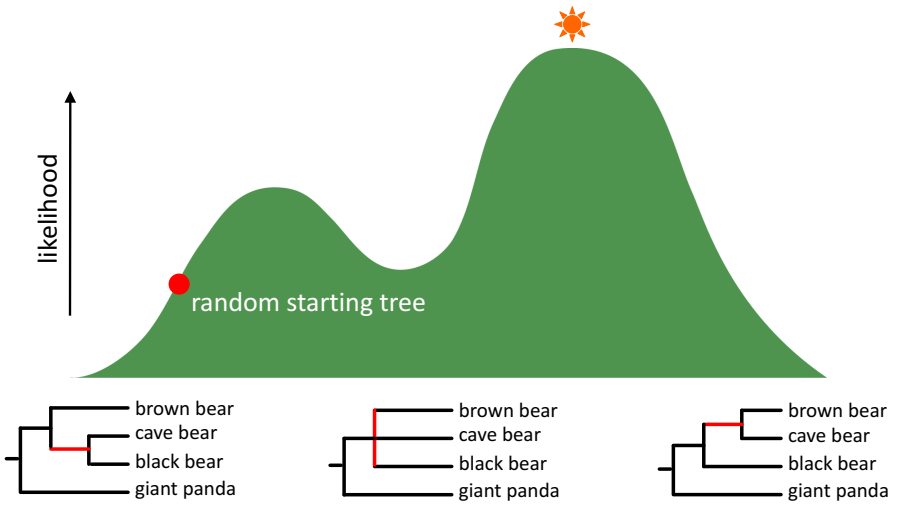
Likelihood optimisation

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

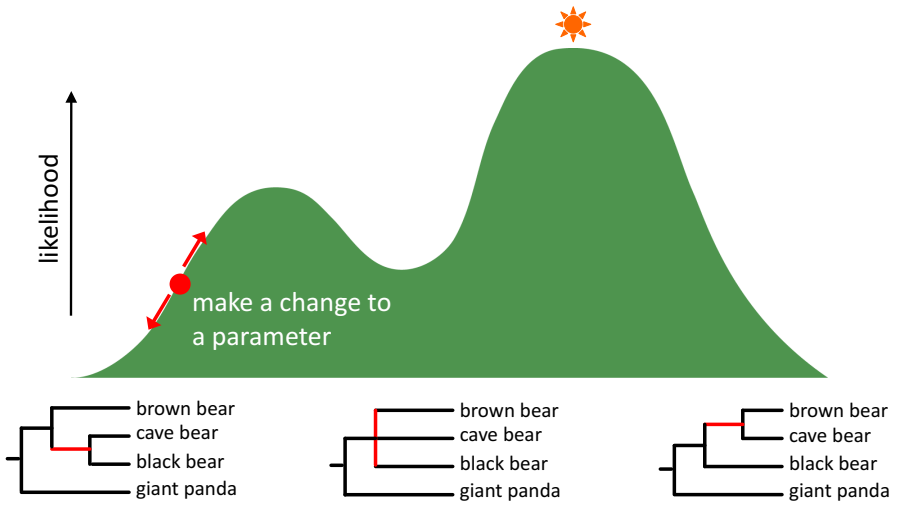
Likelihood optimisation



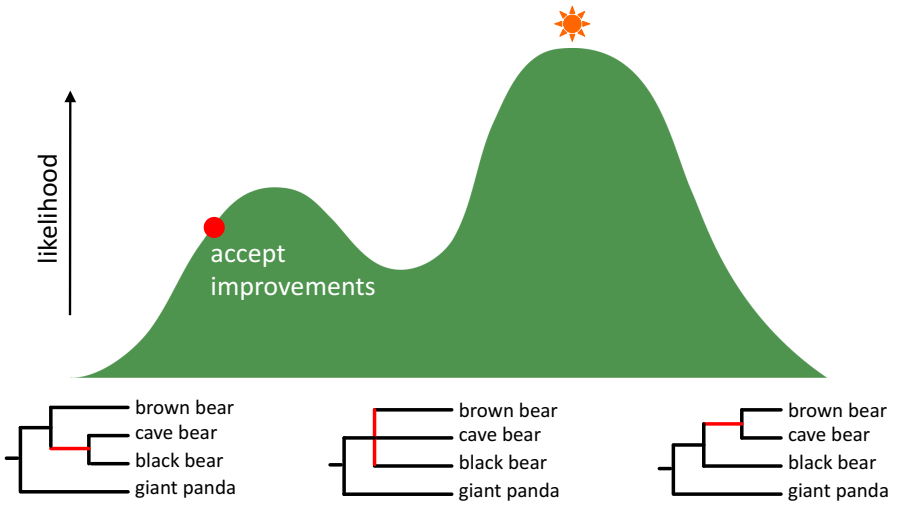
Heuristic search



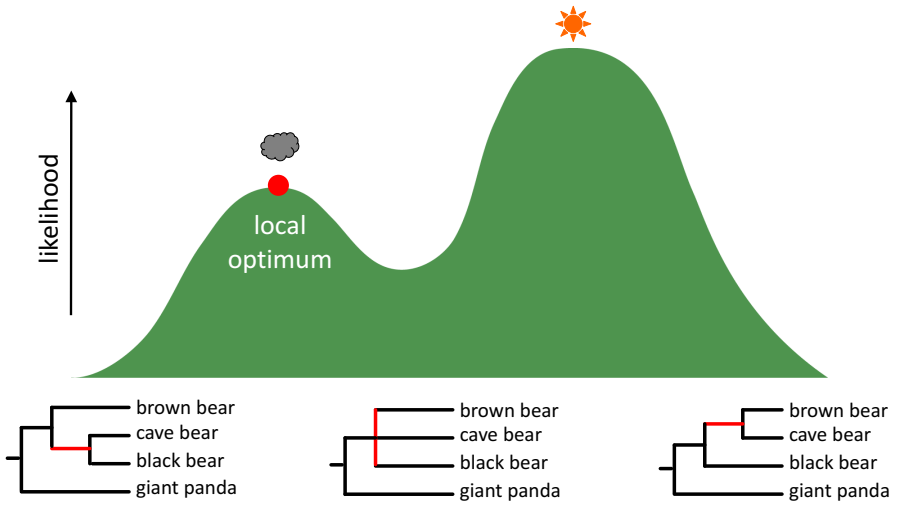
Heuristic search



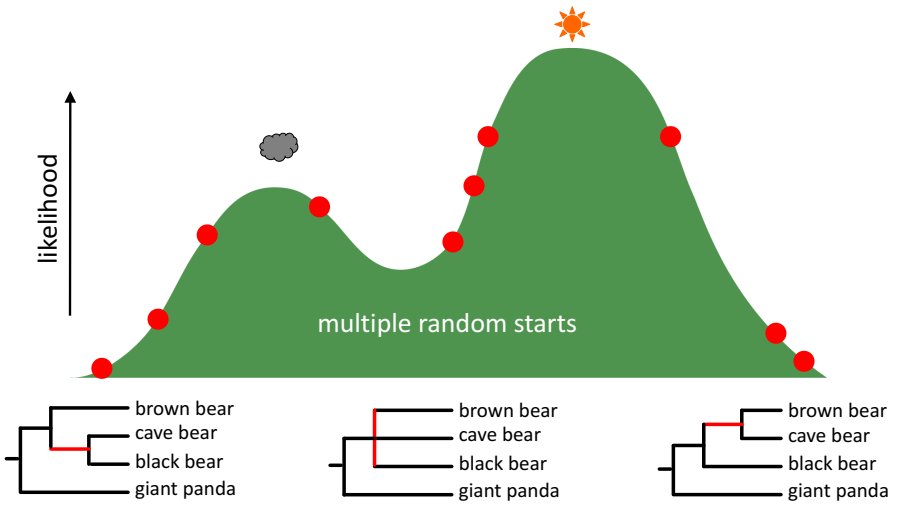
Heuristic search



Heuristic search

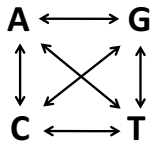


Heuristic search

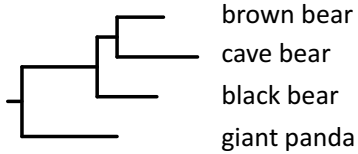


Maximum-likelihood estimates

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

PHYLIP

PAUP

Mesquite

Garli

MEGA

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)

ExaML

- **Exa**scale **M**aximum **L**ikelihood
- Phylogenetic inference on supercomputers
- New MPI parallelisation approach
- Koslov, Aberer, & Stamatakis (2015) *Bioinformatics*

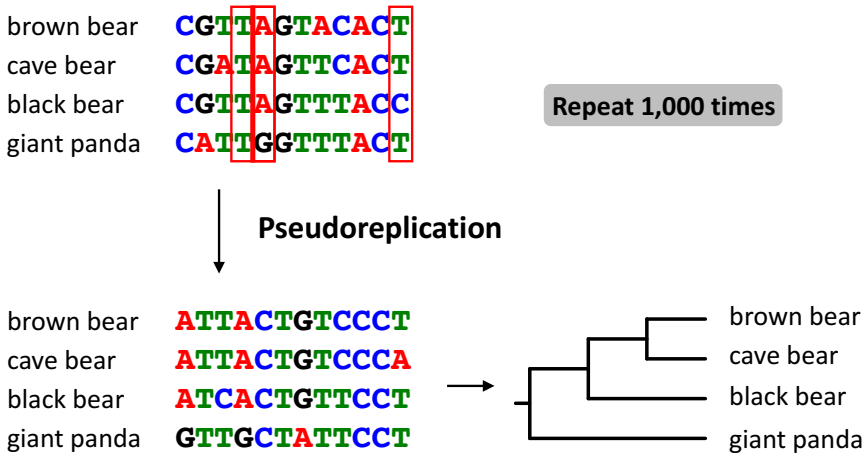
Bootstrapping

Nonparametric bootstrap

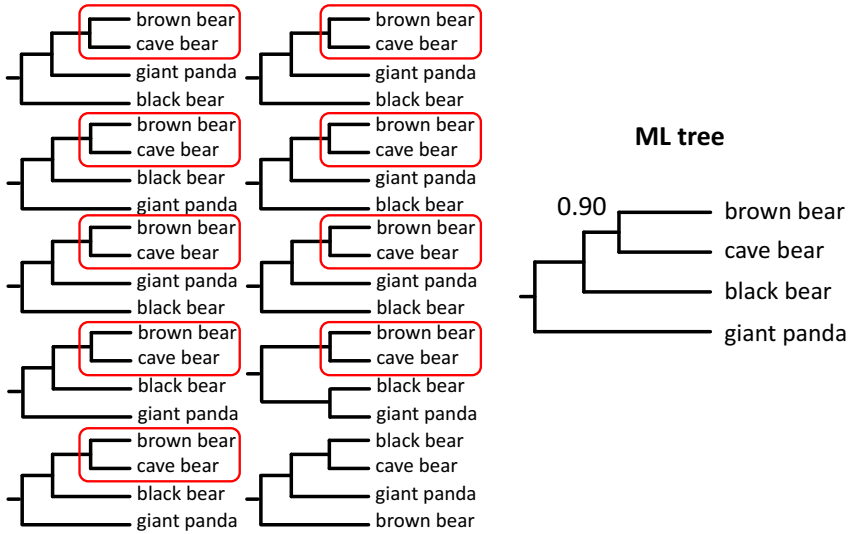
- Uncertainty in the estimate of the tree is inferred indirectly using **bootstrapping analysis**
- "pull oneself up by one's bootstraps"

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

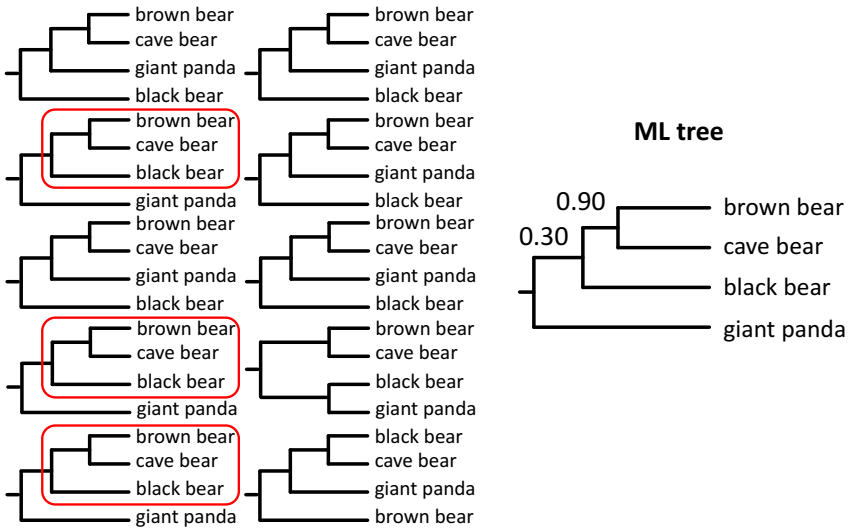
Bootstrapping



Bootstrapping



Bootstrapping



Interpreting bootstrap values

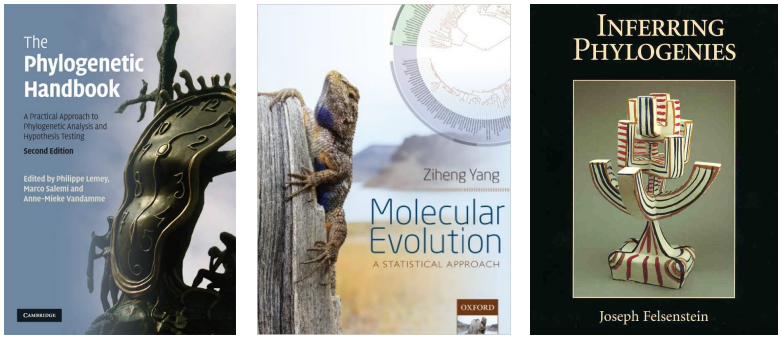
- **Felsenstein (1985)**
  bootstrapping provides a confidence interval that contains the *phylogeny that would be estimated from repeated sampling of many characters from the underlying set of all characters*

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

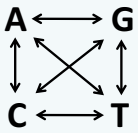
Soltis & Soltis (2003) *Stat Sci*

Useful references

- **Phylogeny estimation and hypothesis testing using maximum likelihood**
  Huelsenbeck & Crandall (1997) *Annu Rev Ecol Syst*, 28: 437–466.



Phylogenetic methods

	Algorithm-based	Optimality criterion	Other
No explicit substitution model	Distance-based methods	Maximum parsimony	
	Distance-based methods	Maximum likelihood	Bayesian inference