Lecture 1.2

Evolutionary Models

Popular phylogenetic methods

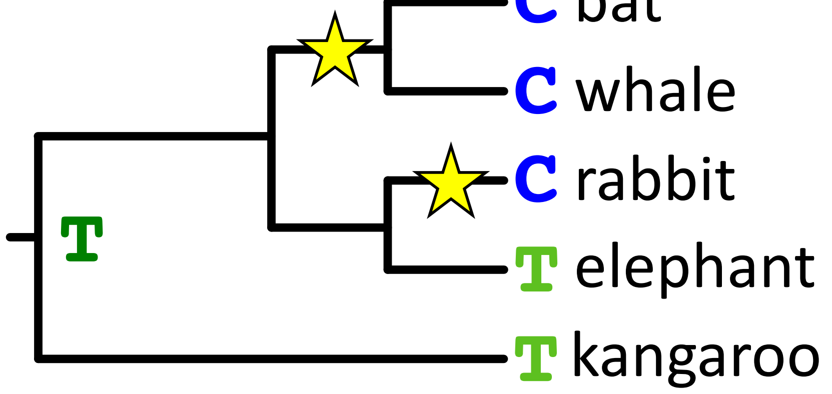
1. Maximum parsimony
2. Distance-based methods
3. Maximum likelihood
4. Bayesian inference

Model-based methods

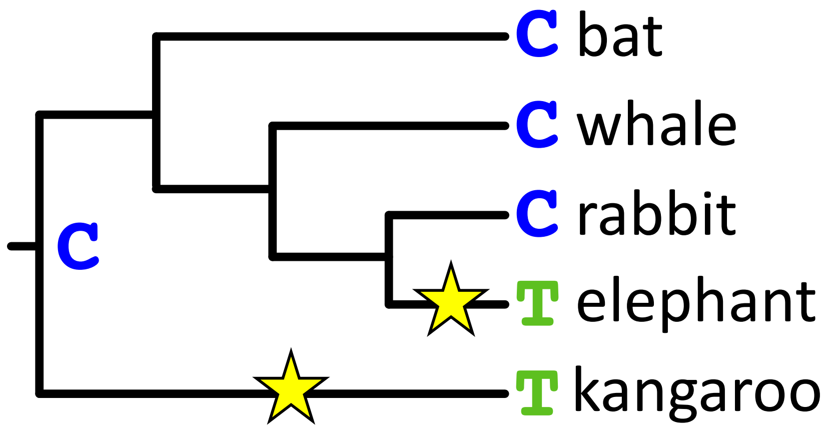
Maximum Parsimony

Maximum parsimony

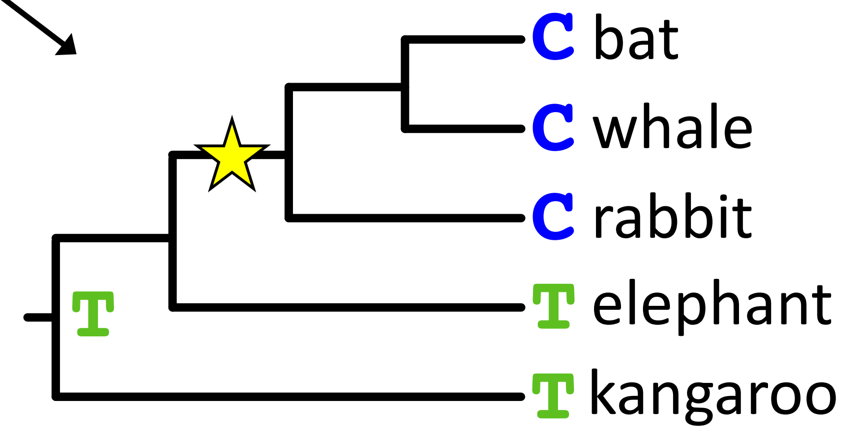
bat	CCGTTAGTAACT
whale	CCGTTAGTAACT
rabbit	CCGATAGTTACT
elephant	TCGTTAGTTACC
kangaroo	TCATTGGTTACT



2 steps

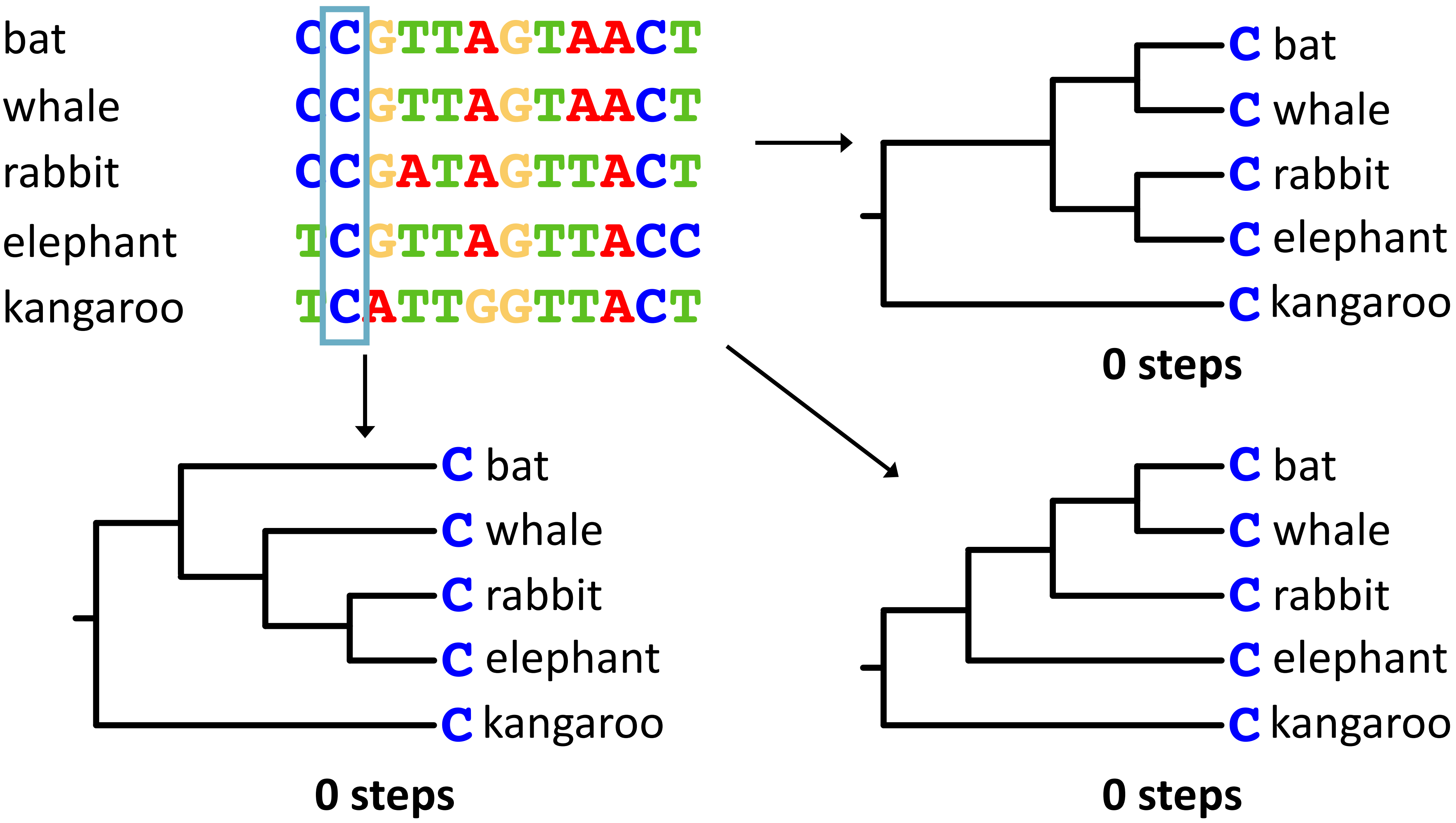


2 steps



1 step

Maximum parsimony



bat	CCGTTAGTAACT
whale	CCGTTAGTAACT
rabbit	CCGATAGTTACT
elephant	TCGTTAGTTACC
kangaroo	TCATTGGTTACT

0 steps

0 steps

0 steps

Maximum parsimony

bat	CCGTTAGTAACT
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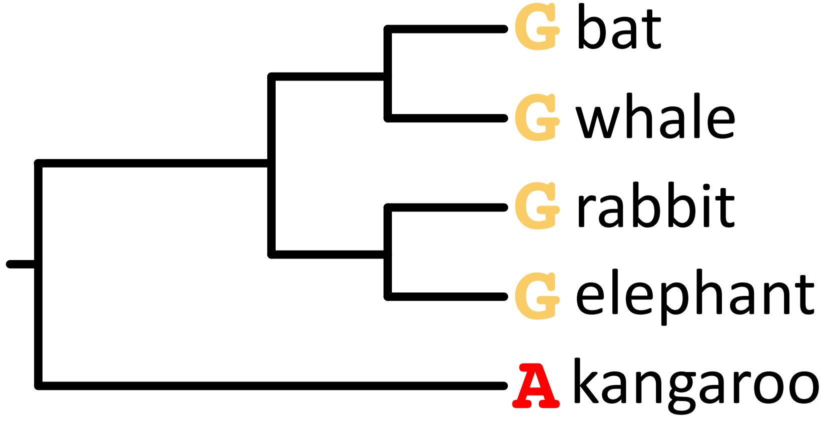
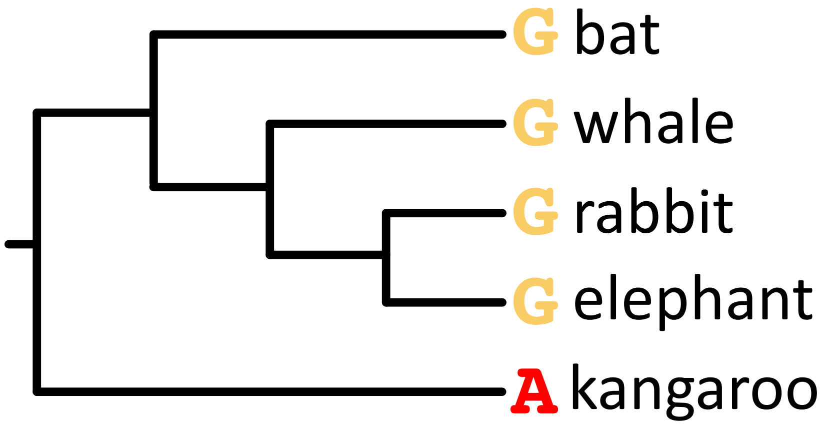
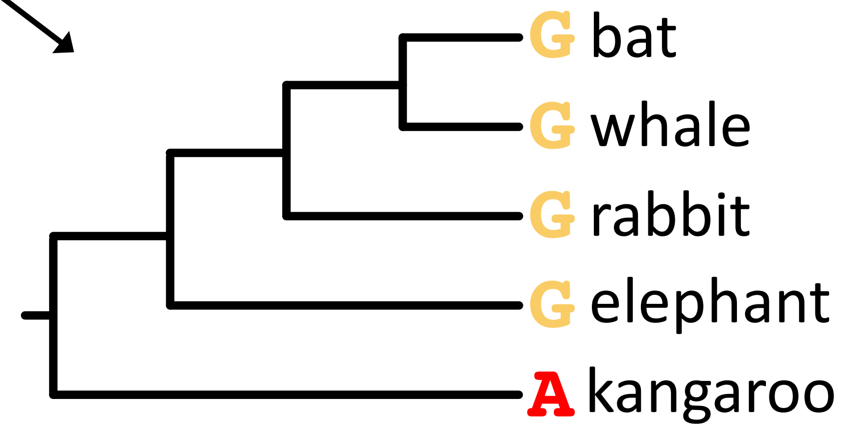


1 step

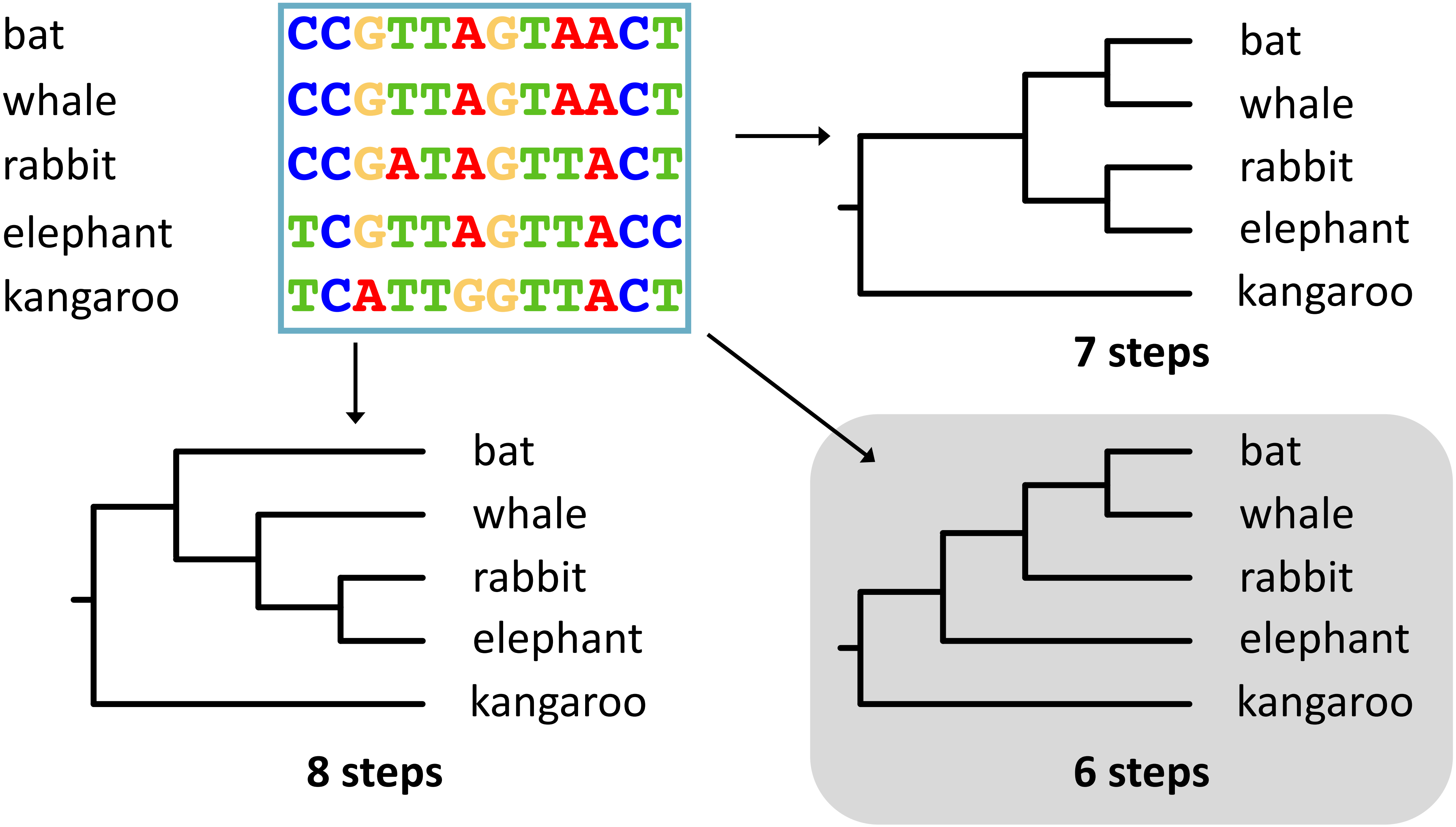


1 step



1 step

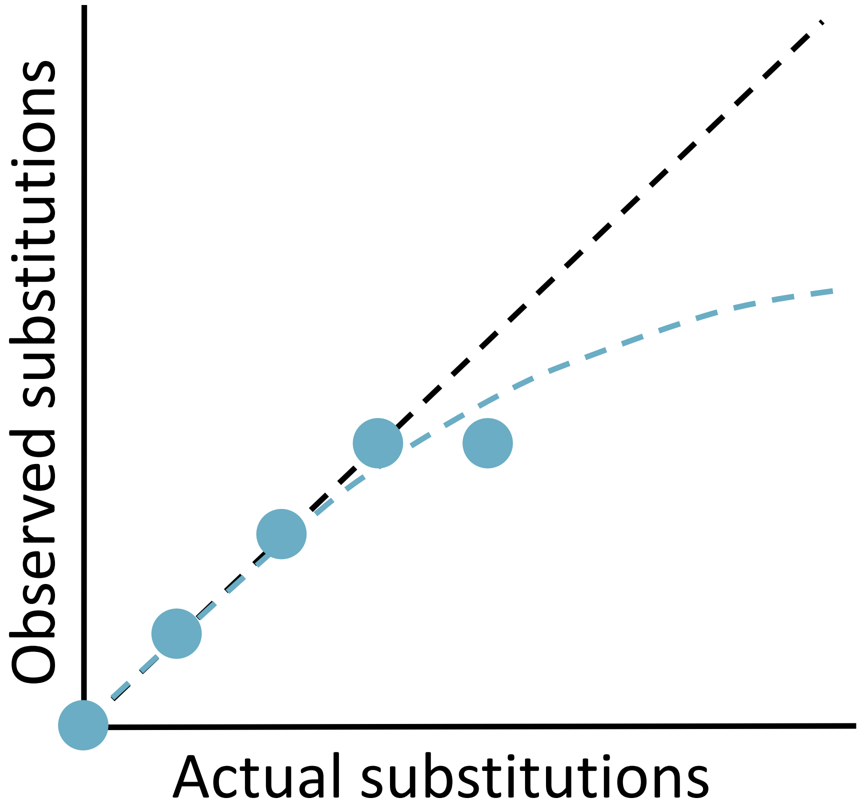
Maximum parsimony



bat	CCGTTAGTAACT
whale	CCGTTAGTAACT
rabbit	CCGATAGTTACT
elephant	TCGTTAGTTACC
kangaroo	TCATTGGTTACT

Maximum parsimony

- Identifies the tree topology that can explain the sequence data, using the smallest number of inferred substitution events
- Commonly used for morphological data
- Now *rarely used* for analysing genetic data
    - Cannot estimate evolutionary rates or timescales
    - Effects of multiple substitutions

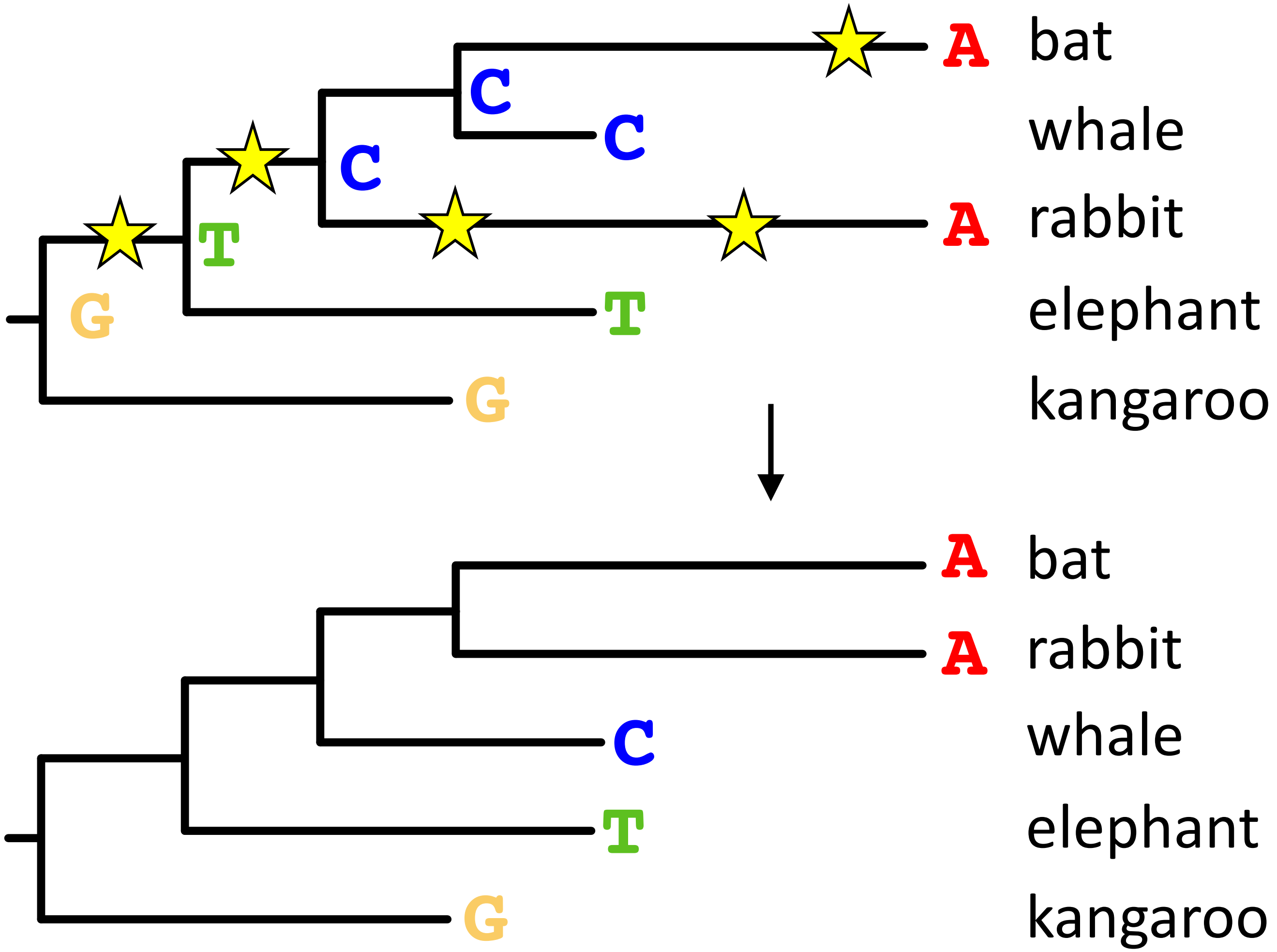


A	A	A	A	A
A	T	T	T	T
C	C	G	G	G
A	A	A	A	A
T	T	T	T	T
T	T	T	T	T
A	A	A	A	A
G	G	G	G	G
T	T	T	A	C

- Maximum parsimony does not correct for multiple substitutions at the same site

- This leads to a problem known as **long-branch attraction**
    - Long branch = many substitutions
    - Similarities arise by chance
    - Long branches cluster together

Long-branch attraction

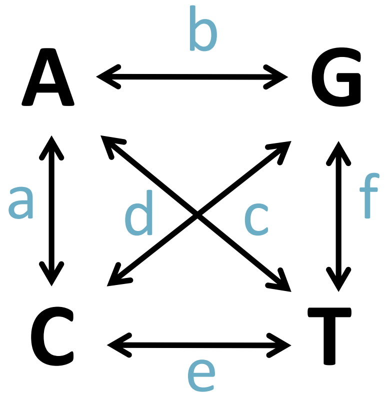


We can correct for multiple hits using substitution models

Substitution Models

Nucleotide substitution models

Rate Matrix

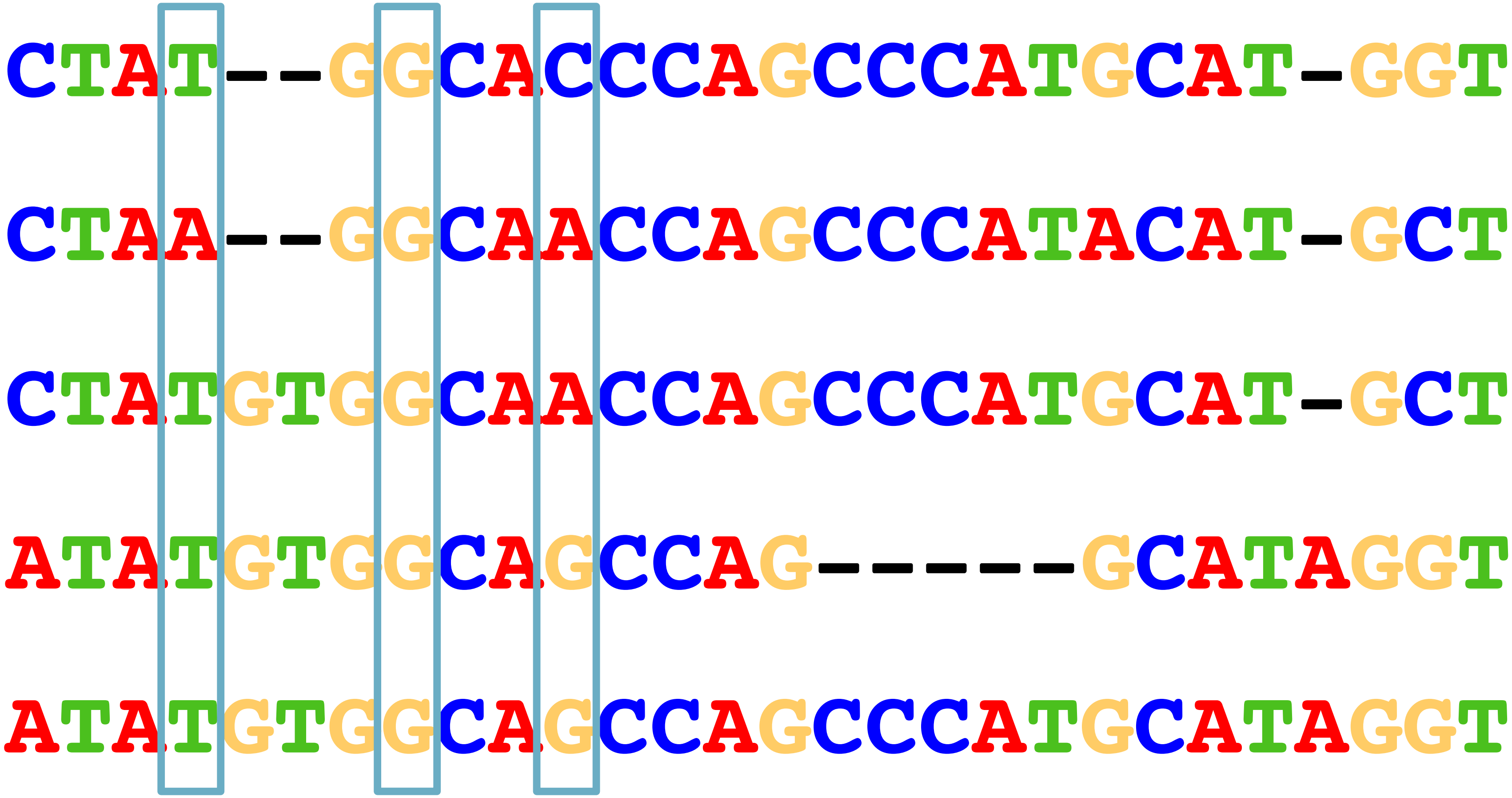


Base Frequencies

$$\pi_A + \pi_C + \pi_G + \pi_T = 1$$

JC	**HKY**	**GTR**
a=b=c=d=e=f	a=c=d=f, b=e	a, b, c, d, e, f
$\pi_A=\pi_C=\pi_G=\pi_T$	$\pi_A, \pi_C, \pi_G, \pi_T$	$\pi_A, \pi_C, \pi_G, \pi_T$

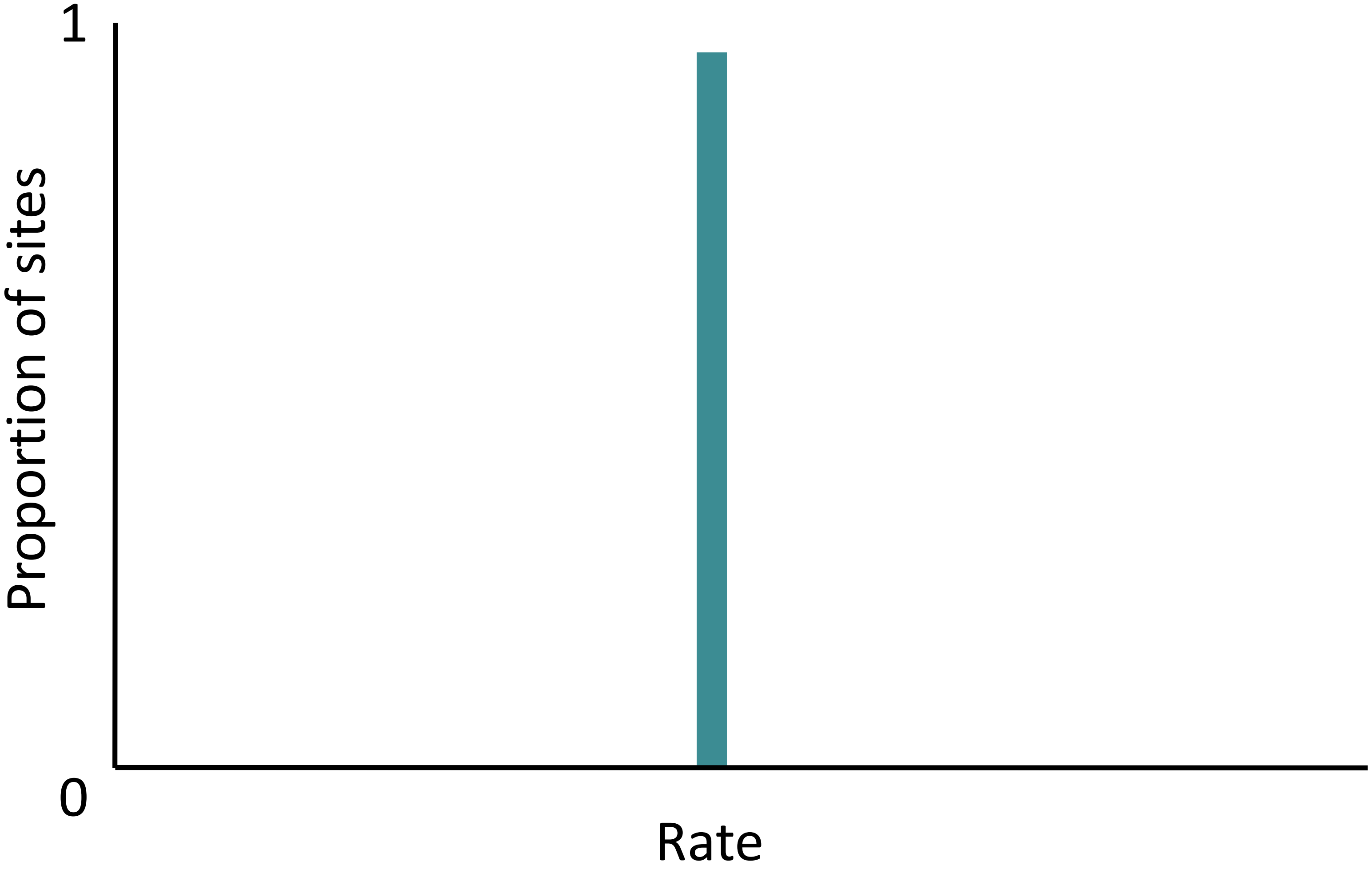
Rate variation across sites



```
CTAT--GGCACCCAGCCCATGCAT-GGT
CTAA--GGCAACCAGCCCATACAT-GCT
CTATGTGGCAACCAGCCCATGCAT-GCT
ATATGTGGCAGCCAG-----GCATAGGT
ATATGTGGCAGCCAGCCCATGCATAGGT
```

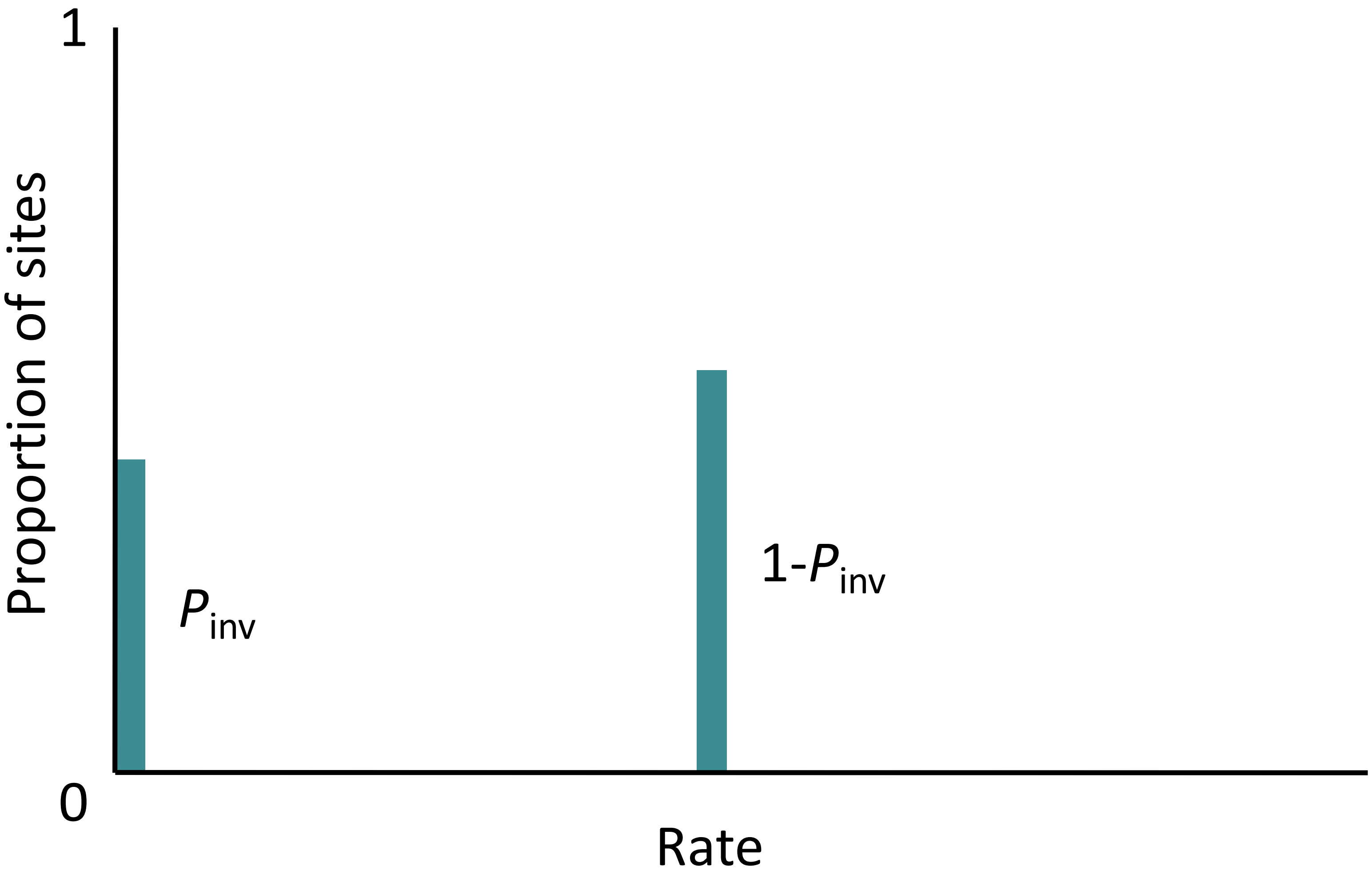
Rate variation across sites

- Equal rates among sites



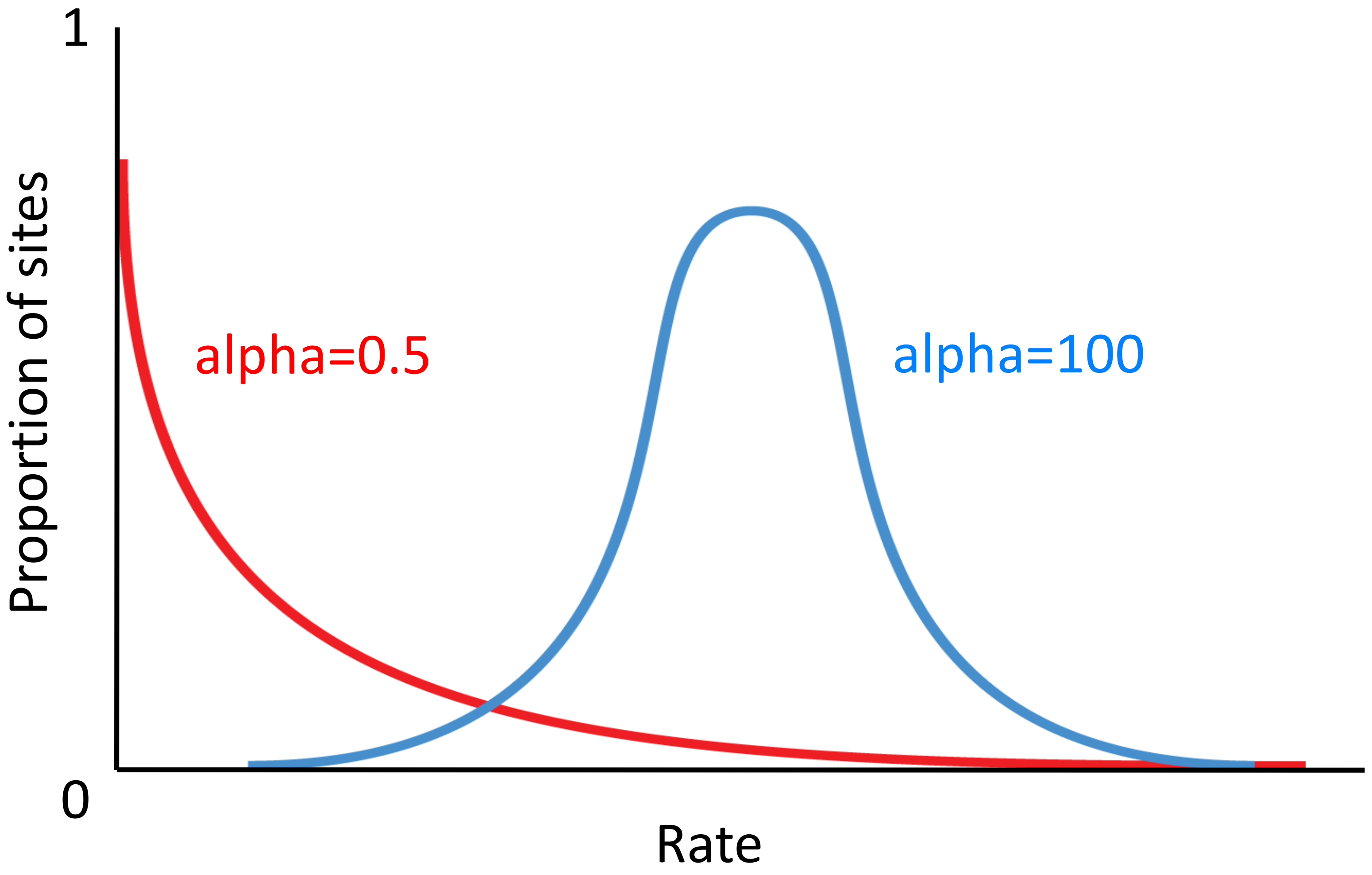
Rate variation across sites

- Proportion of invariable sites (**+I** models)



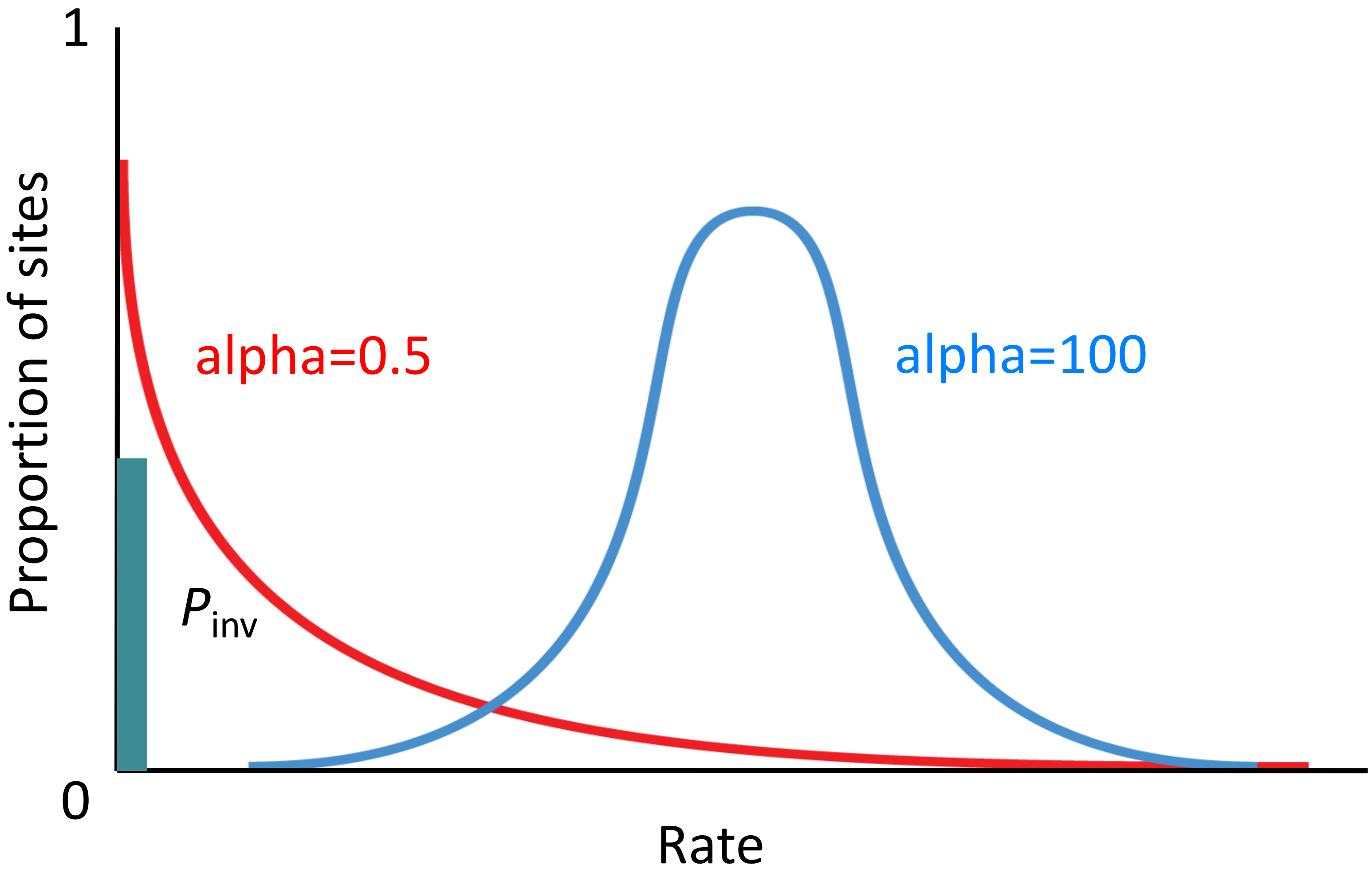
Rate variation across sites

- Gamma-distributed rate variation across sites (**+G** models)



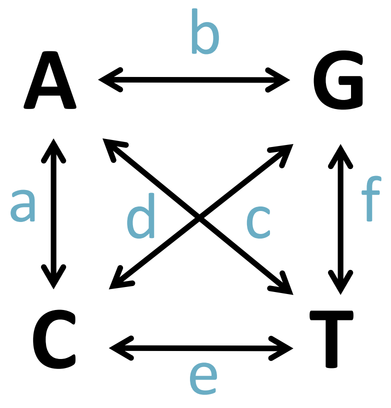
Rate variation across sites

- Gamma-distributed rate variation across sites and a proportion of invariable sites (**+G+I** models)



Nucleotide substitution models

Rate Matrix



Base Frequencies

$\pi_A + \pi_C + \pi_G + \pi_T = 1$

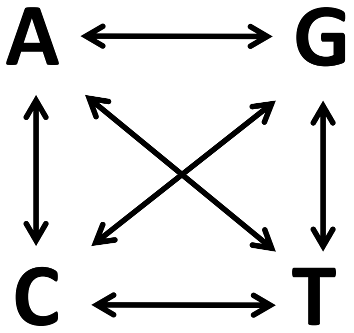
Site Rates

+ I + G

JC	HKY	GTR	GTR+I+G
a=b=c=d=e=f	a=c=d=f, b=e	a, b, c, d, e, f	a, b, c, d, e, f
$\pi_A=\pi_C=\pi_G=\pi_T$	$\pi_A, \pi_C, \pi_G, \pi_T$	$\pi_A, \pi_C, \pi_G, \pi_T$	$\pi_A, \pi_C, \pi_G, \pi_T$ I, G

Nucleotide substitution models

Rate Matrix



Base Frequencies

$\pi_A + \pi_C + \pi_G + \pi_T = 1$

Site Rates

+ I + G

#Models

203 x 15 x 4 = 12,180

In phylogenetics, we typically consider a small subset of these

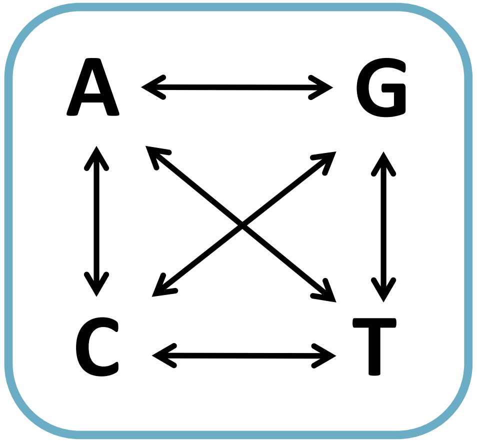
Proportion of invariable sites

- Often overestimated in analyses of intraspecific data
- Unable to distinguish between:
  - Sites that are **invariable** and unable to change
  - Sites that are **constant** and by chance have not mutated
- Not always biologically meaningful
- Slowly evolving sites taken into account by **+G**

Use +G models to account for rate variation across sites

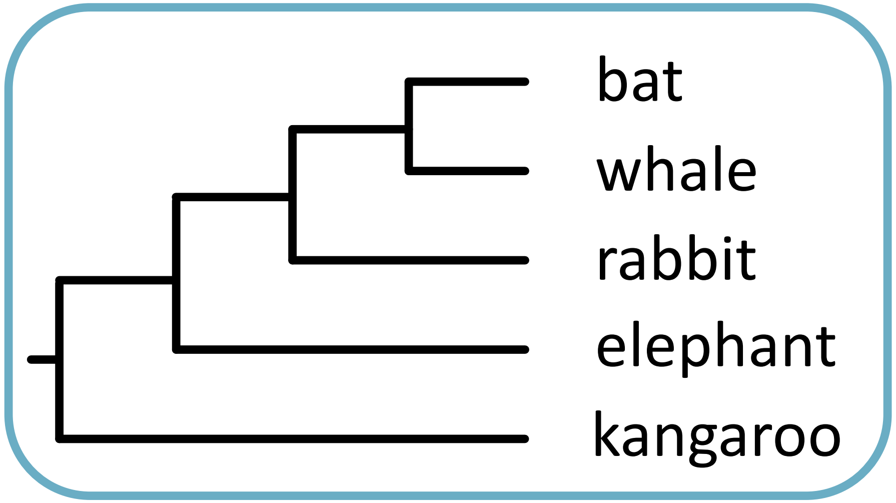
Fundamental assumptions

Reversible



Stationary

$\pi_A + \pi_C + \pi_G + \pi_T = 1$



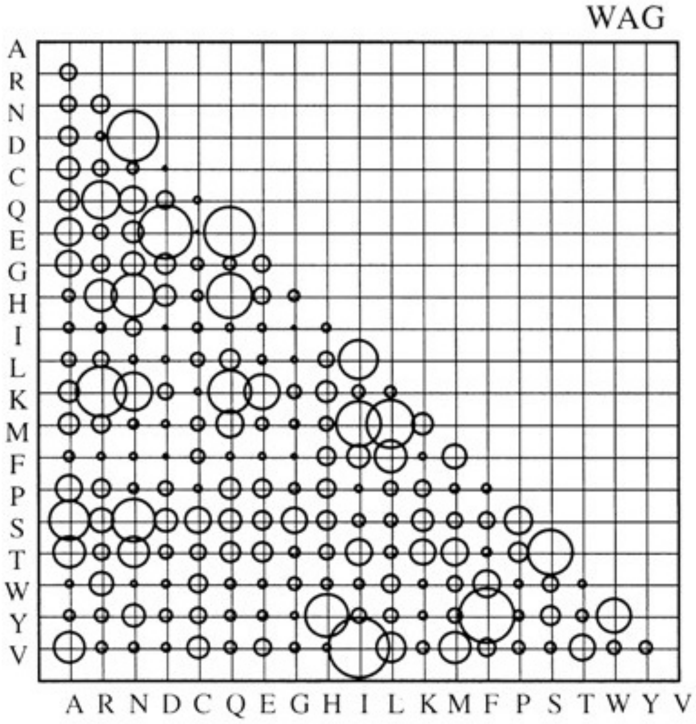
```
CCGTTAGTAACT
CCGTTAGTAACT
CCGATAGTTACT
TCGTTAGTTACC
TCATTGGTTACT
```

Homogeneous

Independent across sites

Amino acid substitution matrices

- 20x20 matrix of substitution probabilities
- Too many parameters to estimate
  - GTR model for DNA: 6 parameters
  - GTR model for proteins: 190 parameters
- Estimate substitution probabilities using large data set
  - PAM
  - BLOSUM
  - JTT
  - WAG



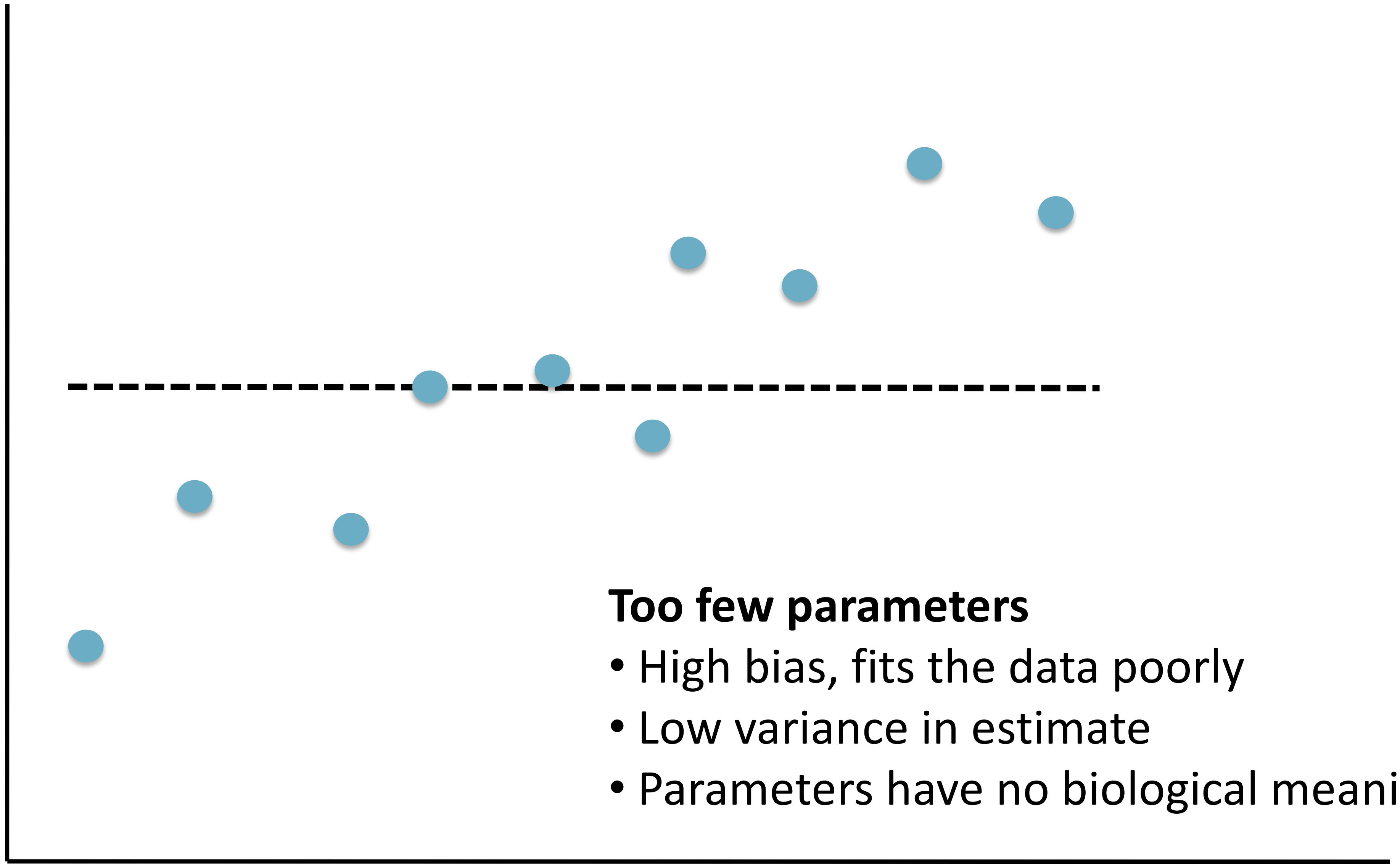
Model Selection

Model selection

1. **Subjective model selection**
    - Pick a model that seems sensible
    - Balance the number of parameters against the amount of data
    - Biological motivation

2. **Objective model selection**
    - Use information theory and let a computer do it for you
    - Statistical motivation

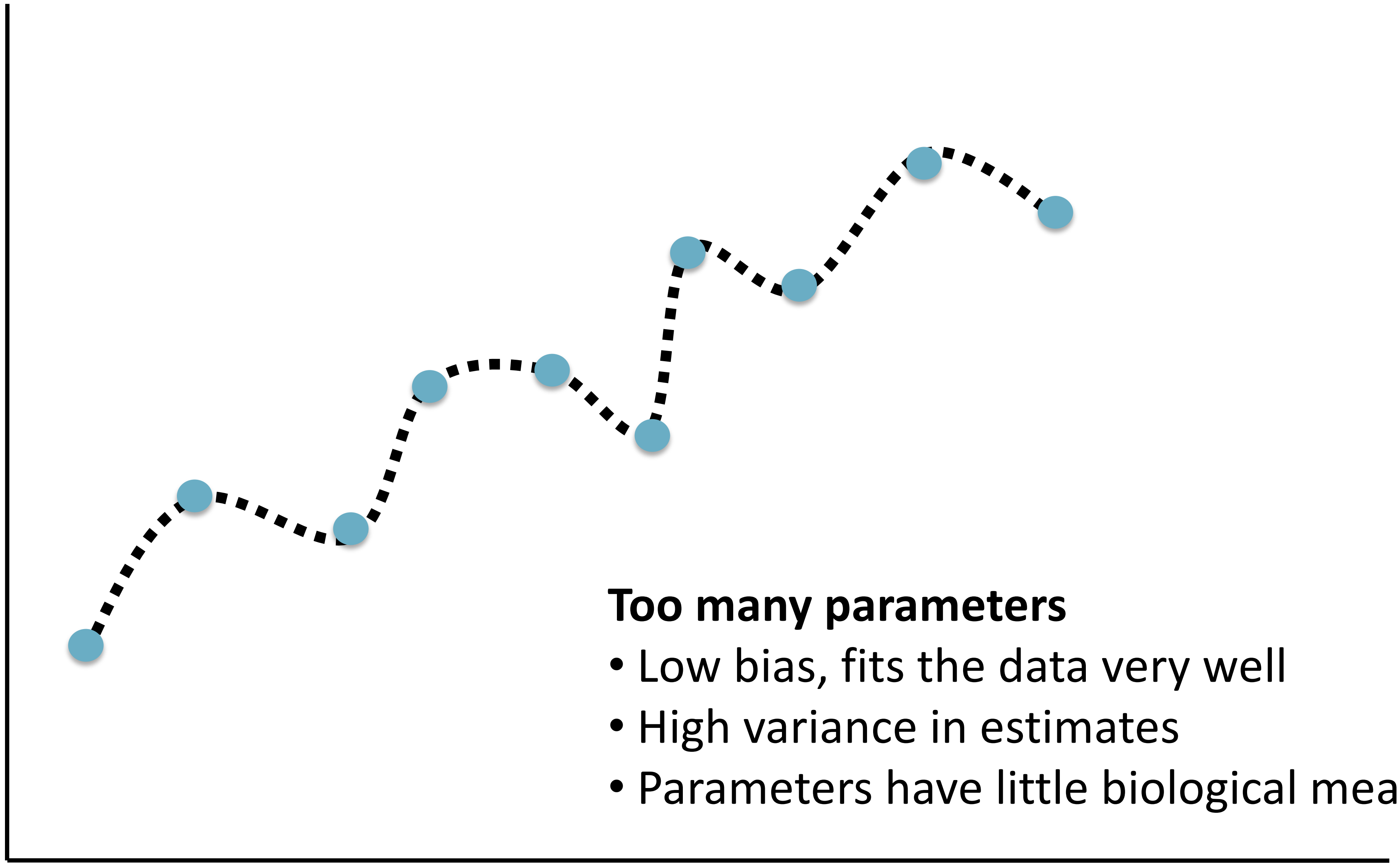
Model selection



Too few parameters

- High bias, fits the data poorly
- Low variance in estimate
- Parameters have no biological meaning

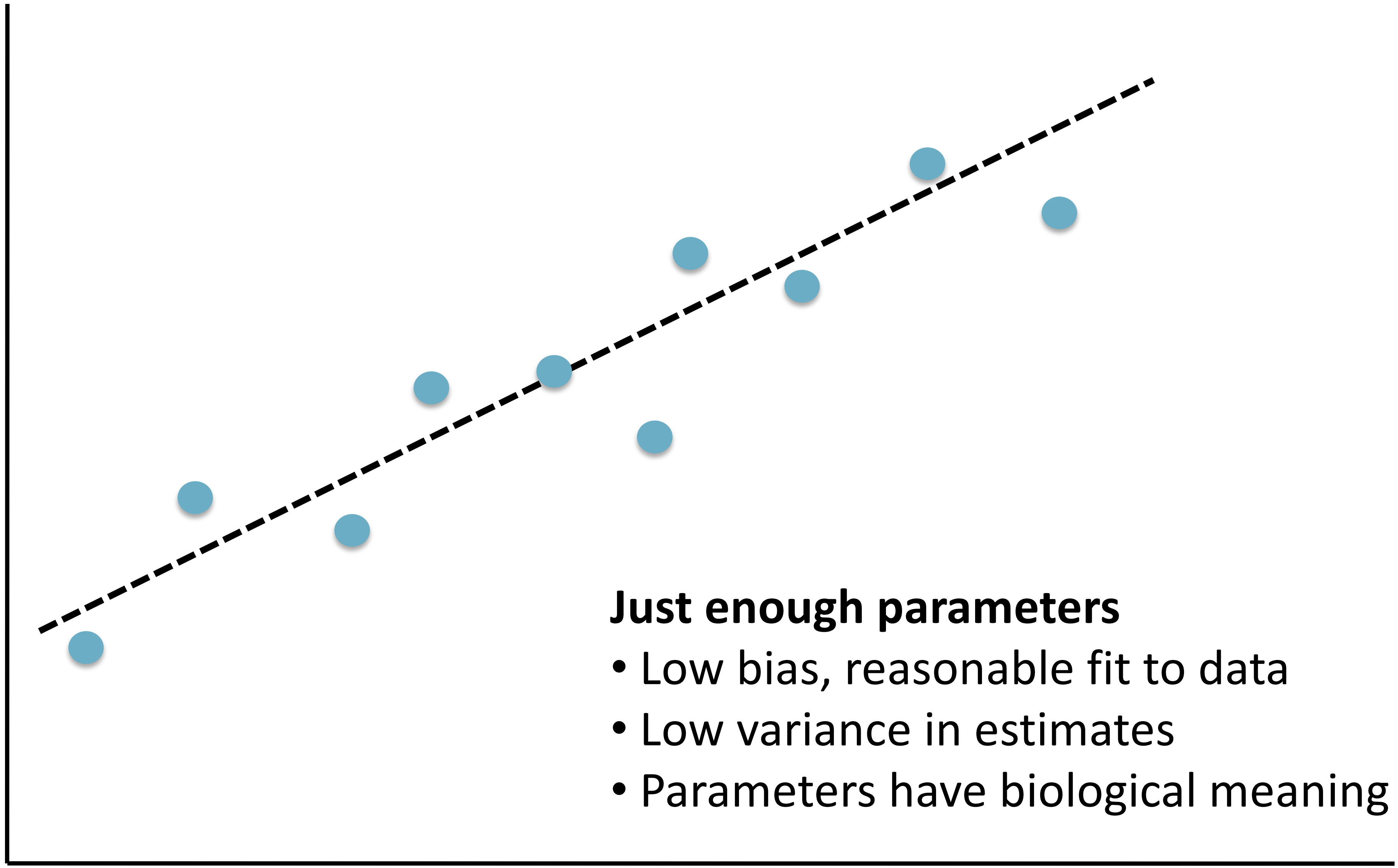
Model selection



Too many parameters

- Low bias, fits the data very well
- High variance in estimates
- Parameters have little biological meaning

Model selection



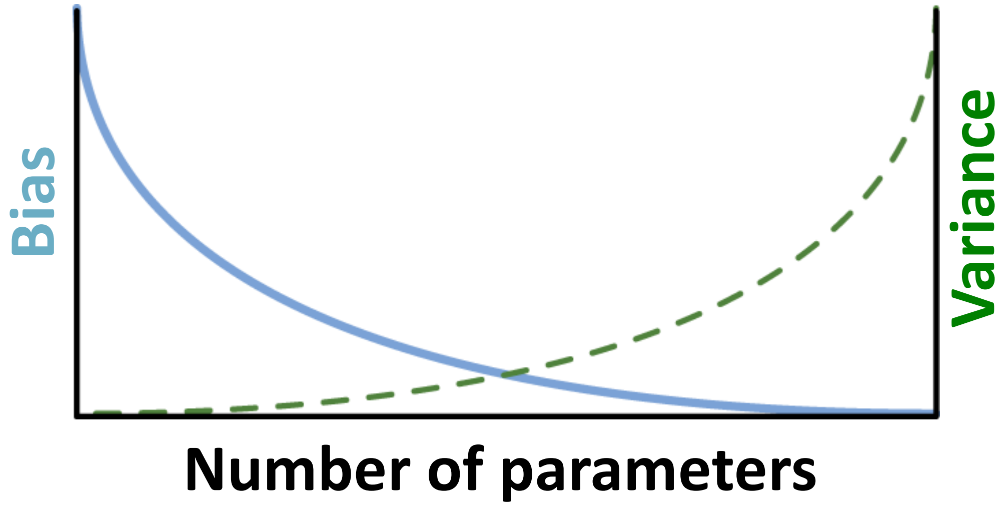
Just enough parameters

- Low bias, reasonable fit to data
- Low variance in estimates
- Parameters have biological meaning

Model selection

- Adding more parameters *always* improves the fit of the model to the observed data
- But more parameters leads to greater variance in the estimates of those parameters

Is the improvement in model fit worth the cost of adding a parameter?



Model selection

- **Likelihood-ratio test (LRT)**
  Used to compare nested models

- **Akaike information criterion (AIC)**
  AIC = -2ln(likelihood) + 2k

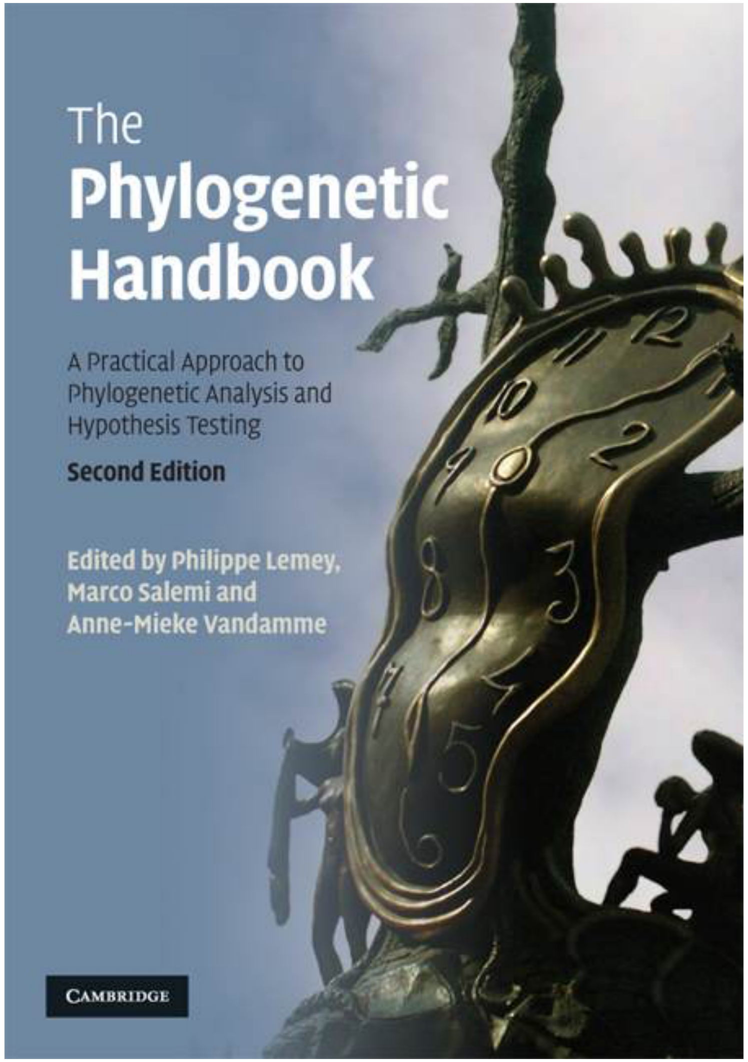
- **Bayesian information criterion (BIC)**
  BIC = -2ln(likelihood) + $k$ln(n)

Phylogenetic estimates are often robust to choice of model

Useful references

- **Model selection in phylogenetics**
  Sullivan & Joyce (2005) *Annual Review of Ecology, Evolution, and Systematics*, 36: 445–466.

- **Model selection may not be a mandatory step for phylogeny reconstruction**
  Abadi et al. (2019)
  Nature Communications, 10: 934.


The
Phylogenetic
Handbook
A Practical Approach to
Phylogenetic Analysis and
Hypothesis Testing
Second Edition
Edited by Philippe Lemey,
Marco Salemi and
Anne-Mieke Vandamme
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