Likelihoods, Bootstraps and Testing Trees

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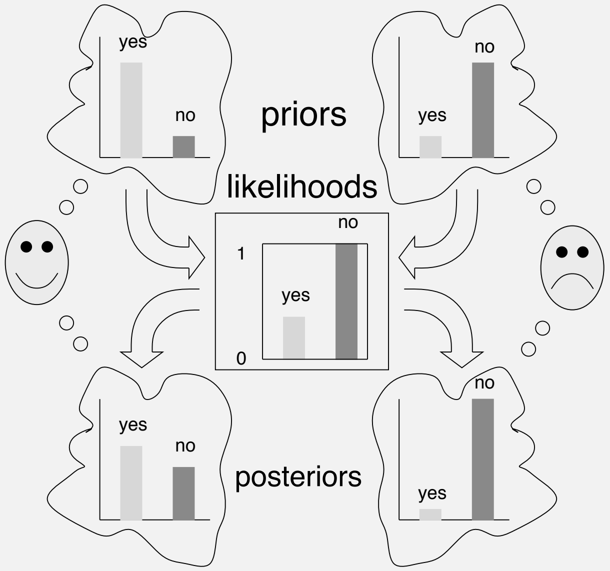
Odds ratio justification for maximum likelihood

D	**the data**
H_1	**Hypothesis 1**
H_2	**Hypothesis 2**
$\mid$	**the symbol for “given”**

$$\underbrace{\frac{\mathrm{Prob}\,(H_1)}{\mathrm{Prob}\,(H_2)}}_{\text{Prior odds ratio}} \quad \underbrace{\frac{\mathrm{Prob}\,(D \mid H_1)}{\mathrm{Prob}\,(D \mid H_2)}}_{\text{Likelihood ratio}} \quad = \quad \underbrace{\frac{\mathrm{Prob}\,(H_1 \mid D)}{\mathrm{Prob}\,(H_2 \mid D)}}_{\text{Posterior odds ratio}}$$

If a space probe finds no Little Green Men on Mars


priors

likelihoods

posteriors

$$\frac{4}{1} \times \frac{1/3}{1} = \frac{4}{3} \qquad\qquad \frac{1}{4} \times \frac{1/3}{1} = \frac{1}{12}$$

The likelihood ratio term ultimately dominates

If we see one Little Green Man, the likelihood calculation does the right thing:

$$\frac{1}{4} \times \frac{2/3}{0} = \frac{\infty}{1}$$

(put this way, this is OK but not mathematically kosher)

If we send n space probes and keep seeing none, the likelihood ratio term is

$$\left(\frac{1}{3}\right)^{n}$$

It dominates the calculation, overwhelming the prior.
Thus even if we don't have a prior we can believe in, we may be interested in knowing which hypothesis the likelihood ratio is recommending ...

Likelihood in Simple Coin-Tossing

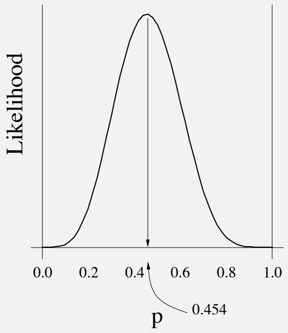
Tossing a coin n times, with probability p of heads, the probability of outcome HHTHTTTTHTTH is

$$pp(1-p)p(1-p)(1-p)(1-p)(1-p)p(1-p)(1-p)p$$

which is

$$L = p^5(1-p)^6$$

Plotting L against p to find its maximum:



Differentiating to find the maximum:

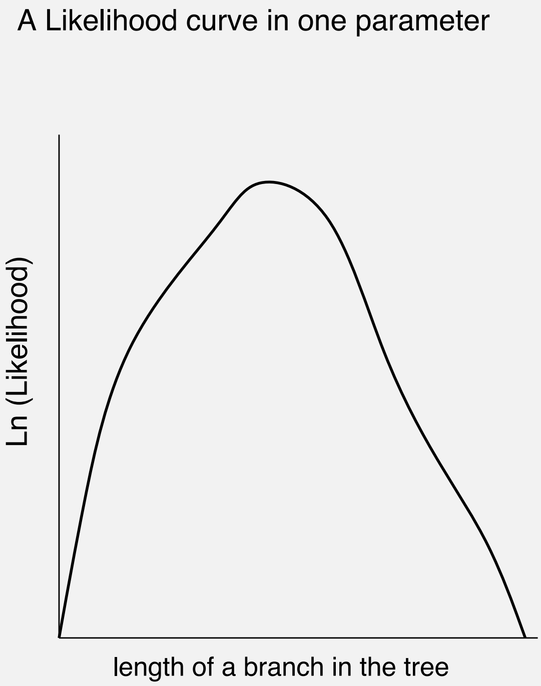
Differentiating the expression for L with respect to p and equating the derivative to 0, the value of p that is at the peak is found (not surprisingly) to be $p = 5/11$:

$$\frac{\partial L}{\partial p} \;=\; \left(\frac{5}{p} - \frac{6}{1-p}\right) p^5(1-p)^6 \;=\; 0$$

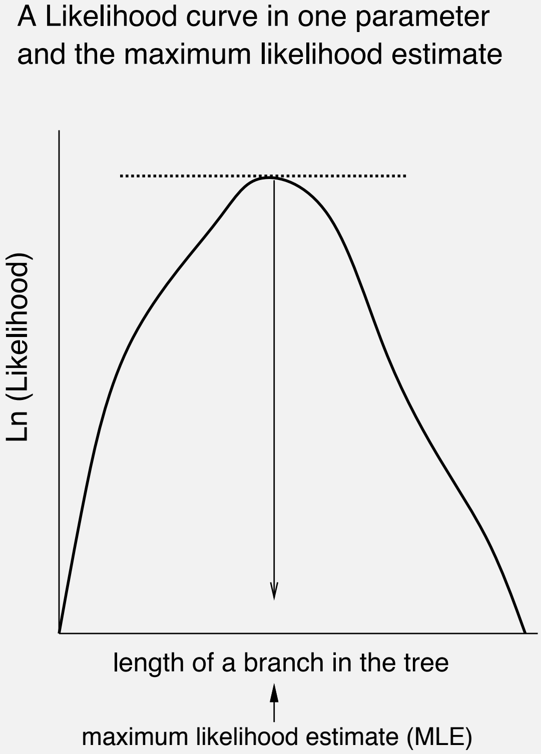
$$5 - 11\,p \;=\; 0$$

$$\hat{p} \;=\; \frac{5}{11}$$

A log-likelihood curve

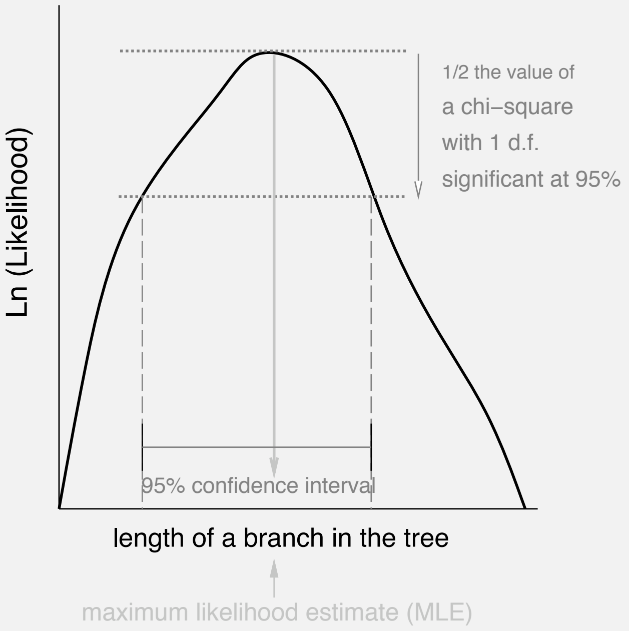


Its maximum likelihood estimate

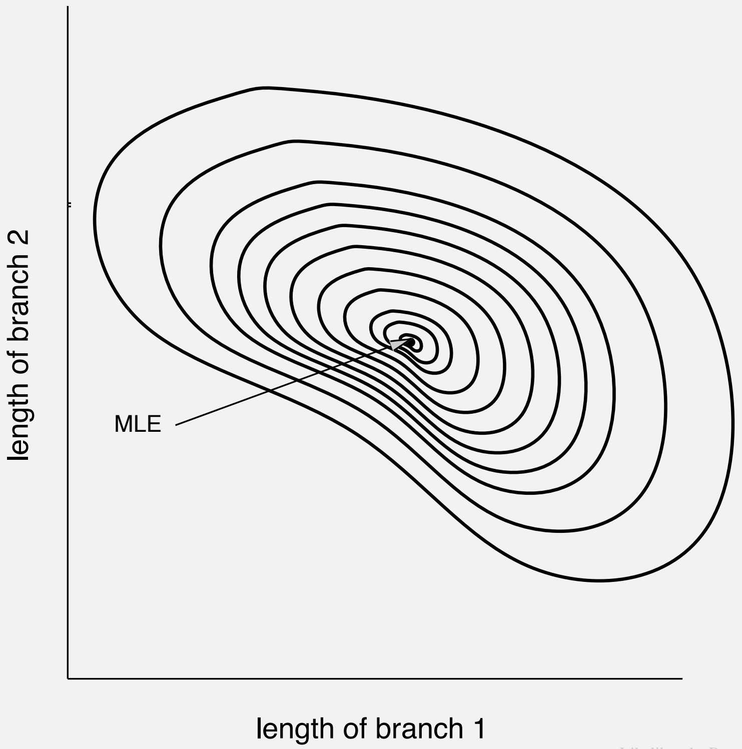


The (approximate, asymptotic) confidence interval

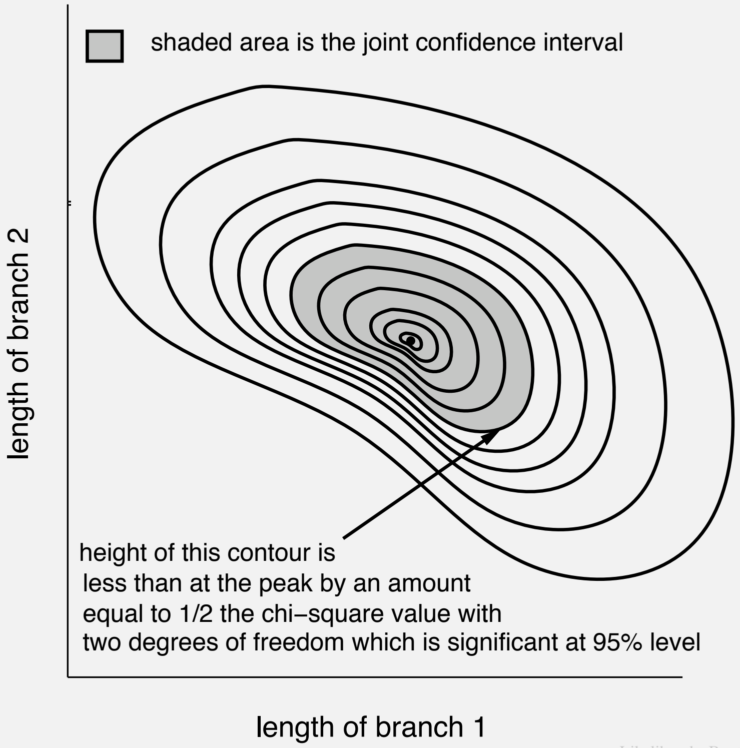
A Likelihood curve in one parameter
and the maximum likelihood estimate and
confidence interval derived from it



Contours of a log-likelihood surface in two dimensions



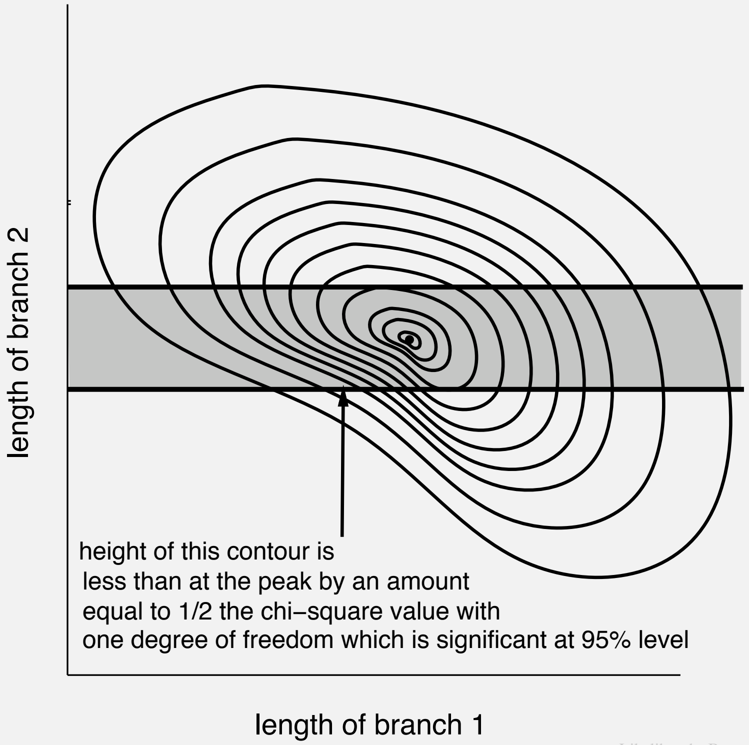
Log-likelihood-based confidence set for two variables



▨ shaded area is the joint confidence interval

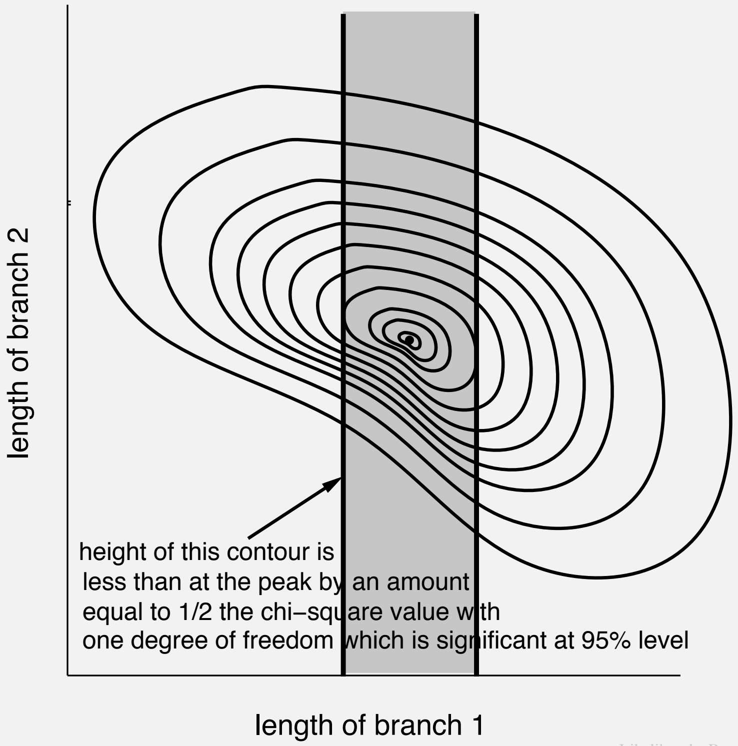
height of this contour is
less than at the peak by an amount
equal to 1/2 the chi−square value with
two degrees of freedom which is significant at 95% level

Confidence interval for one variable



height of this contour is
less than at the peak by an amount
equal to 1/2 the chi−square value with
one degree of freedom which is significant at 95% level

Confidence interval for the other variable



height of this contour is less than at the peak by an amount equal to 1/2 the chi−square value with one degree of freedom which is significant at 95% level

Calculating the likelihood of a tree

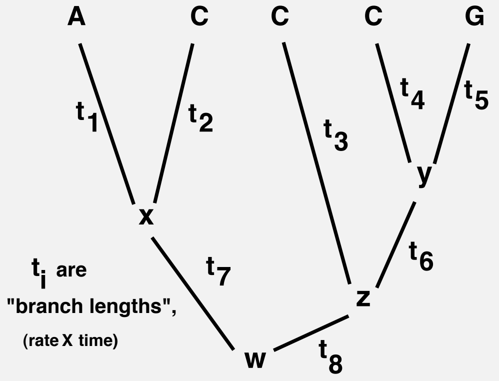
If we have molecular sequences on a tree, the likelihood is the product over sites of the data $D^{[i]}$ for each site (if those evolve independently):

$$L \;=\; \mathrm{Prob}\,(D\,|\,T) \;=\; \prod_{i=1}^{\mathrm{sites}} \mathrm{Prob}\,(D^{[i]}\,|\,T)$$

With log-likelihoods, the product becomes a sum:

$$\ln L \;=\; \ln\;\mathrm{Prob}\,(D\,|\,T) \;=\; \sum_{i=1}^{\mathrm{sites}} \ln\;\mathrm{Prob}\,(D^{[i]}\,|\,T)$$

Calculating the likelihood for site i on a tree



t_i are "branch lengths", (rate X time)

Sum over all possible states (bases) at interior nodes:

$$\begin{aligned} L^{(i)} \quad = \quad & \sum_x \sum_y \sum_z \sum_w \mathrm{Prob}\,(w)\ \ \mathrm{Prob}\,(x\,|\,w,t_7) \\ & \times \mathrm{Prob}\,(A\,|\,x,t_1)\ \mathrm{Prob}\,(C\,|\,x,t_2)\ \mathrm{Prob}\,(z\,|\,w,t_8) \\ & \times \mathrm{Prob}\,(C\,|\,z,t_3)\ \mathrm{Prob}\,(y\,|\,z,t_6)\ \mathrm{Prob}\,(C\,|\,y,t_4)\ \mathrm{Prob}\,(G\,|\,y,t_5) \end{aligned}$$

Calculating the likelihood for site i on a tree

We use the conditional likelihoods: $L_j^{(i)}(s)$

These compute the probability of everything at site i at or above node j on the tree, given that node j is in state s. Thus it assumes something (s) that we don't know in practice – so we compute these for all states s.

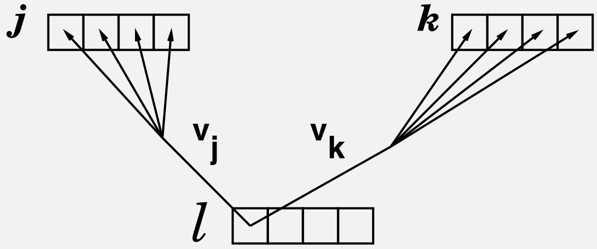
At the tips we can define these quantities: if the observed state is (say) C, the vector of L's is

$$(0, 1, 0, 0)$$

.
If we observe an ambiguity, say R (purine), they are

$$(1, 0, 1, 0), \qquad \textit{not} \quad (1/2, 0, 1/2, 0)$$

The “pruning" algorithm:



$$
\begin{aligned}
\mathsf{L}_{\ell}^{(\mathsf{i})}(\mathsf{s}) \quad &= \quad \left[\sum_{\mathsf{s_j}} \mathrm{Prob}\left(\mathsf{s_j} \mid \mathsf{s}, \mathsf{v_j}\right) \mathsf{L}_{\mathsf{j}}^{(\mathsf{i})}(\mathsf{s_j}) \right] \\
& \quad \times \left[\sum_{\mathsf{s_k}} \mathrm{Prob}\left(\mathsf{s_k} \mid \mathsf{s}, \mathsf{v_k}\right) \mathsf{L}_{\mathsf{k}}^{(\mathsf{i})}(\mathsf{s_k}) \right]
\end{aligned}
$$

(Felsenstein, 1973; 1981).

and at the bottom of the tree:

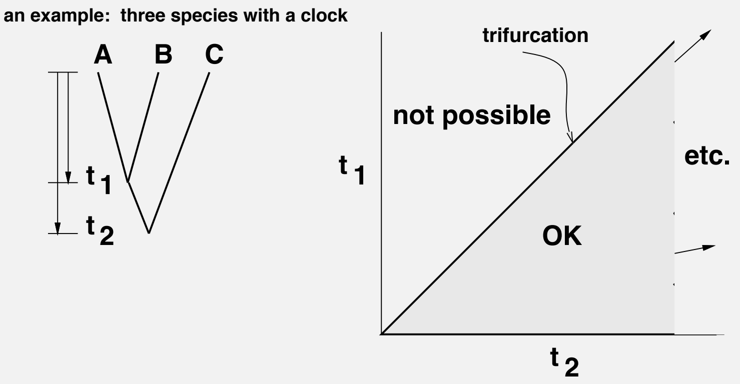
$$
\mathsf{L}_0^{(\mathsf{i})} \;=\; \sum_{\mathsf{s}} \pi_{\mathsf{s}} \, \mathsf{L}_0^{(\mathsf{i})}(\mathsf{s})
$$

(Felsenstein, 1973, 1981)

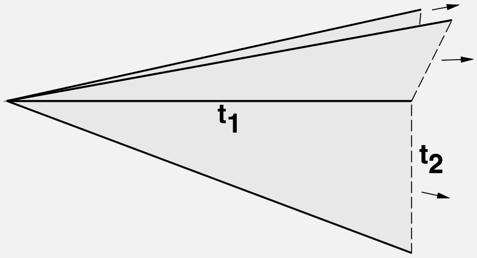
and having gotten the likelihoods for each site:

$$
\mathsf{L} \;=\; \prod_{\mathsf{i}=1}^{\text{sites}} \mathsf{L}_0^{(\mathsf{i})}
$$

What does “tree space" (with branch lengths) look like?

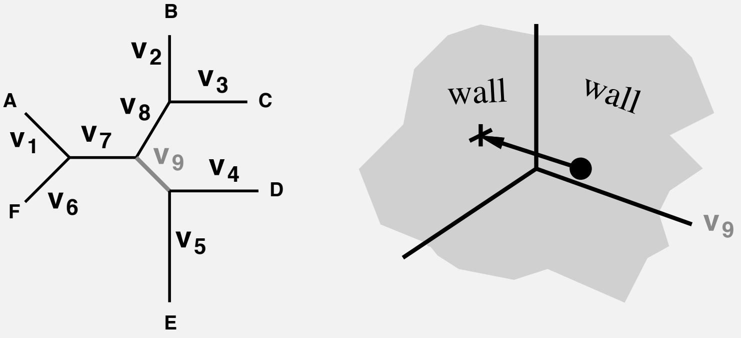


when we consider all three possible topologies, the space looks like:



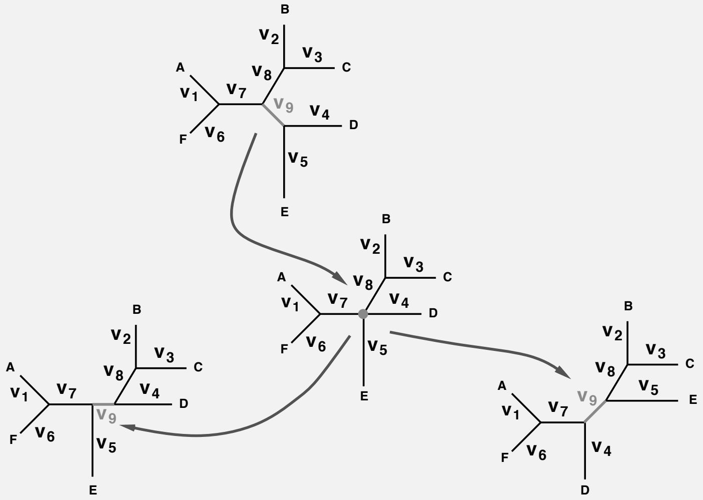
For one tree topology

The space of trees varying all $2n - 3$ branch lengths, each a nonegative number, defines an “orthant" (open corner) of a $(2n - 3)$-dimensional real space:



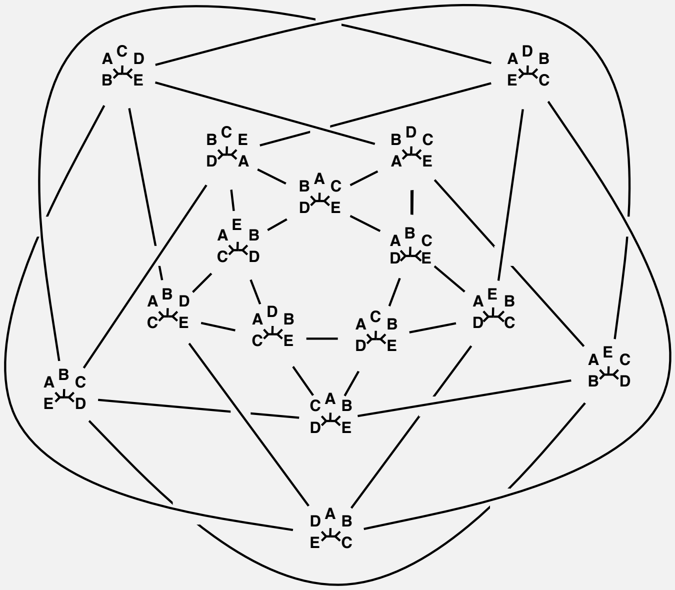
Through the looking-glass

Shrinking one of the $n - 1$ interior branches to 0, we arrive at a trifurcation:



Here, as we pass “through the looking glass" we are also touch the space for two other tree topologies, and we could enter either.

The graph of all trees of 5 species



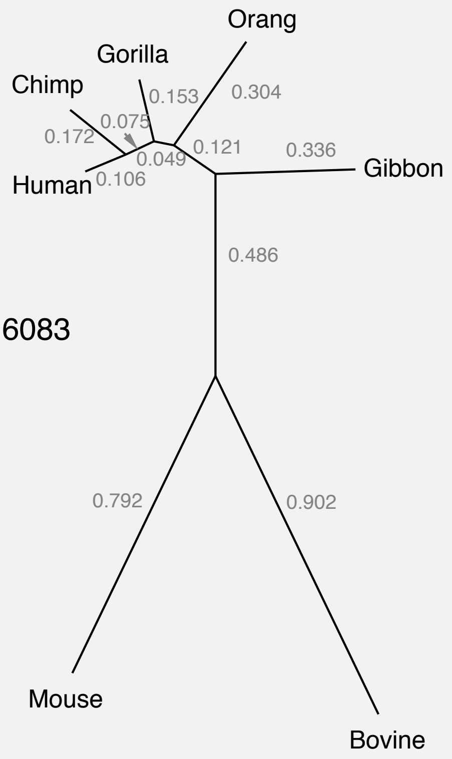
The Schoenberg graph (all 15 trees of size 5 connected by NNI’s)

A data example: mitochondrial D-loop sequences

```
Bovine    CCAAACCTGT CCCCACCATC TAACACCAAC CCACATATAC AAGCTAAACC AAAAATACCA
Mouse     CCAAAAAAAC ATCCAAACAC CAACCCCAGC CCTTACGCAA TAGCCATACA AAGAATATTA
Gibbon    CTATACCCAC CCAACTCGAC CTACACCAAT CCCCACATAG CACACAGACC AACAACCTCC
Orang     CCCCACCCGT CTACACCAGC CAACACCAAC CCCCACCTAC TATACCAACC AATAACCTCT
Gorilla   CCCCATTTAT CCATAAAAAC CAACACCAAC CCCCATCTAA CACACAAACT AATGACCCCC
Chimp     CCCCATCCAC CCATACAAAC CAACATTACC CTCCATCCAA TATACAAACT AACAACCTCC
Human     CCCCACTCAC CCATACAAAC CAACACCACT CTCCACCTAA TATACAAATT AATAACCTCC

          TACTACTAAA AACTCAAATT AACTCTTTAA TCTTTATACA ACATTCCACC AACCTATCCA
          TACAACCATA AATAAGACTA ATCTATTAAA ATAACCCATT ACGATACAAA ATCCCTTTCG
          CACCTTCCAT ACCAAGCCCC GACTTTACCG CCAACGCACC TCATCAAAAC ATACCTACAA
          CAACCCCTAA ACCAAACACT ATCCCCAAAA CCAACACACT CTACCAAAAT ACACCCCCAA
          CACCCTCAAA GCCAAACACC AACCCTATAA TCAATACGCC TTATCAAAAC ACACCCCCAA
          CACTCTTCAG ACCGAACACC AATCTCACAA CCAACACGCC CCGTCAAAAC ACCCCTTCAG
          CACCTTCAGA ACTGAACGCC AATCTCATAA CCAACACACC CCATCAAAGC ACCCCTCCAA

          CACAAAAAAA CTCATATTTA TCTAAATACG AACTTCACAC AACCTTAACA CATAAACATA
          TCTAGATACA AACCACAACA CACAATTAAT ACACACCACA ATTACAATAC TAAACTCCCA
          CACAAACAAA TGCCCCCCCA CCCTCCTTCT TCAAGCCCAC TAGACCATCC TACCTTCCTA
          TTCACATCCG CACACCCCCA CCCCCCCTGC CCACGTCCAT CCCATCACCC TCTCCTCCCA
          CATAAACCCA CGCACCCCCA CCCCTTCCGC CCATGCTCAC CACATCATCT CTCCCCTTCA
          CACAAATTCA TACACCCCTA CCTTTCCTAC CCACGTTCAC CACATCATCC CCCCCTCTCA
          CACAAACCCG CACACCTCCA CCCCCCTCGT CTACGCTTAC CACGTCATCC CTCCCTCTCA

          CCCCAGCCCA ACACCCTTCC ACAAATCCTT AATATACGCA CCATAAATAA CA
          TCCCACCAAA TCACCCTCCA TCAAATCCAC AAATTACACA ACCATTAACC CA
          GCACGCCAAG CTCTCTACCA TCAAACGCAC AACTTACACA TACAGAACCA CA
          ACACCCTAAG CCACCTTCCT CAAAATCCAA AACCCACACA ACCGAAACAA CA
```

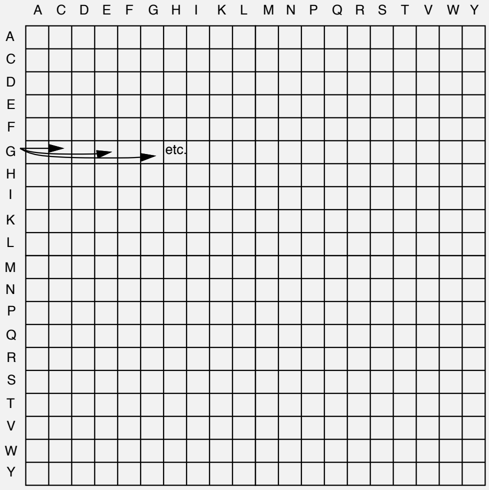
which gives the ML tree

ln L = −1405.6083



Maximum likelihood tree for the Hasegawa 232-site mitochondrial D-loop data set, with Ts/Tn set to 2, analyzed with maximum likelihood (DNAML)

Models with amino acids



Dayhoff PAM model

Jones−Taylor−Thornton model

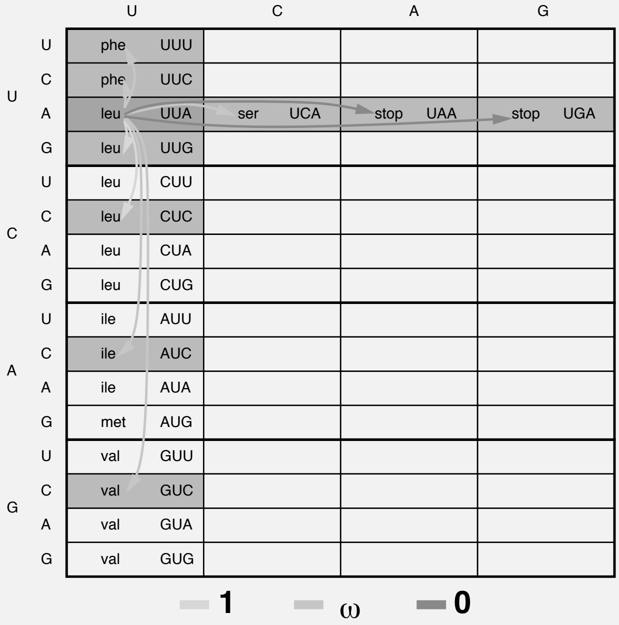
specific models for secondary−structure contexts or membrane proteins

Models adapted from Henikoff BLOSUM scoring

But ... how to take DNA sequence into account? Constraints of code?

Codon models

Goldman & Yang, 1994; Muse & Gaut, 1994)

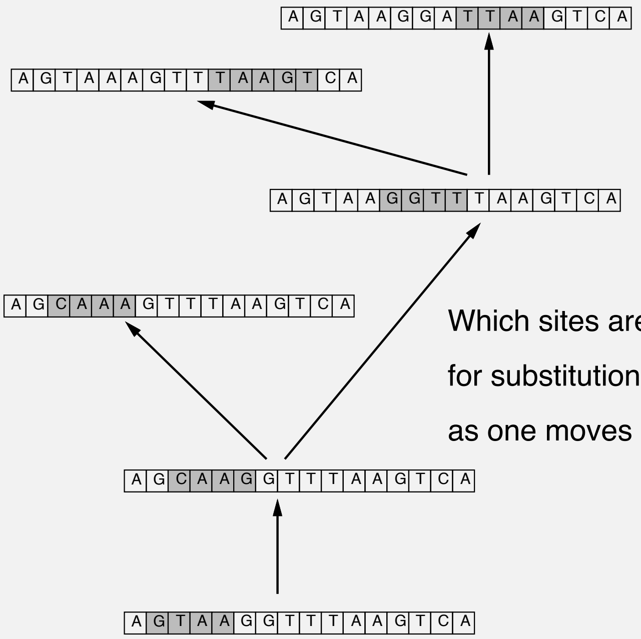


		U	C	A	G
U	U	phe UUU			
	C	phe UUC			
	A	leu UUA	ser UCA	stop UAA	stop UGA
	G	leu UUG			
C	U	leu CUU			
	C	leu CUC			
	A	leu CUA			
	G	leu CUG			
A	U	ile AUU			
	C	ile AUC			
	A	ile AUA			
	G	met AUG			
G	U	val GUU			
	C	val GUC			
	A	val GUA			
	G	val GUG			

Probabilities of change vary depending on whether amino acid is changing, and to what

Covarion models?

(Fitch and Markowitz, 1970)



Which sites are available

for substitutions changes

as one moves along the tree

How to calculate likelihood with rate variation

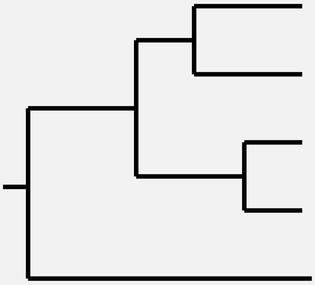
Easy! Since branch lengths always come into transition probability formulas as $r \times t$, can just multiply lengths of branches by the appropriate factor to calculate the likelihood for a site.

(Branch lengths are usually scaled by assuming a rate of 1.)

Rate variation among sites

Sites

Phylogeny



1	2	3	4	5	6	7	8	
C	A	C	G	A	C	G	A	
C	G	T	A	A	C	G	A	
C	G	A	G	A	C	G	G	...
C	A	A	A	A	C	G	G	
A	A	G	T	G	C	G	C	

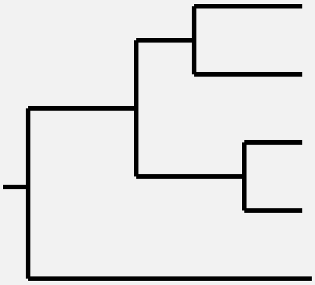
Rates at different sites:

Rates of evolution									
10.0			○			○			
2.0		○			○			○	•••
0.3	○			○			○		

Hidden Markov Model of rate variation among sites

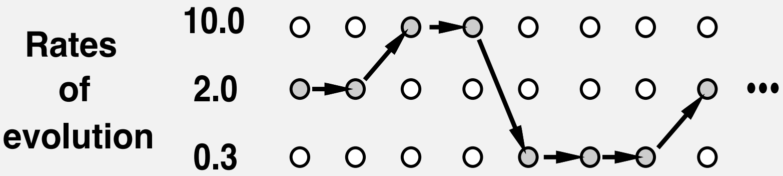
Sites

Phylogeny



1	2	3	4	5	6	7	8	
C	A	C	G	A	C	G	A	
C	G	T	A	A	C	G	A	
C	G	A	G	A	C	G	G	...
C	A	A	A	A	C	G	G	
A	A	G	T	G	C	G	C	

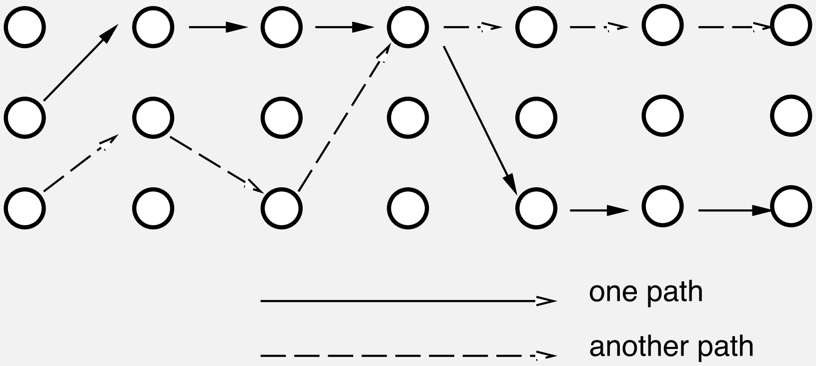
Hidden Markov chain that assigns rates:



Hidden Markov Models sum up over all paths

The Hidden Markov Chain method sums up likelihoods over all possible paths through the states:

$$\text{Prob (Data l tree)} \;=\; \sum_{\text{paths}} \text{Prob(Datal tree, path)}\;\; \text{Prob(path)}$$

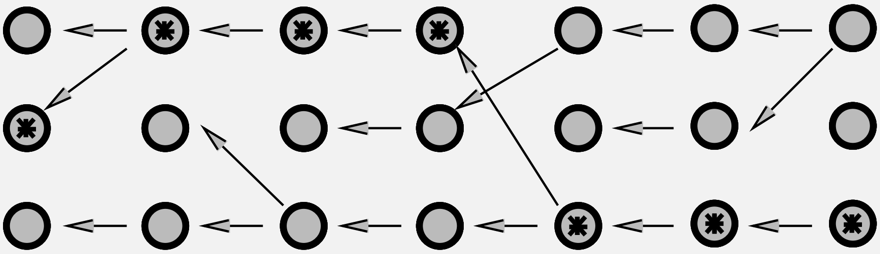


This is done using a recursive algorithm known as the Forwards

The rate combination contributing the most:

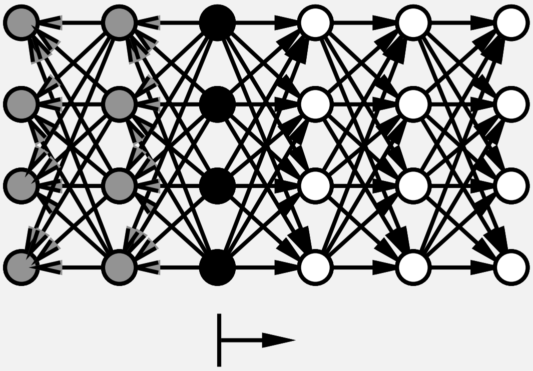
We can leave behind pointers that allow us to backtrack

This can be done by a dynamic programming algorithm called the Viterbi Algorithm, well-known in the HMM literature.



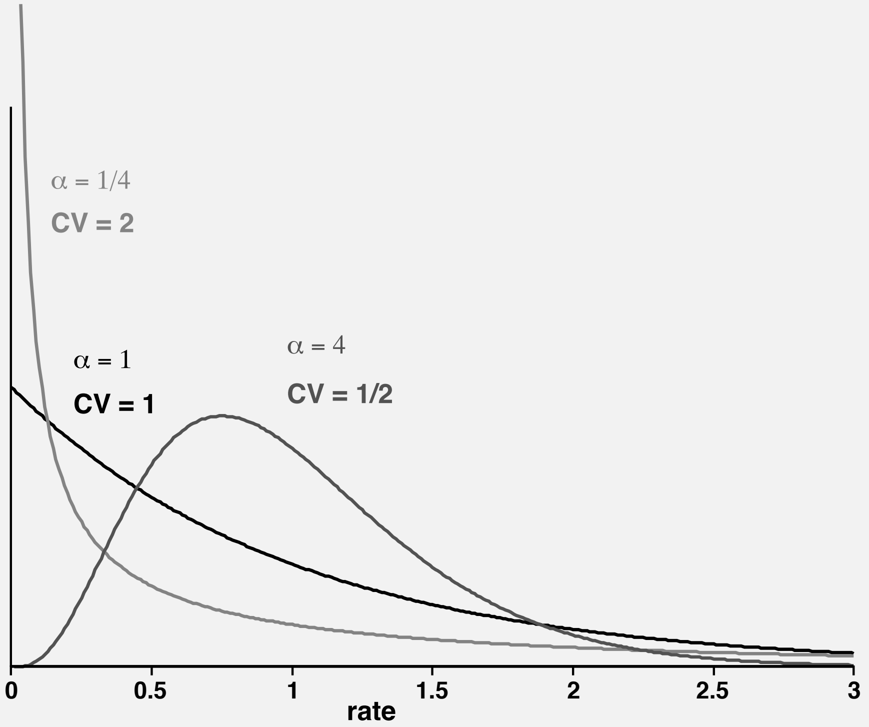
(Of course, this one might account for only 0.001 of the likelihood)

Forwards-Backwards algorithm (marginal probabilities)



The Forwards–Backwards algorithm
can calculate the contribution of one rate
at a given site to the overall likelihood
(a little different from the Viterbi calculation)

The Gamma distribution, used for rates



A numerical example. Cyochrome B

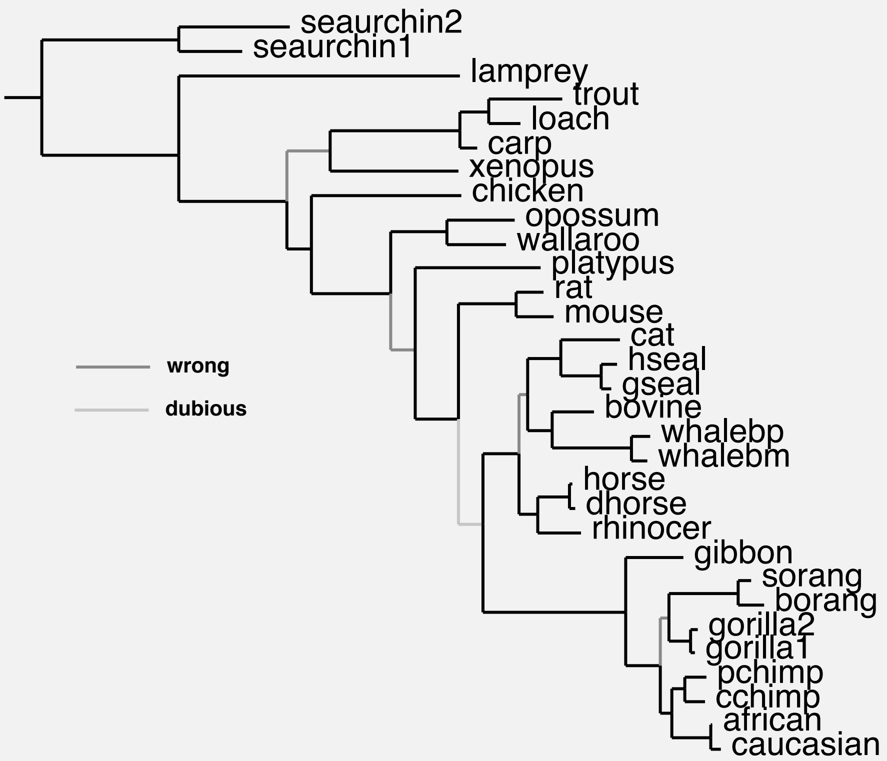
We analyze 31 cytochrome B sequences, aligned by Naoko Takezaki, using the Proml protein maximum likelihood program. Assume a Hidden Markov Model with 3 states, rates:

category	rate	probability
1	0.0	0.2
2	1.0	0.4
3	3.0	0.4

and expected block length 3.

We get a reasonable, but not perfect, tree with the best rate combination inferred to be

The cytochrome B tree from the above run



(It’s not perfect).

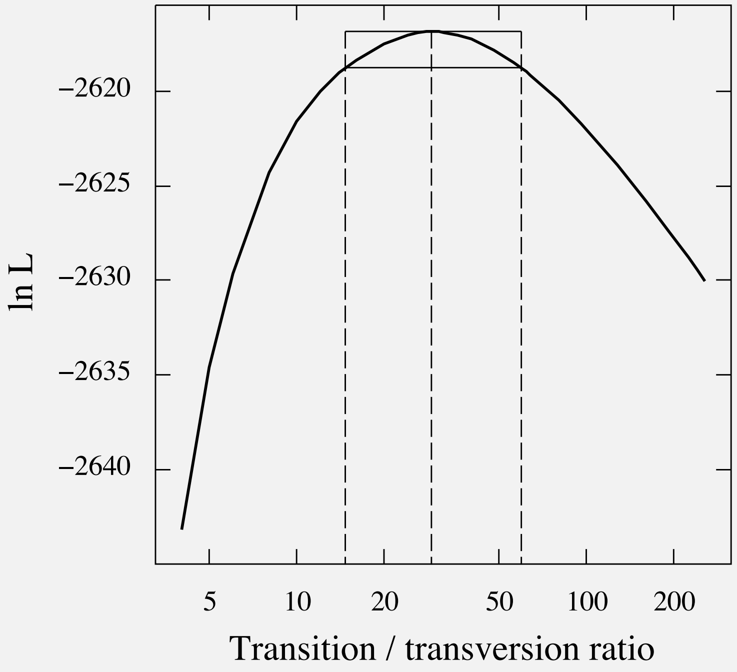
Rates inferred from Cytochrome B

```
             1333333311 3222322313 3321113222 2133111111 1331133123 112211111
african      M-----TPMRK INPLMKLINH SFIDLPTPSN ISAWWNFGSL LGACLILQIT TGLFLAM
caucasian    .......... .........R .......... .......... ..T....... .........
cchimp       .......T.. .......... .......... .......... .......... .........
pchimp       .......T.. .......... .......... ..T....... .......... .........
gorilla1     .......... T...A..... .......... ..T....... .......... .........
gorilla2     .......... T...A..... .......... ..T....... .......... .........
borang       .......... T......... .L........ .......... ......I.TI .........
sorang       ......ST.. T......... .L........ .......... ......I... .........
gibbon       .......L.. T......... .L....A... ..M....... .........I .........
bovine       ......NI.. SH....IV.N A.....A... ..S....... ..I......L .........
whalebm      ......NI.. TH....I..D A......... ..S....... ..L...V..L .........
whalebp      ......NI.. TH....IV.D A.V....... ..S....... ..L...M..L .........
dhorse       ......NI.. SH..I.I... ......A... ..S....... ..I......L .........
horse        ......NI.. SH..I.I... .......... ..S....... ..I......L .........
rhinocer     ......NI.. SH..V.I... .......... ..S....... ..I......L .........
cat          ......NI.. SH..I.I... ......A... .......... ..V..T...L .........
gseal        ......NI.. TH....I..N .......... .......... ..I......L .........
hseal        ......NI.. TH....I..N .......... .......... ..I......L .........
mouse        ......N... TH..F.I... ......A... ..S....... ..V..MV..I .........
rat          ......NI.. SH..F.I... ......A... ..S....... ..V..MV..L .........
platypus     .....NNL.. TH..I.IV.. .......... ..S....... ..L...I..L .........
wallaroo     ......NL.. SH..I.IV.. ......A... .......... ......I..L .........
opossum      ......NI.. TH....I..D .......... .......... ..V...I..L .........
chicken      ....APNI.. SH..L.M..N .L....A... .......... .AV..MT..L ...L.....
xenopus      ....APNI.. SH..I.I..N .......... ..SL...... ..V...A..I .........
carp         ....A-SL.. TH..I.IA.D ALV....... .......... ..L...T..L .........
loach        ....A-SL.. TH..I.IA.D ALV...A... ..V....... ..L...T..L .........
trout        ....A-NL.. TH..L.IA.D ALV...A... ..V....... ..L..AT..L .........
lamprey      .SHQPSII.. TH..LS.G.S MLV...S.A. .......... .SL......I ...I.....
seaurchin1   -...LG.L.. EH.IFRIL.S T.V...L... L.I....... ..L...T..L .........
seaurchin2   -...AG.L.. EH.IFRIL.S T.V...L... L.M....... ..L...I.LI ..I......
```

Rates inferred from Cytochrome B

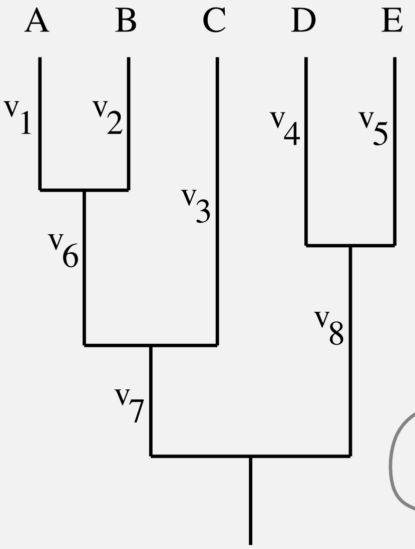
```
             2223311112 2222222222 2222232112 2222222223 1222221112 333311112
african      PDASTAFSSI AHITRDVNYG WIIRYLHANG ASMFFICLFL HIGRGLYYGS FLYSETWN
caucasian    .......... .......... .......... .......... .......... .........
cchimp       .......... .......... .......... .......... .......... ...L.....
pchimp       .......... .......... .......... ...L...... .V........ ...L.....
gorilla1     .......... .......... .T........ .......... .......... ..HQ.....
gorilla2     .......... .......... .T........ .......... .......... ..HQ.....
borang       ...T...... .......... .M..H..... ...L...... .......... .THL.....
sorang       .......... .......... .M..H..... .......... .......... .THL.....
gibbon       .........V .......... .......... .......... .......... ...L.....
bovine       S.TT.....V T..C...... .....M.... ........YM .V........ YTFL.....
whalebm      ..TM.....V T..C...... .V........ ........YA .M........ HAFR.....
whalebp      ..TT.....V T..C...... .......... ........YA .M........ YAFR.....
dhorse       S.TT.....V T..C...... .......... .........I .V........ YTFL.....
horse        S.TT.....V T..C...... .......... .........I .V........ YTFL.....
rhinocer     ..TT.....V T..C...... .M........ .........I .V........ YTFL.....
cat          S.TM.....V T..C...... .......... ........YM .V...M.... YTF......
gseal        S.TT.....V T..C...... .......... ........YM .V........ YTFT.....
hseal        S.TT.....V T..C...... .......... ........YM .V........ YTFT.....
mouse        S.TM.....V T..C...... .L...M.... .......... .V........ YTFM.....
rat          S.TM.....V T..C...... .L....Q... .......... .V........ YTFL.....
platypus     S.T......V ...C...... .L...M.... ..L..M.I.. .......... YTQT.....
wallaroo     S.TL.....V ...C...... .L..N..... .....M.... .V...I.... Y..K.....
opossum      S.TL.....V ...C...... .L..NI.... .....M.... .V...I.... Y..K.....
chicken      A.T.L....V ..TC.N.Q.. .L..N..... ..F....I.. .......... Y..K....T
xenopus      A.T.M....V ...CF..... LL..N..... L.F....IY. .......... ...K.....
carp         S.I......V T..C...... .L..NV.... ..F....IYM ..A....... Y..K.....
loach        S.I......V ...C...... .L..NI.... ..F.....Y. ..A....... Y..K.....
trout        S.I......V C..C...S.. .L..NI.... ..F....IYM ..A....... Y..K.....
lamprey      ANTEL....V M..C....N. .LM.N..... .......IYA .....I.... Y..K....V
seaurchin1   A.I.L....A S..C...... .LL.NV.... ..L....MYC .........G SNKI....V
seaurchin2   A.INL....V S..C...... .LL.NV...C ..L....MYC .........L TNKI....V
```

Likelihood curve and its confidence interval



(This is for the 14-species primates data available for download).

Constraints on a tree for a clock



Constraints for a clock

$v_1 = v_2$

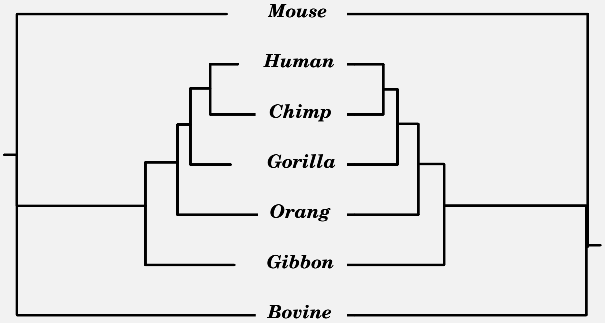
$v_4 = v_5$

$v_1 + v_6 = v_3$

$v_3 + v_7 = v_4 + v_8$

Does not constrain the branch length on the unrooted tree

Likelihood-ratio test of molecular clock



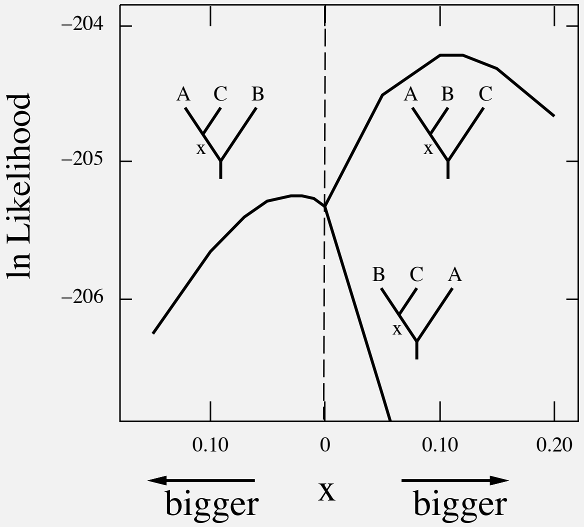
	log–likelihood	parameters
Without clock	−1405.608	11
With clock	−1407.085	6
Difference	1.477	5

$\chi^2 =$ 2.954 df = 5

(non–significant)

(This is for this 7-species subset of the primates data).

Likelihood surface for three clocklike trees



(These are “profile likelihoods" as they show the largest likelihood for that value of x , maximizing over the other branch length in the tree.)

Two trees to be tested using KHT test

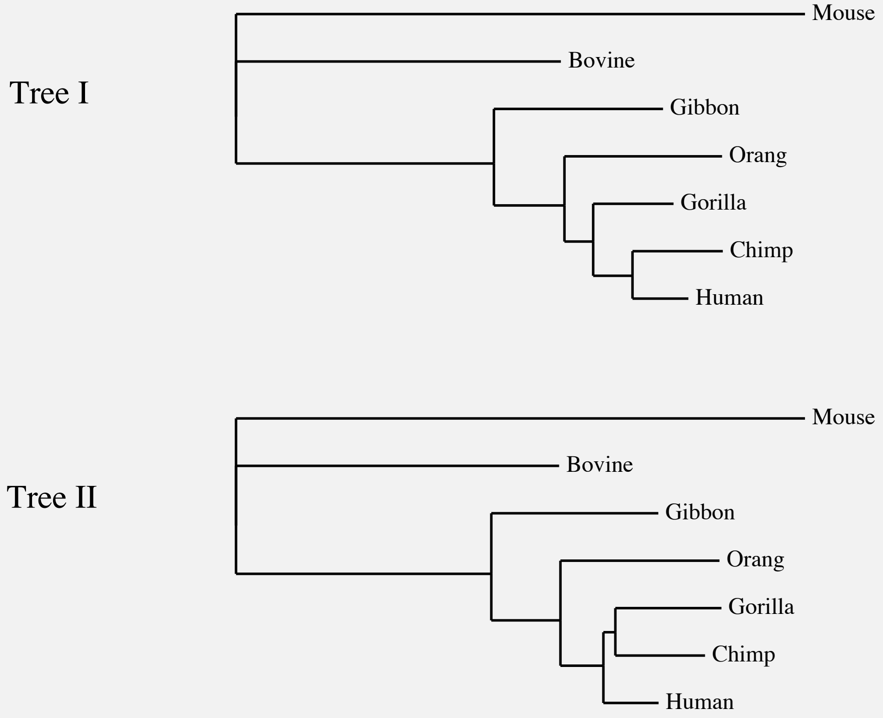
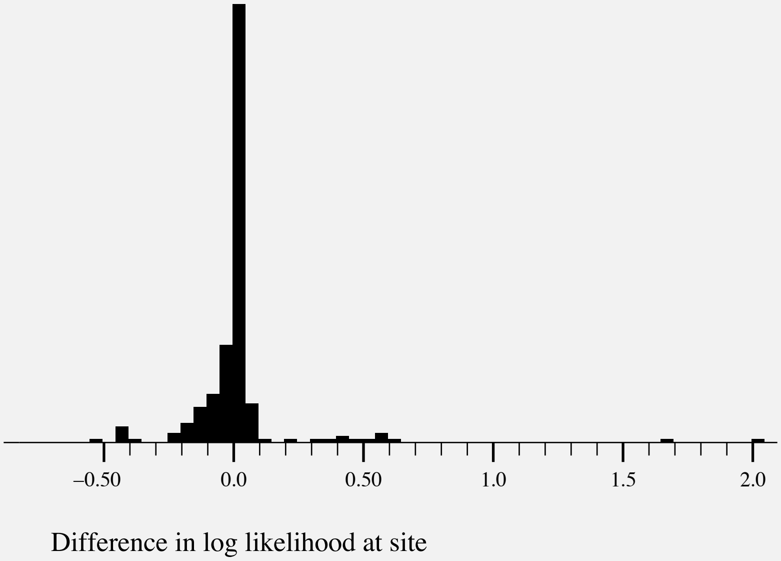


Table of differences in log-likelihood

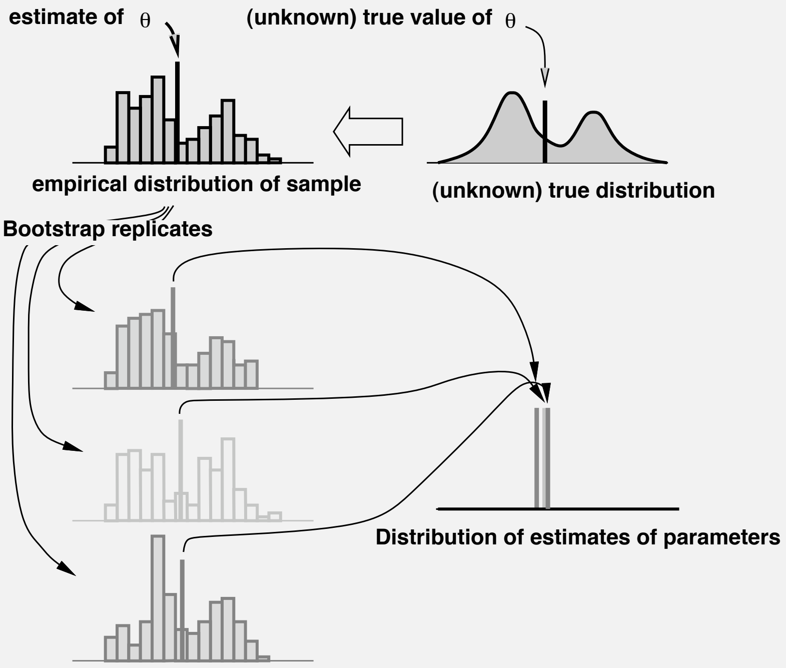
Tree \ site	1	2	3	4	5	6		231	232	ln L
I	−2.971	−4.483	−5.673	−5.883	−2.691	−8.003	…	−2.971	−2.691	−1405.61
II	−2.983	−4.494	−5.685	−5.898	−2.700	−7.572	…	−2.987	−2.705	−1408.80
Diff	+0.012	+0.111	+0.013	+0.015	+0.010	−0.431	…	+0.012	+0.010	+3.19

Histogram of those differences



Do sign test, or t-test, or similar nonparametric tests.

Bootstrap sampling (with mixtures of normals)

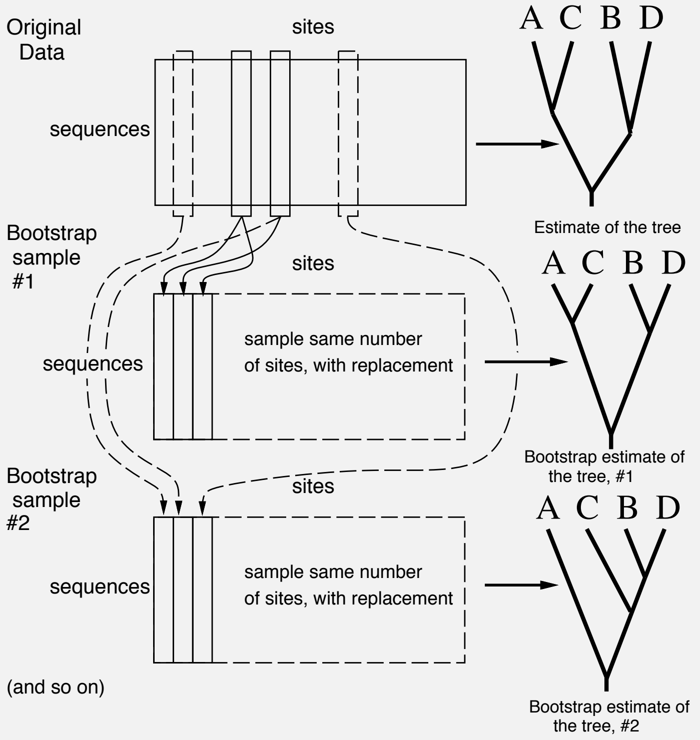

estimate of θ
(unknown) true value of θ
empirical distribution of sample
(unknown) true distribution
Bootstrap replicates
Distribution of estimates of parameters

Bootstrap sampling

To infer the error in a quantity, θ, estimated from a sample of points $x_1, x_2, \ldots, x_n$ we can

- Do the following R times ($R = 1000$ or so)
- Draw a “bootstrap sample" by sampling n times with replacement from the sample. Call these $x_1^*, x_2^*, \ldots, x_n^*$. Note that some of the original points are represented more than once in the bootstrap sample, some once, some not at all.
- Estimate θ from each of the bootstrap samples, call these $\hat{\theta}_k^*$ ($k = 1, 2, \ldots, R$)
- When all R bootstrap samples have been done, the distribution of $\hat{\theta}_i^*$ estimates the distribution one would get if one were able to draw repeated samples of n data points from the unknown true distribution.

Bootstrap sampling of phylogenies

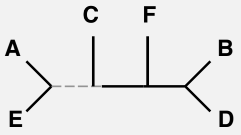

Original Data
sites
sequences
A C B D
Estimate of the tree
Bootstrap sample #1
sites
sequences
sample same number of sites, with replacement
A C B D
Bootstrap estimate of the tree, #1
Bootstrap sample #2
sites
sequences
sample same number of sites, with replacement
A C B D
Bootstrap estimate of the tree, #2
(and so on)

Analyzing bootstraps with phylogenies

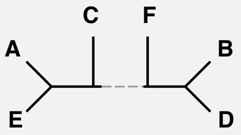
The sites are assumed to have evolved independently given the tree. They are the entities that are sampled (the x_i). The trees play the role of the parameter. One ends up with a cloud of R sampled trees.

To summarize this cloud, we ask, for each branch in the tree, how frequently it appears among the cloud of trees. We make a tree that summarizes this for all the most frequently occurring branches. This is the majority rule consensus tree of the bootstrap estimates of the tree.

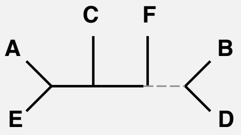
Partitions from branches in an (unrooted) tree



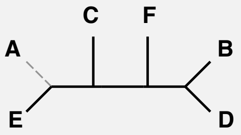
AE | BCDF



ACE | BDF



ACEF | BD

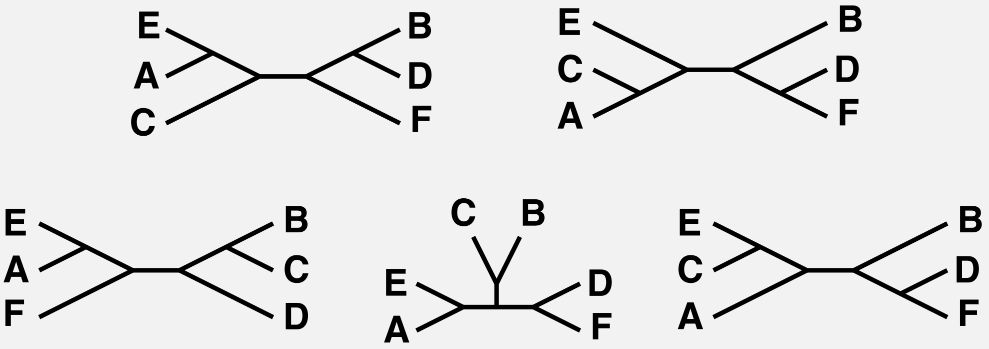


A | CEFBD

and so on for all the other external (tip) branches

The majority-rule consensus tree

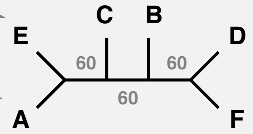
Trees:



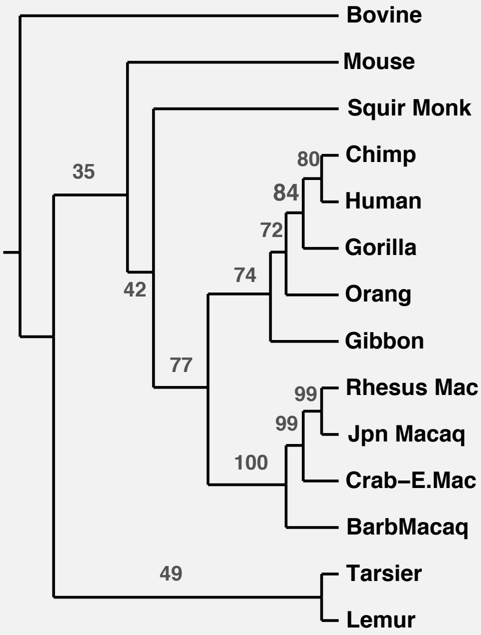
How many times each partition of species is found:

AE I BCDF	3
ACE I BDF	3
ACEF I BD	1
AC I BDEF	1
AEF I BCD	1
ADEF I BC	2
ABDF I EC	1
ABCE I DF	3

Majority−rule consensus tree of the unrooted trees:



Bootstrap sampling of a phylogeny

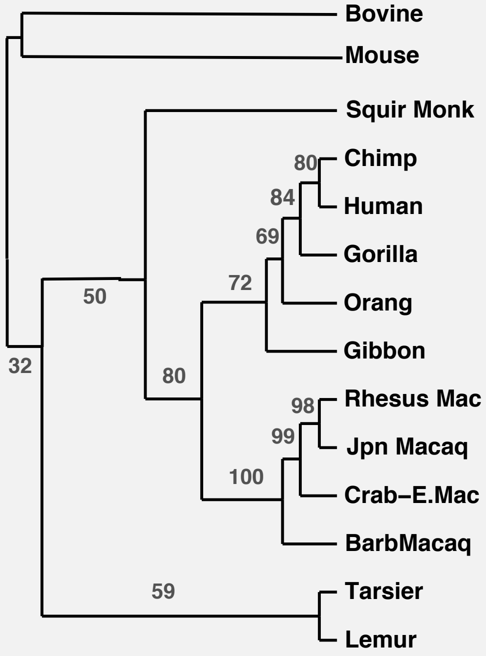


In this example, parsimony was used to infer the tree.

Potential problems with the bootstrap

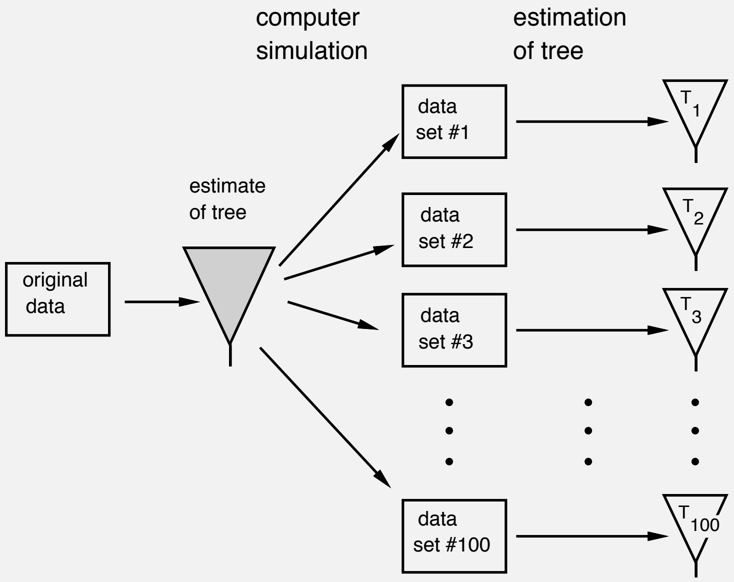
- Sites may not evolve independently
- Sites may not come from a common distribution (but you can consider them to be sampled from a mixture of possible distributions)
- If do not know which branch is of interest at the outset, a “multiple-tests" problem means that the most extreme P values are overstated
- P values are biased (too conservative)
- Bootstrapping does not correct biases in phylogeny methods

Delete-half jackknife P values



In this example, parsimony was used to infer the tree.

A diagram of the parametric bootstrap



computer simulation

estimation of tree

original data

estimate of tree

data set #1

data set #2

data set #3

data set #100

T_1

T_2

T_3

T_{100}

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Likelihood

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