CS 394C
March 21, 2012

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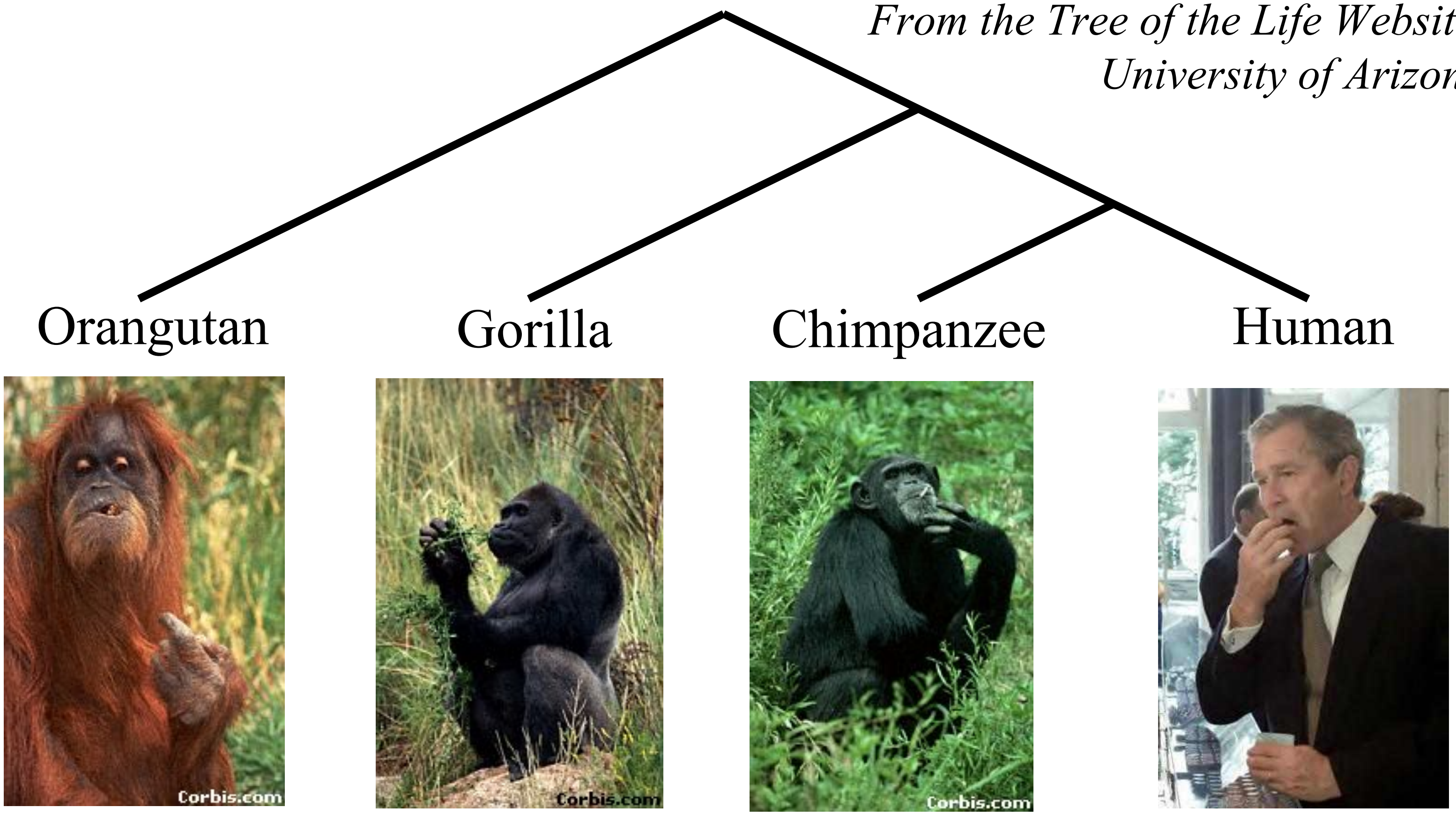
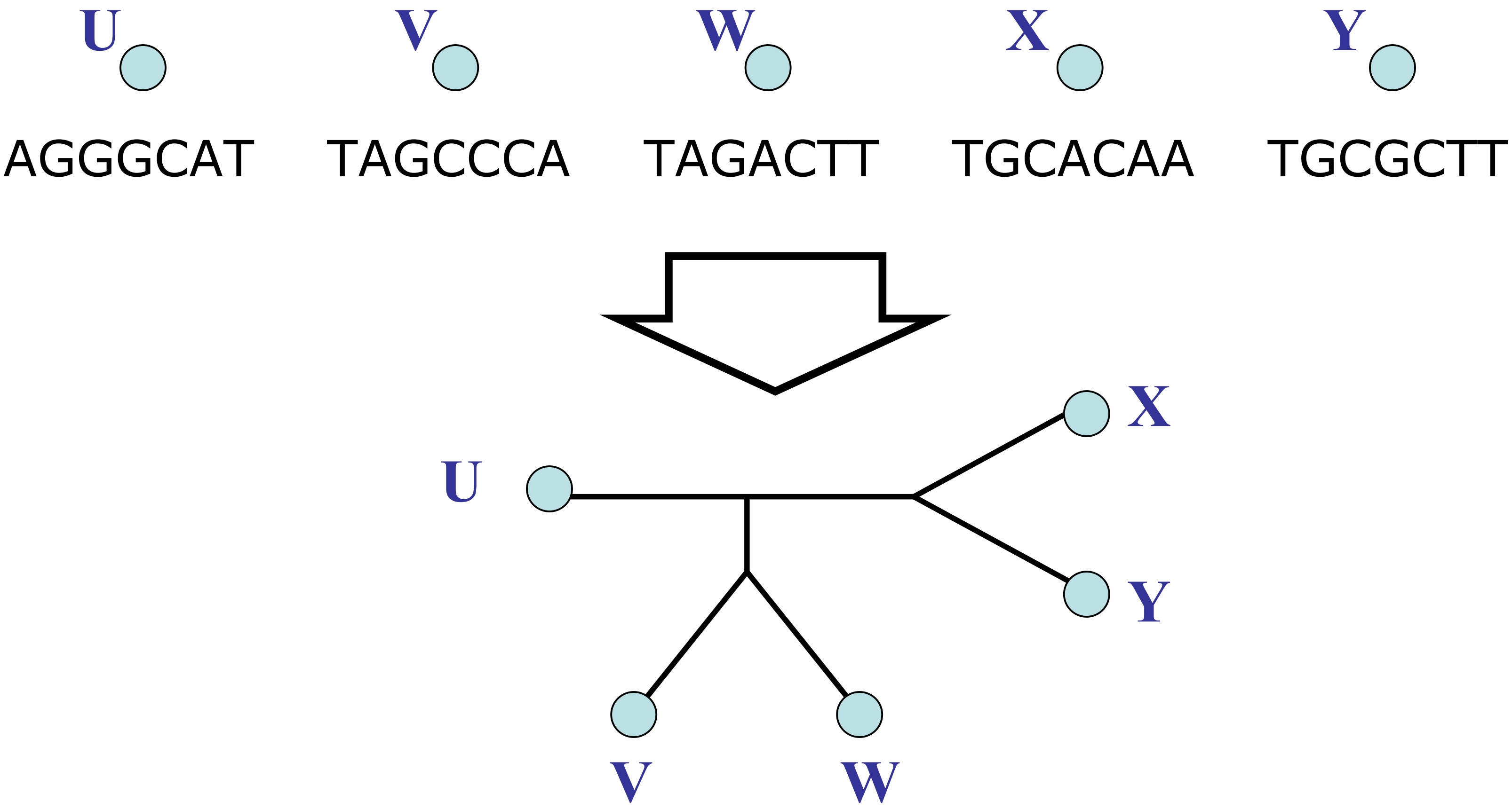
Phylogeny



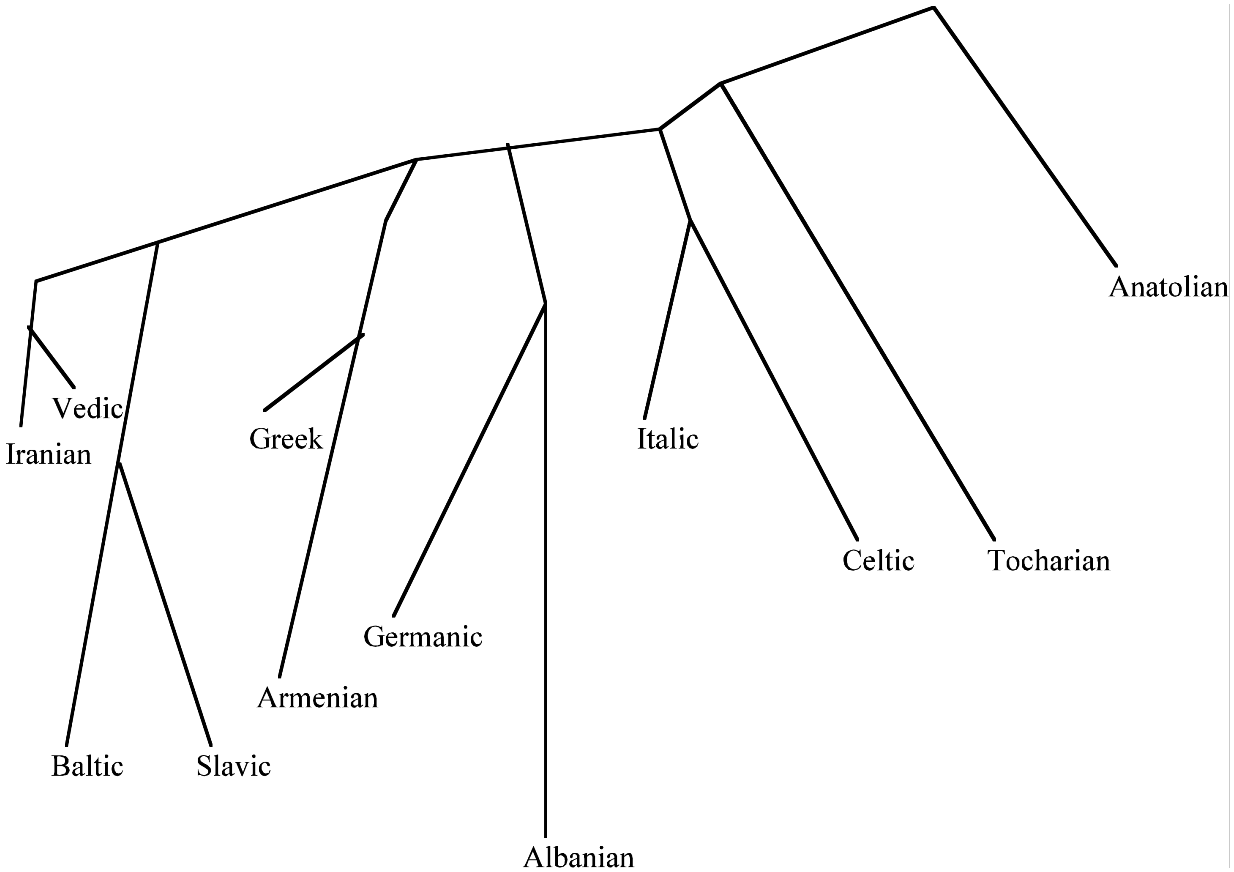
From the Tree of the Life Website,
University of Arizona

Phylogeny Problem



AGGGCAT TAGCCCA TAGACTT TGCACAA TGCGCTT

Possible Indo-European tree (Ringe, Warnow and Taylor 2000)

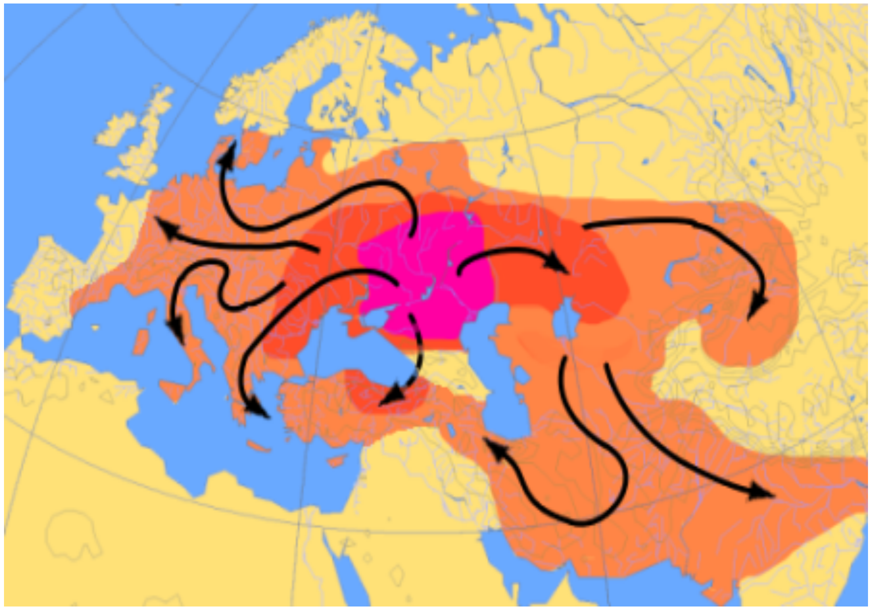


Questions about Indo-European (IE)

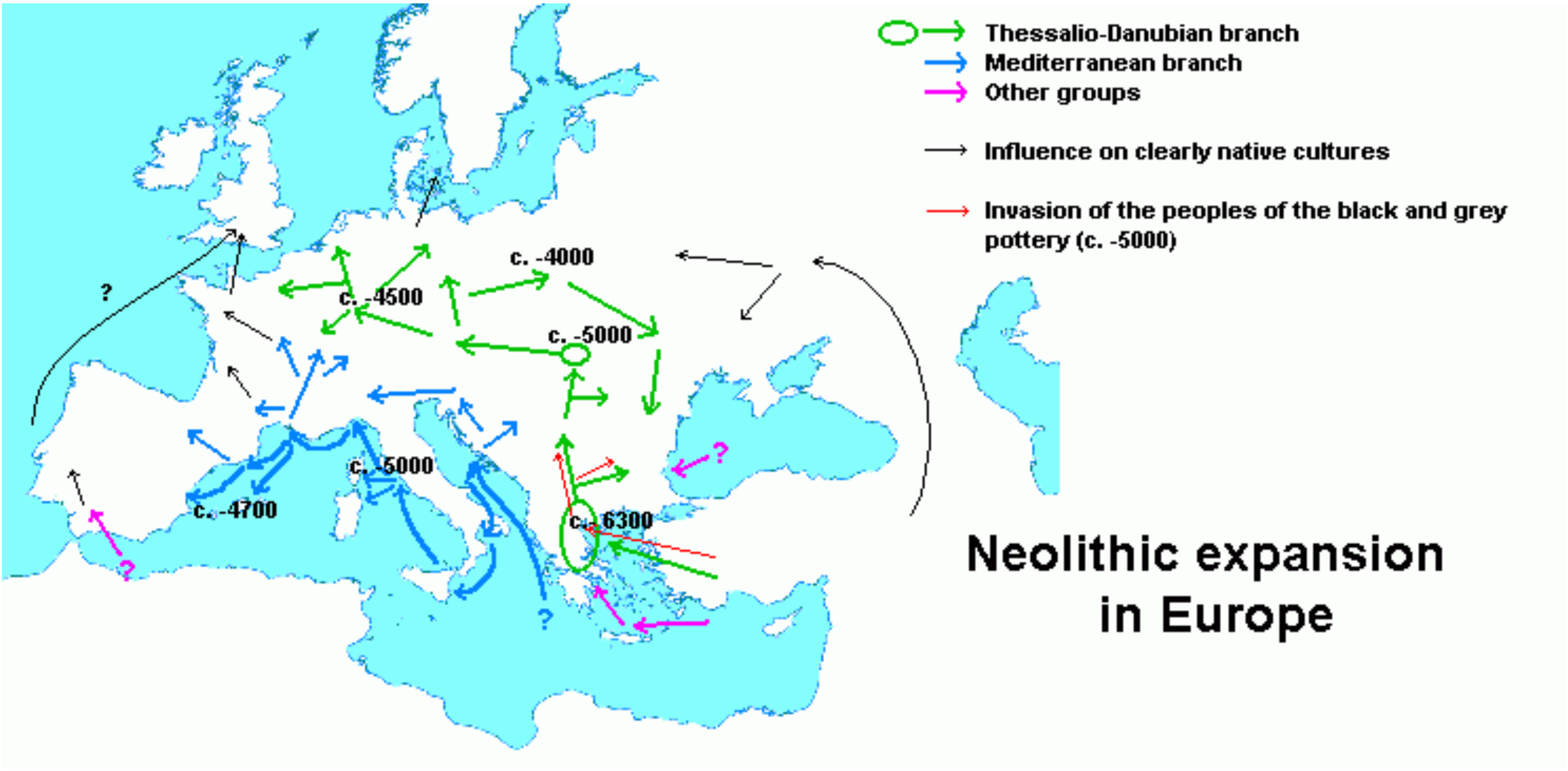
- How did the IE family of languages evolve?
- Where is the IE homeland?
- When did Proto-IE “end”?
- What was life like for the speakers of proto-Indo-European (PIE)?

The Kurgan Expansion

- Date of PIE ~4000 BCE.
- Map of Indo-European migrations from ca. 4000 to 1000 BC according to the Kurgan model
- From http://indo-european.eu/wiki



The Anatolian hypothesis
(from wikipedia.org)



Date for PIE ~7000 BCE

Historical Linguistic Data

- A character is a function that maps a set of languages, L, to a set of states.
- Three kinds of characters:
  - Phonological (sound changes)
  - Lexical (meanings based on a wordlist)
  - Morphological (especially inflectional)

Phylogenies of Languages

- Languages evolve over time, just as biological species do (geographic and other separations induce changes that over time make different dialects incomprehensible -- and new languages appear)
- The result can be modelled as a rooted tree
- The interesting thing is that many characteristics of languages evolve without back mutation or parallel evolution (i.e., homoplasy-free) -- so a "perfect phylogeny" is possible!

Estimating the date and homeland of the proto-Indo-Europeans

- Step 1: Estimate the phylogeny
- Step 2: Reconstruct words for proto-Indo-European (and for intermediate proto-languages)
- Step 3: Use archaeological evidence to constrain dates and geographic locations of the proto-languages

Our objectives

How to estimate the phylogeny?

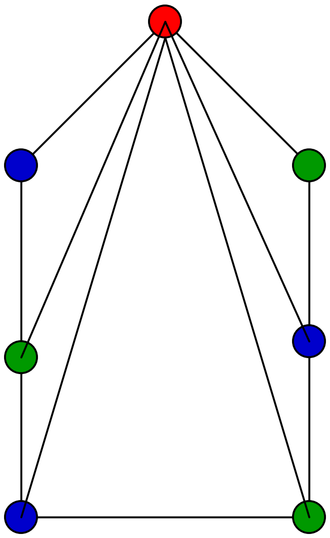
How to model linguistic character evolution?

Part 1

- Triangulating colored graphs
- Perfect phylogenies

Triangulated Graphs

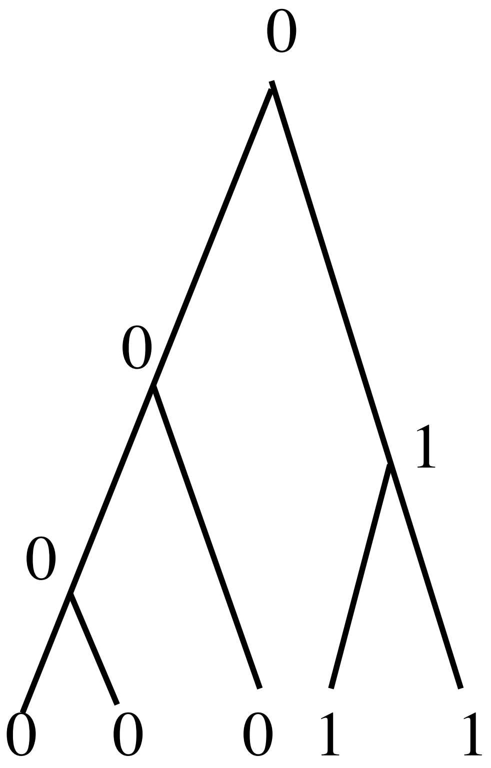
- Definition: A graph is triangulated if it has no simple cycles of size four or more.



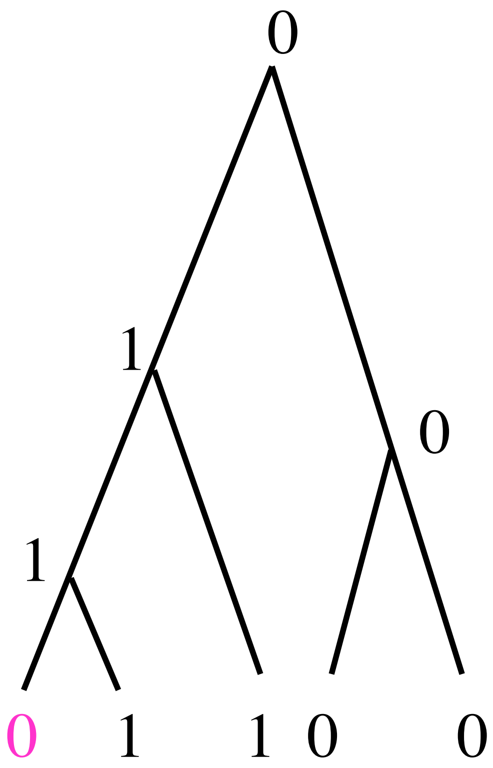
Triangulated graphs and phylogeny estimation

- The "Triangulating Colored Graphs" problem and an application to historical linguistics (this talk)
- Using triangulated graphs to improve the accuracy and sequence length requirements phylogeny estimation in biology (absolute-fast converging methods)
- Using triangulated graphs to speed-up heuristics for NP-hard phylogenetic estimation problems (Rec-I-DCM3-boosting)

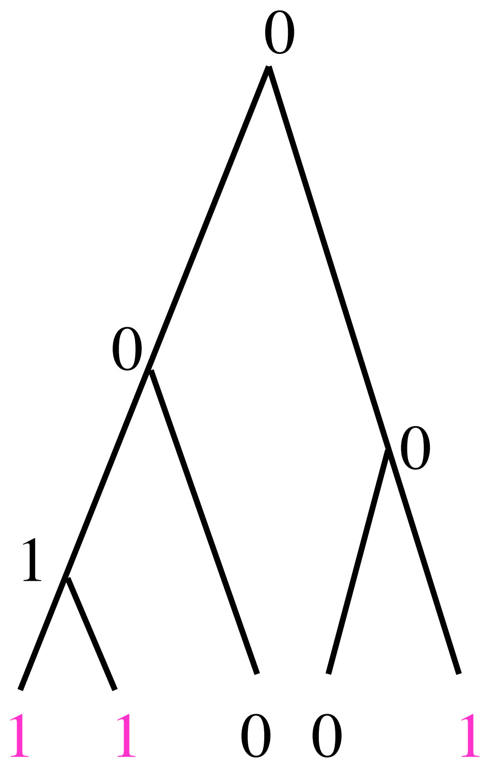
Some useful terminology: homoplasy



no homoplasy



back-mutation



parallel evolution

Perfect Phylogeny

- A phylogeny T for a set S of taxa is a perfect phylogeny if each state of each character occupies a subtree (no character has back-mutations or parallel evolution)

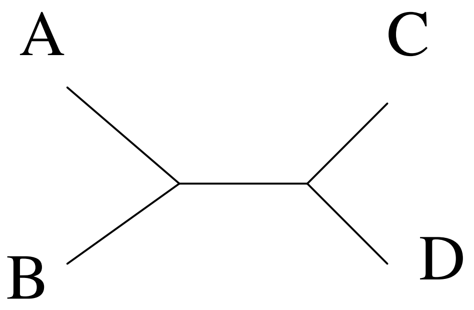
Perfect phylogenies, cont.

- A=(0,0), B=(0,1), C=(1,3), D=(1,2) has a perfect phylogeny!

- A=(0,0), B=(0,1), C=(1,0), D=(1,1) does not have a perfect phylogeny!

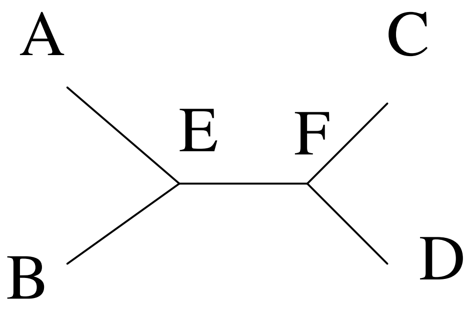
A perfect phylogeny

- A = 0 0
- B = 0 1
- C = 1 3
- D = 1 2



A perfect phylogeny

- A = 0 0
- B = 0 1
- C = 1 3
- D = 1 2
- E = 0 3
- F = 1 3



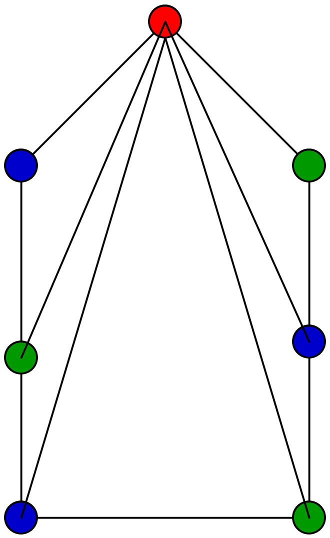
The Perfect Phylogeny Problem

- Given a set S of taxa (species, languages, etc.) determine if a perfect phylogeny T exists for S.

- The problem of determining whether a perfect phylogeny exists is NP-hard (McMorris *et al*. 1994, Steel 1991).

Triangulated Graphs

- Definition: A graph is triangulated if it has no simple cycles of size four or more.

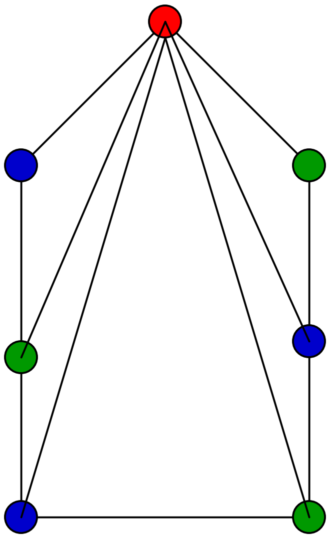


Triangulated graphs and trees

- A graph G=(V,E) is triangulated if and only if there exists a tree T so that G is the intersection graph of a set of subtrees of T.
  - vertices of G correspond to subtrees (f(v) is a subtree of T)
  - (v,w) is an edge in G if and only if f(v) and f(w) have a non-empty intersection

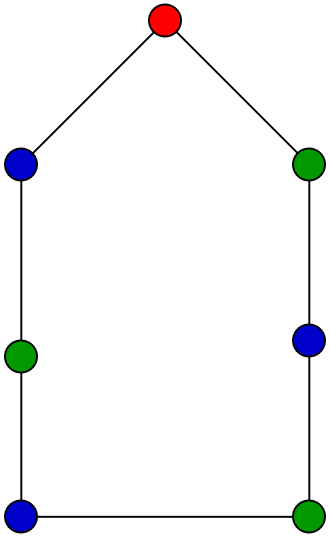
c-Triangulated Graphs

- A vertex-colored graph is c-triangulated if it is triangulated, but also properly colored!



Triangulating Colored Graphs: An Example

A graph that can be c-triangulated



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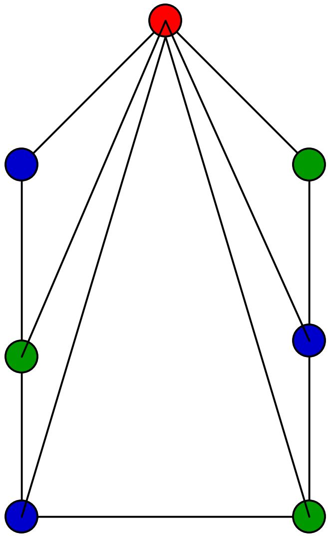
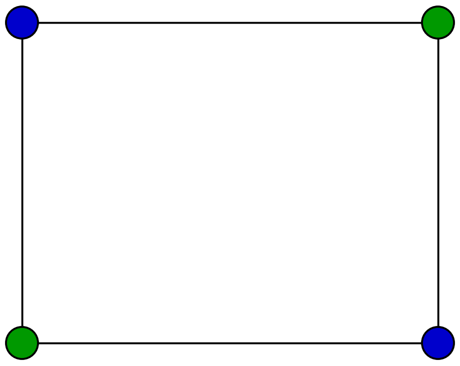
A graph that can be c-triangulated



Triangulating Colored Graphs: An Example

A graph that cannot be c-triangulated



Triangulating Colored Graphs (TCG)

Triangulating Colored Graphs: given a vertex-colored graph G, determine if G can be c-triangulated.

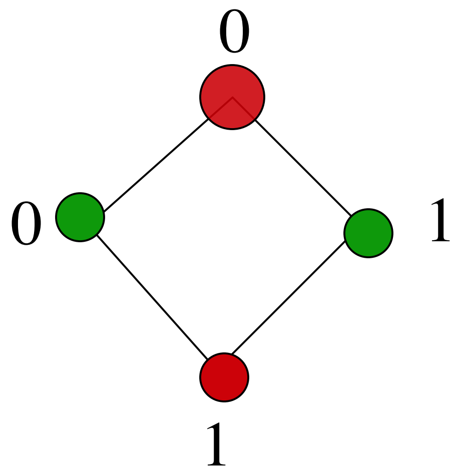
The PP and TCG Problems

- **Buneman's Theorem:**
  A perfect phylogeny exists for a set S *if and only if* the associated character state intersection graph can be *c*-triangulated.

- The PP and TCG problems are polynomially equivalent and NP-hard.

A no-instance of Perfect Phylogeny

- A = 0 0
- B = 0 1
- C = 1 0
- D = 1 1

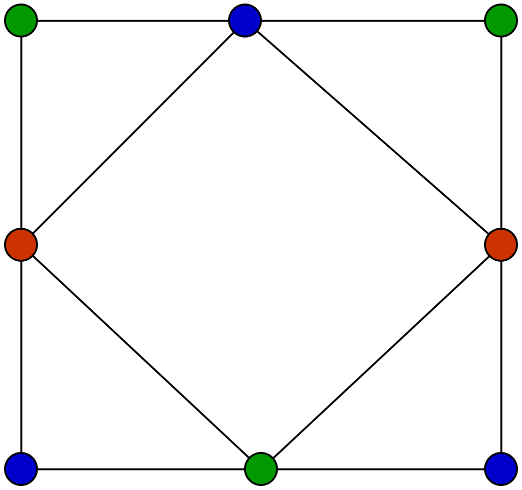


An input to perfect phylogeny (left) of four sequences described by two characters, and its character state intersection graph. Note that the character state intersection graph is 2-colored.

Solving the PP Problem Using Buneman’s Theorem

“Yes” Instance of PP:

	c1	c2	c3
s1	3	2	1
s2	1	2	2
s3	1	1	3
s4	2	1	1



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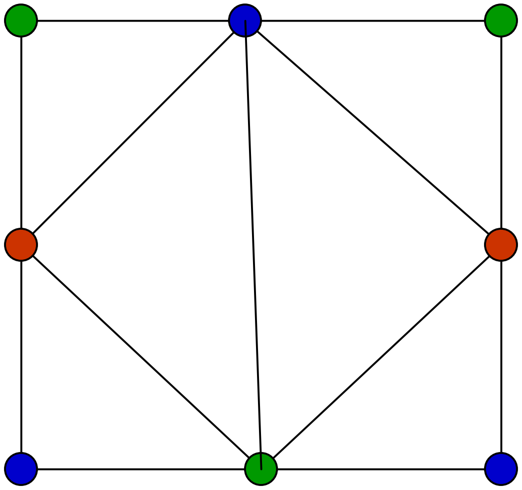


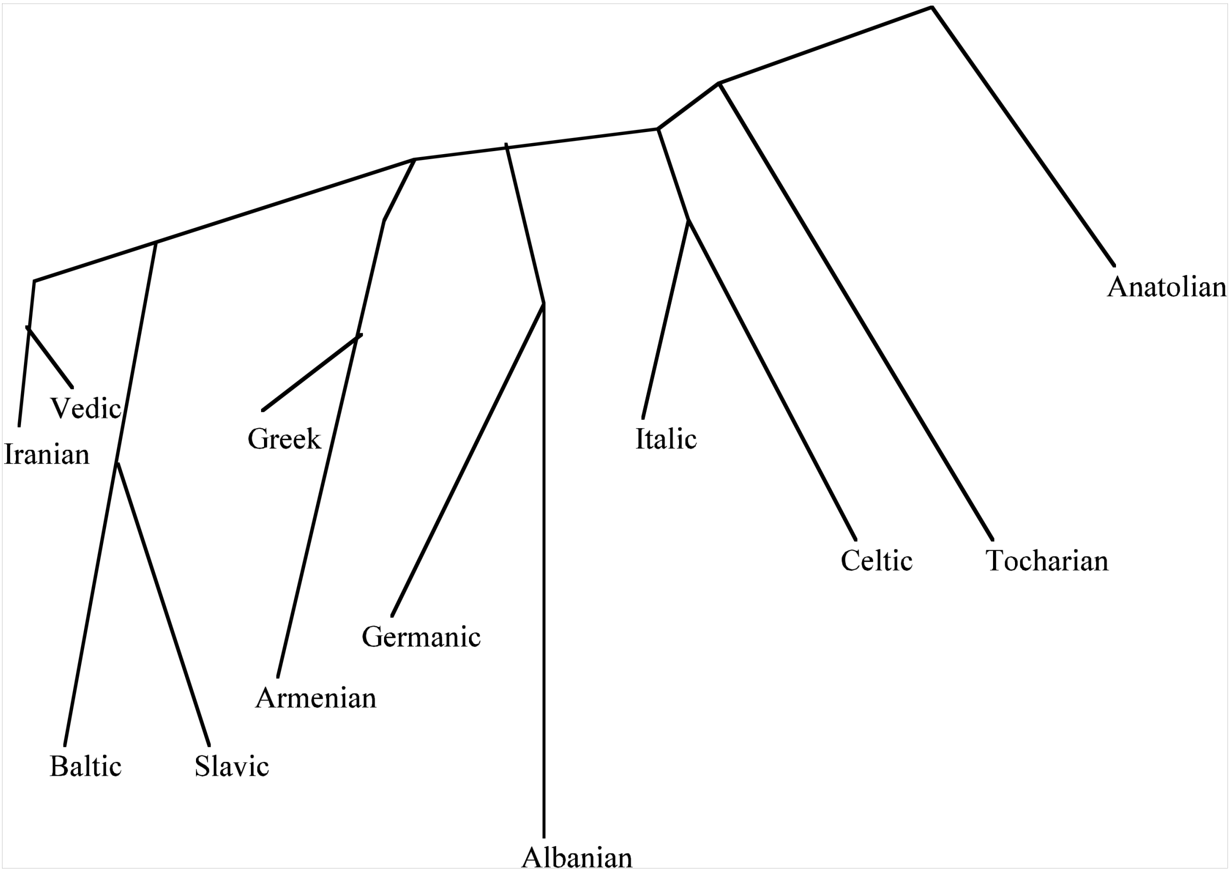
Some special cases are easy

- Binary character perfect phylogeny solvable in linear time
- r-state characters solvable in polynomial time for each r (combinatorial algorithm)
- Two character perfect phylogeny solvable in polynomial time (produces 2-colored graph)
- k-character perfect phylogeny solvable in polynomial time for each k (produces k-colored graphs -- connections to Robertson-Seymour graph minor theory)

Part II

- Historical Linguistics data
- Phylogenetic tree estimation methods
- Phylogenetic network estimation methods
- Stochastic models for linguistic evolution
- Trees and Networks for Indo-European
- Comments about IE history

Possible Indo-European tree (Ringe, Warnow and Taylor 2000)



Phylogenies of Languages

- Languages evolve over time, just as biological species do (geographic and other separations induce changes that over time make different dialects incomprehensible -- and new languages appear)
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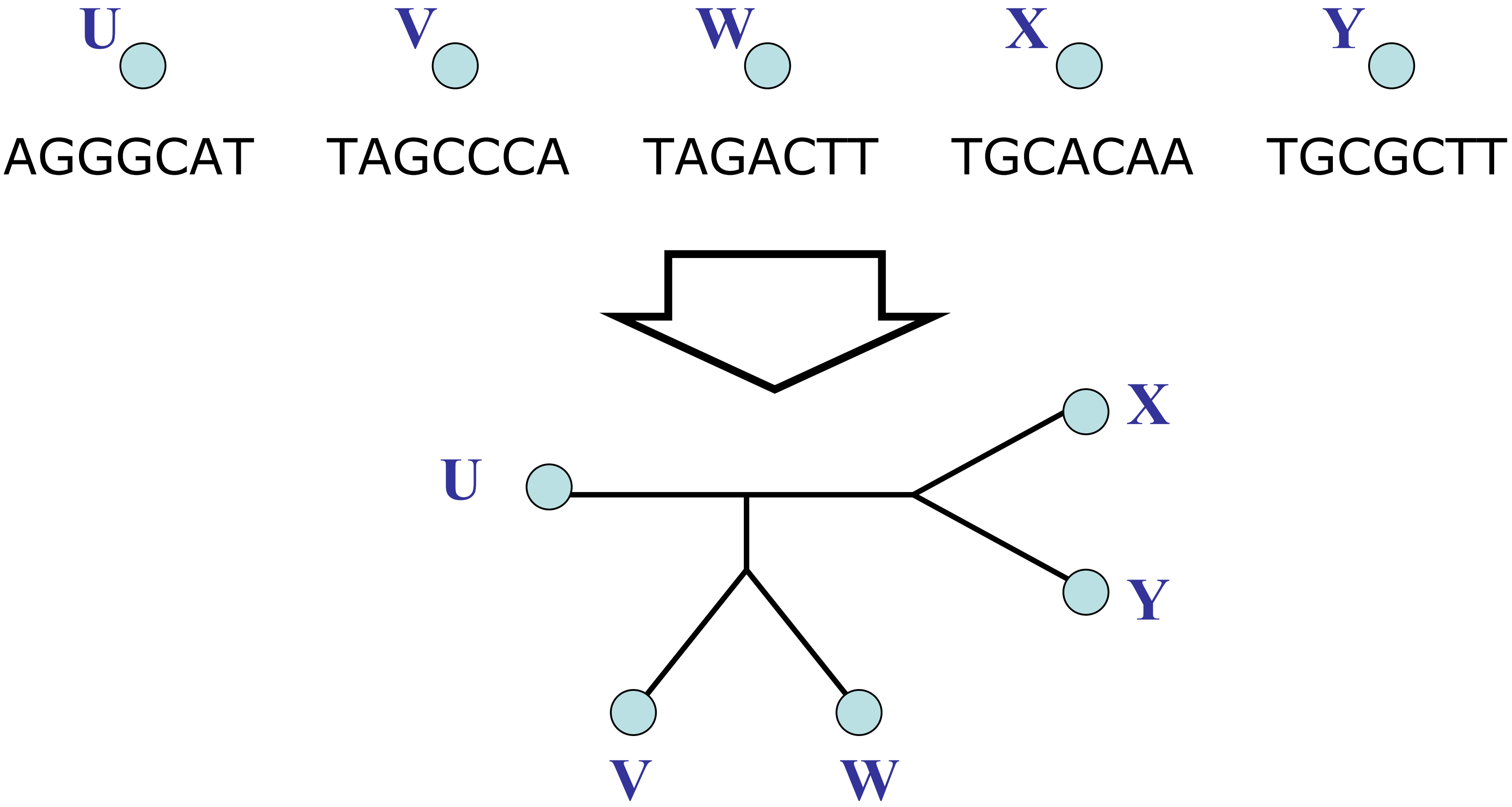
- The interesting thing is that many characteristics of languages evolve without back mutation or parallel evolution -- so a “perfect phylogeny” is possible!

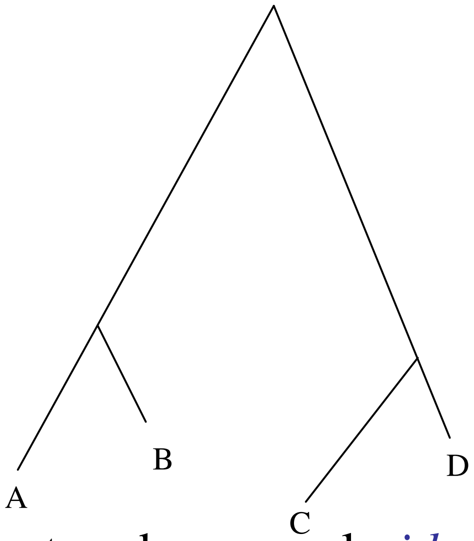


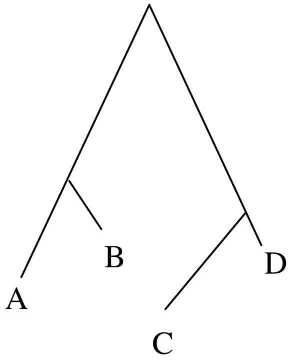
AGGGCAT TAGCCCA TAGACTT TGCACAA TGCGCTT

Standard Markov models of biomolecular sequence evolution

- Sequences evolve just with substitutions
- There are a finite number of states (four for DNA and RNA, 20 for aminoacids)
- Sites (i.e., positions) evolve identically and independently, and have "rates of evolution" that are drawn from a common distribution (typically gamma)
- Numerical parameters describe the probability of substitutions of each type on each edge of the tree

Rates-across-sites

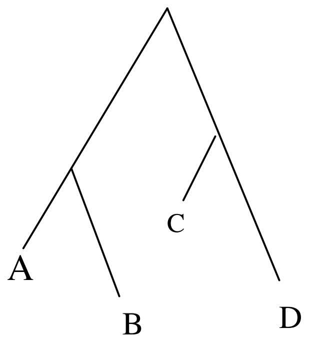


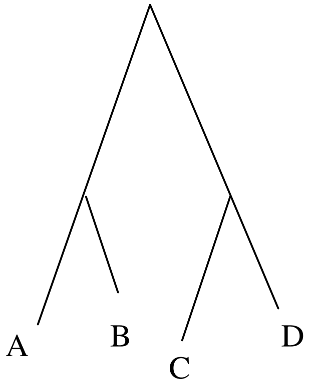


- Dates at nodes are only *identifiable* under rates-across-sites models with simple distributions, and also requires an approximate lexical clock.

Violating the rates-across-sites assumption

- The tree is fixed, but do not just scale up and down.
- Dates are not identifiable.





Linguistic character evolution

- Homoplasy is much less frequent: most changes result in a new state (and hence there is an *unbounded* number of possible states).
- The rates-across-sites assumption is unrealistic
- The lexical clock is known to be false
- Borrowing between languages occurs, but can often be detected.

These properties are very different from models for molecular sequence evolution. Phylogeny estimation requires different techniques.

Dating nodes requires both an approximate lexical clock and also the rates-across-sites assumption. *Neither is likely to be true*.

Historical Linguistic Data

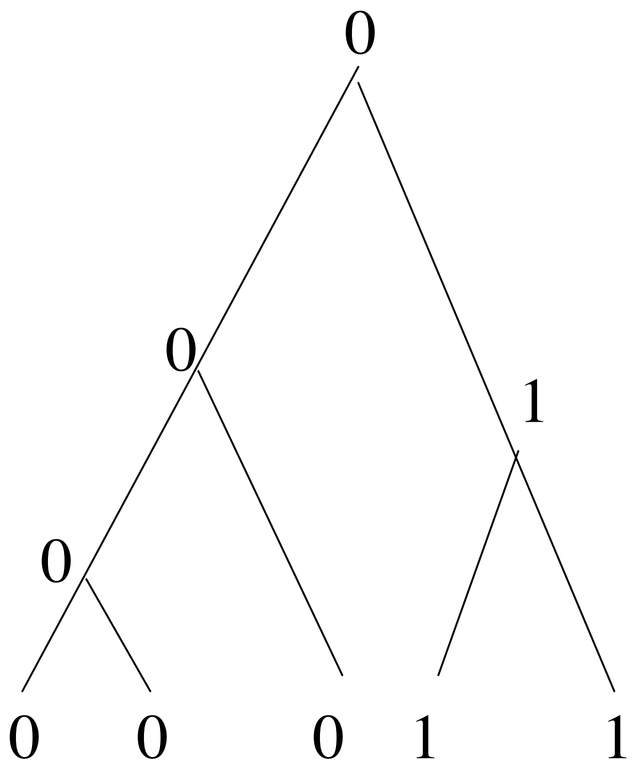
- A character is a function that maps a set of languages, L, to a set of states.
- Three kinds of characters:
  - Phonological (sound changes)
  - Lexical (meanings based on a wordlist)
  - Morphological (especially inflectional)

Sound changes

- Many sound changes are natural, and should not be used for phylogenetic reconstruction.
- Others are bizarre, or are composed of a sequence of simple sound changes. These are useful for subgrouping purposes. Example: Grimm’s Law.
    1. Proto-Indo-European voiceless stops change into voiceless fricatives.
    2. Proto-Indo-European voiced stops become voiceless stops.
    3. Proto-Indo-European voiced aspirated stops become voiced fricatives.

Homoplasy-free evolution

- When a character changes state, it changes to a new state not in the tree
- In other words, there is no homoplasy (character reversal or parallel evolution)
- First inferred for *weird innovations* in phonological characters and morphological characters in the 19th century, and used to establish all the major subgroups within Indo-European.



An Indo-European lexical character: ‘hand’.

Data.

Hittite	kissar	Lithuanian	rankà	Old Prussian	rānkan (acc.)
Armenian	jeṙn	Old English	hand	Latvian	ròka
Greek	xe€r /k^{h}é:r/	Old Irish	lám	Gothic	handus
Albanian	dorë	Latin	manus	Old Norse	hǫnd
Tocharian B	ṣar	Luvian	īssaris	OHG	hant
Vedic	hástas	Lycian	izredi (instr.)	Welsh	llaw
Avestan	zastō	Tocharian A	tsar	Oscan	manim (acc.)
OCS	rǫka	Old Persian	dasta	Umbrian	manf (acc. pl.)

Justification of coding.

Note that “>” means “developed by regular sound change into”; this is important, because developments by regular sound change are mathematically demonstrable. On the other hand, “→” means “developed by process(es) other than regular sound change”; a hypothesis of such a development is not mathematically demonstrable, but it can be highly probable, since many changes are of known types with dozens of well-understood examples.

In the following table each form is descended from the last form which is one tab to the left.

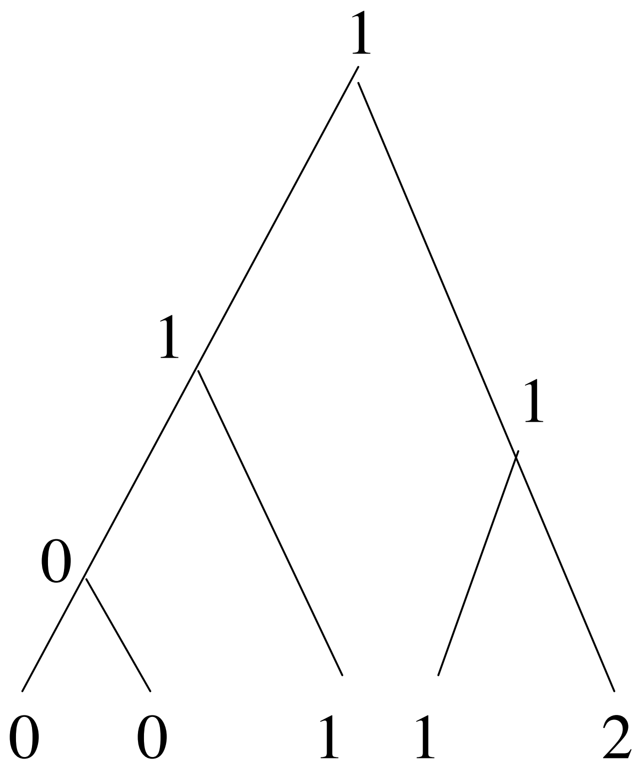
Proto-Indo-European *pĺ̥$h_2$meh_2 ‘flat hand’ (cf. Homeric Greek palãmh) >
Proto-Celtic
*lāmā ‘hand’
> Old Irish *lám*
> Welsh *llaw*
Proto-Germanic *handuz ‘hand’
> Gothic *handus*
>→ Runic Norse *handu (ending influenced by a different class of feminine nouns) > Old Norse *hǫnd*
> Proto-West Germanic *handu
> Old English *hand*
> Old High German *hant*
Proto-Italic *man- ‘hand’
> Latin *manus* (transferred into the u-stems)
>→ Proto-Sabellian *man-
>→ Oscan *manis > *mans, accusative *manim* (transferred into the i-stems)
> Umbrian *man-, accusative plural *manf*

Coding.

Hittite	1
Armenian	1
Greek	1
Albanian	1
Tocharian B	1
Vedic	1a
Avestan	1a
OCS	2
Lithuanian	2
Old English	3
Old Irish	4
Latin	5
Luvian	1
Lycian	1
Tocharian A	1
Old Persian	1a
Old Prussian	2
Latvian	2
Gothic	3
Old Norse	3
OHG	3
Welsh	4
Oscan	5
Umbrian	5

Lexical characters can also evolve without homoplasy

- For every cognate class, the nodes of the tree in that class should form a connected subset - *as long as there is no undetected borrowing nor parallel semantic shift.*



Phylogeny estimation

- Linguists estimate the phylogeny through intensive analysis of a relatively small amount of data
  - a few hundred lexical items, plus
  - a small number of morphological, grammatical, and phonological features
- All data preprocessed for homology assessment and cognate judgments
- All "homoplasy" (parallel evolution, back mutation, or borrowing) must be explained and linguistically believable

Tree estimation methods

- (weighted) Maximum Parsimony
- (weighted) Maximum Compatibility
- Neighbor-joining on distances between languages
- Analyses based upon binary-encodings of linguistic data

Methods based upon binary encoding

- Each multi-state character is split into several binary characters
- The resultant binary character matrix can be analyzed using most phylogeny estimation methods (distance-based methods, maximum parsimony, maximum compatibility, likelihood-based methods)

Binary character likelihood-based methods

- You need to specify the model (and so the probability of 0->1 and 1->0) for each binary character. For example, you may constrain 0->1 to be as likely as 1-> 0 (Cavender-Farris), or not.
- Rates-across-sites issues
- Note the lack of independence between characters.

Likelihood-based approaches

- Gray and Atkinson used a Bayesian method to estimate a distribution on trees for Indo-European, using binary encodings of lexical data.
- Others have done similar analyses on binary encodings of multi-state characters, but treated the binary matrices differently
- Other approaches have used finite-state characters, and assumed a Jukes-Cantor model for those finite states, and analyzed linguistic data.
- Many analyses are restricted to lexical characters
- Trees estimated by different groups have been quite different, in interesting ways
- IE analyses are particularly “hot” (and also “heated”)
- Our own group has proposed an infinite-states model, and showed how to calculate likelihoods efficiently under the model (but not done analyses of lexical data under the model).

Our (RWT) Data

- Ringe & Taylor (2002)
  - 259 lexical
  - 13 morphological
  - 22 phonological
- These data have cognate judgments estimated by Ringe and Taylor, and vetted by other Indo-Europeanists. (Alternate encodings were tested, and mostly did not change the reconstruction.)
- Polymorphic characters, and characters known to evolve in parallel, were removed.

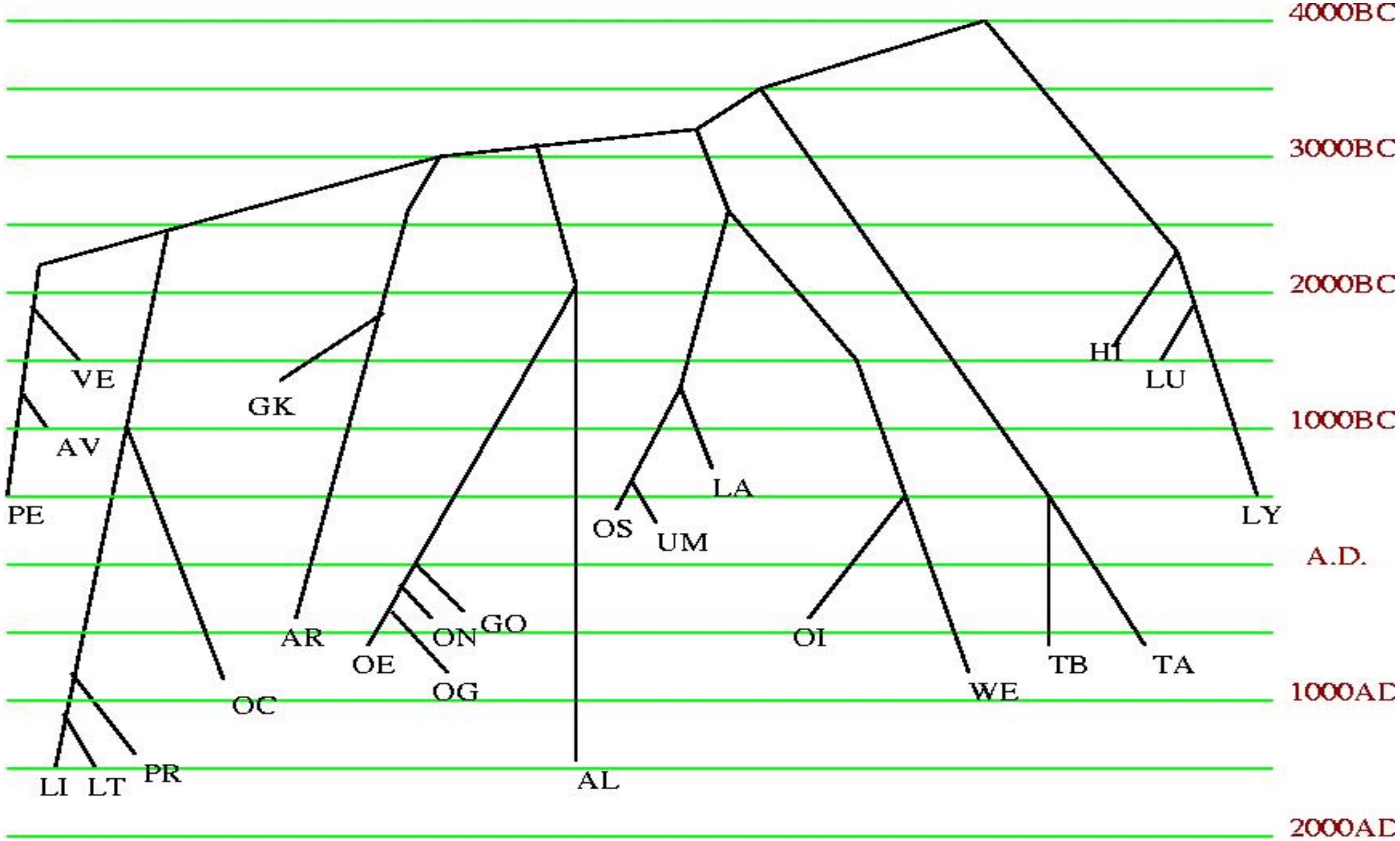
First analysis:
“Weighted Maximum Compatibility”

- Input: set L of languages described by characters
- Output: Tree with leaves labelled by L, such that the number of homoplasy-free (compatible) characters is maximized (while *requiring that certain of the morphological and phonological characters be compatible)*.
- NP-hard.

The WMC Tree

dates are approximate

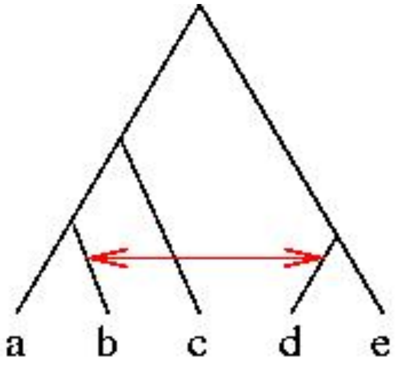
95% of the characters are compatible

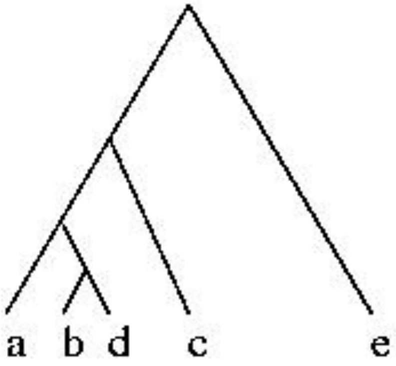


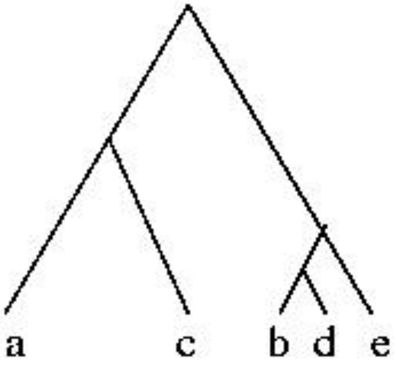
Our methods/models

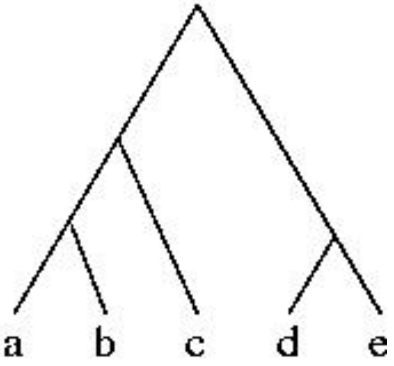
- Ringe & Warnow "Almost Perfect Phylogeny": most characters evolve without homoplasy under a no-common-mechanism assumption (various publications since 1995)
- Ringe, Warnow, & Nakhleh "Perfect Phylogenetic Network": extends APP model to allow for borrowing, but assumes homoplasy-free evolution for all characters (Language, 2005)
- Warnow, Evans, Ringe & Nakhleh "Extended Markov model": parameterizes PPN and allows for homoplasy provided that homoplastic states can be identified from the data. Under this model, trees and some networks are identifiable, and likelihood on a tree can be calculated in linear time (Cambridge University Press, 2006)
- Ongoing work: incorporating unidentified homoplasy and polymorphism (two or more words for a single meaning)

Modelling borrowing: Networks and Trees within Networks

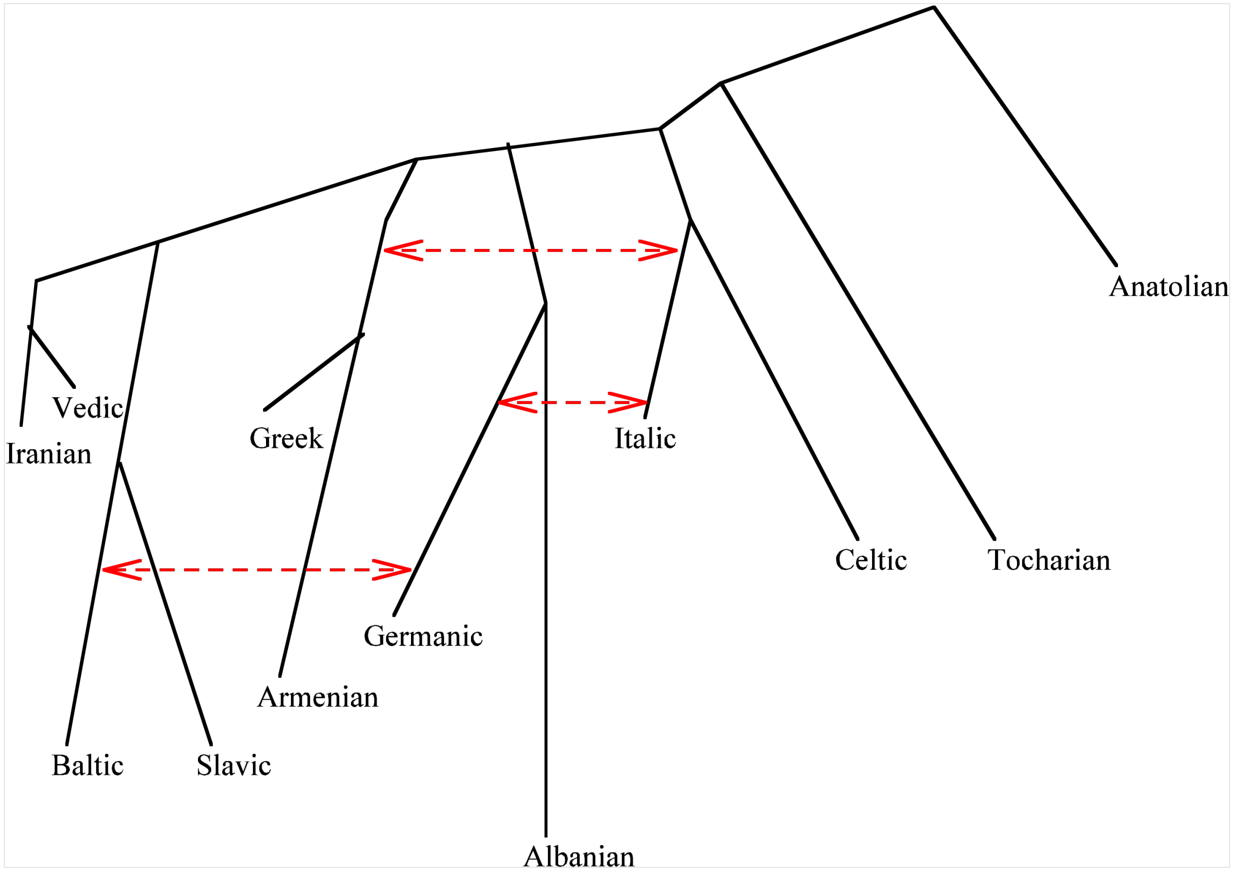








“Perfect Phylogenetic Network” (all characters compatible)



Extended Markov model

- Each character evolves down the tree.
- There are two types of states: those that can arise more than once, and those that can only arise once. We also know which type each state is.
- Characters evolve independently but not identically, nor in a rates-across-sites fashion.
- *Essentially this is a linguistic version of the no-common-mechanism model, but allowing for an infinite number of states.*

Initial results

- Under very mild conditions (substitution probabilities bounded away from 1 and 0), the model tree is identifiable - even without identically distributed sites.
- Fast, statistically consistent, methods exist for reconstructing the tree (and the network, under some conditions).
- Maximum Likelihood and Bayesian analyses are also feasible, since likelihood calculations can be done in linear time.

What about PIE homeland and date?

- Linguists have “reconstructed” words for ‘wool’, ‘horse’, ‘thill’ (harness pole), and ‘yoke’, for Proto-Indo-European, and for ‘wheel’ for the ancestor of the “core” (IE minus Anatolian and Tocharian).
- Archaeological evidence (positive and negative) for these objects used to constrain the date and location for proto-IE to be *after* the “secondary products revolution”, and somewhere with horses (wild or domesticated).
- Combination of evidence supports the date for PIE within 3000-5500 BCE (some would say 3500-4500 BCE), and location *not* Anatolia, thus ruling out the Anatolian hypothesis.

For more information

- Please see **http://www.cs.rice.edu/~nakhleh/CPHL** (the Computational Phylogenetics for Historical Linguistics web site) for data and papers

How old is PIE?

(1) Words for 'yoke' and 'draw, pull (on sledge)' reconstruct to PIE, hence PIE dispersed **after** the development of animal traction.

(2) Words for 'wool' reconstruct to PIE, hence PIE dispersed **after** the development of woolly sheep. (Ancestral sheep and goats have short hair -- unspinnable, unfeltable.)

(3) A verb for 'milk (an animal)' reconstructs to PIE, hence PIE dispersed **after** the "secondary products revolution".

(4) Words for 'wheel', 'thill' (harness pole), and 'convey (in a vehicle) reconstruct to at least core IE and maybe all PIE, hence PIE dispersed after (or **not too long before)** the development of wheeled transport.

How old is PIE?

(1) Words for 'yoke' and 'draw, pull (on sledge)' reconstruct to PIE, hence PIE dispersed **after** the development of animal traction.

northern Mesopotamia, c. 4000 BCE

spread from Mesopotamia c. 3000 BCE

Darden, Bill J. 2001. On the question of the Anatolian origin of Indo-Hittite. In Robert Drews, ed., *Greater Anatolia and The Indo-Hittite Language Family,* 184-228. Washington, DC: Institute for the Study of Man.

Sherratt, Andrew. 1981. Plough and pastoralism: Aspects of the secondary product revolution. In I. Hodder, G. Isaac and G. Hammond, eds., *Pattern of the Past: Studies in Honour of David Clarke,* 261-205. Cambridge: Cambridge University Press.

How old is PIE?

(2) Words for 'wool' reconstruct to PIE, hence PIE dispersed **after** the development of woolly sheep.

(Ancestral sheep and goats have short hair -- unspinnable, unfeltable.)

woolly sheep: eastern Iran, after 7000 BCE (maybe)

wool: Sumeria, North Caucasus steppe after 4000 BCE

Barber, E. J. W. 1991. *Prehistoric Textiles: The Development of Cloth in the Neolithic and Bronze Ages*. Princeton: Princeton University Press.

Darden, Bill J. 2001. On the question of the Anatolian origin of Indo-Hittite. In Robert Drews, ed., *Greater Anatolia and The Indo-Hittite Language Family,* 184-228. Washington, DC: Institute for the Study of Man.

Shishlina, N. I., O. V. Orfinskaja and V. P. Golikov. 2003. Bronze Age textiles from the North Caucasus: New evidence of fourth millennium BC fibres and fabrics. *Oxford Journal of Archaeology* 22.331-344.

How old is PIE?

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How old is PIE?

(4) Words for 'wheel', 'thill' (harness pole), and 'convey (in a vehicle)' reconstruct to at least core IE and maybe all PIE, hence PIE dispersed **after (or not long before)** the development of wheeled transport.

c. 4000-3500 BCE in or near today's Ukraine, Romania

Anthony, David W. 2007. *The Horse, the Wheel, and Language: How Bronze Age Riders From the Eurasian Steppes Shaped the Modern World*. Princeton, NJ: Princeton University Press.

Darden, Bill J. 2001. On the question of the Anatolian origin of Indo-Hittite. In Robert Drews, ed., *Greater Anatolia and The Indo-Hittite Language Family,* 184-228. Washington, DC: Institute for the Study of Man.

Parpola, Asko. Proto-Indo-European speakers of the Late Tripolye culture as the inventors of wheeled vehicles: Linguistic and archaeological considerations of the PIE homeland problem. In Karlene Jones-Bley, Martin E. Huld, Angela Della Volpe and Miriam Robbins Dexter, eds., *Proceedings of the 19th Annual UCLA Indo-European Conference,* 1-59. Washington, DC: Institute for the Study of Man.

How old is PIE?

Couldn't these words have been borrowed into the IE daughter branches millennia **after** the PIE dispersal?

NO! Words borrowed separately into distant languages would look very different, as with medieval Arabic loans into European languages:

Spanish	algodon *	química (reshaped!) *
Frenchcoton *		chemie *
English	cotton (< French!) †	chemistry (reshaped!) †
German	Baumwolle (coinage!) †	Chemie (from French!) †
Russian	xlopok (lit. 'fluff': coinage!)	ximija (via Greek!)

* Can't even reconstruct Proto-Romance!

† Can't even reconstruct Proto-Germanic!

Acknowledgements

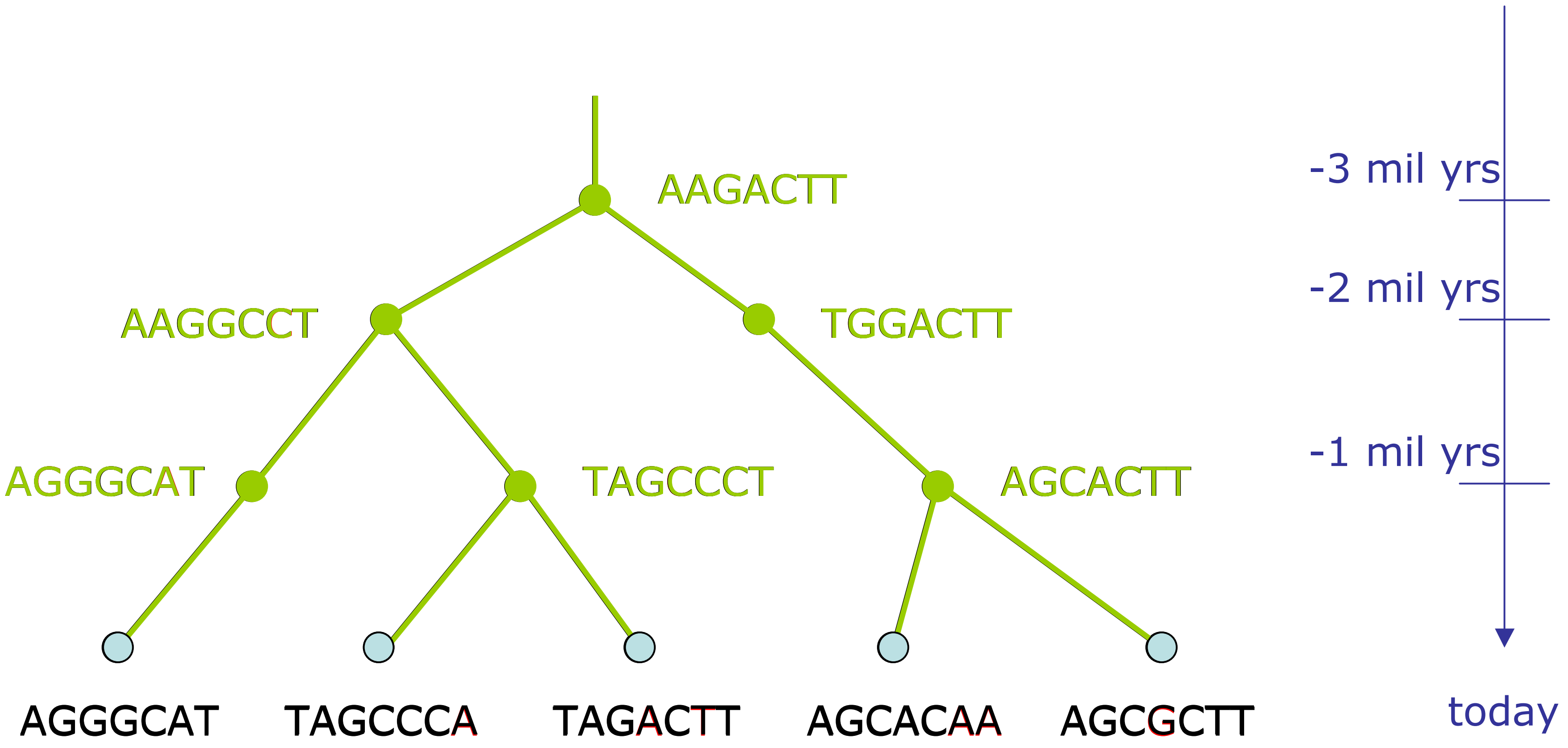
- Financial Support: The David and Lucile Packard Foundation, the National Science Foundation, The Program for Evolutionary Dynamics at Harvard, The Radcliffe Institute for Advanced Studies, and the Institute for Cellular and Molecular Biology at UT-Austin.
- Collaborators: Don Ringe (Penn), Steve Evans (Berkeley), and Luay Nakhleh (Rice)
- Thanks also to Don Ringe (Penn), Craig Melchert (UCLA), and Johanna Nichols (Berkeley) for discussions related to the date and homeland for PIE
- Please see **http://www.cs.utexas.edu/users/tandy/histling.html** for papers and data

Part 2: Phylogeny estimation in biology

- Using triangulated graphs to improve the topological accuracy of distance-based methods

- Using triangulated graphs to speed up heuristics for NP-hard optimization problems

DNA Sequence Evolution



AAGACTT

AAGGCCT

TGGACTT

AGGGCAT

TAGCCCT

AGCACTT

AGGGCAT TAGCCCA TAGACTT AGCACAA AGCGCTT

-3 mil yrs

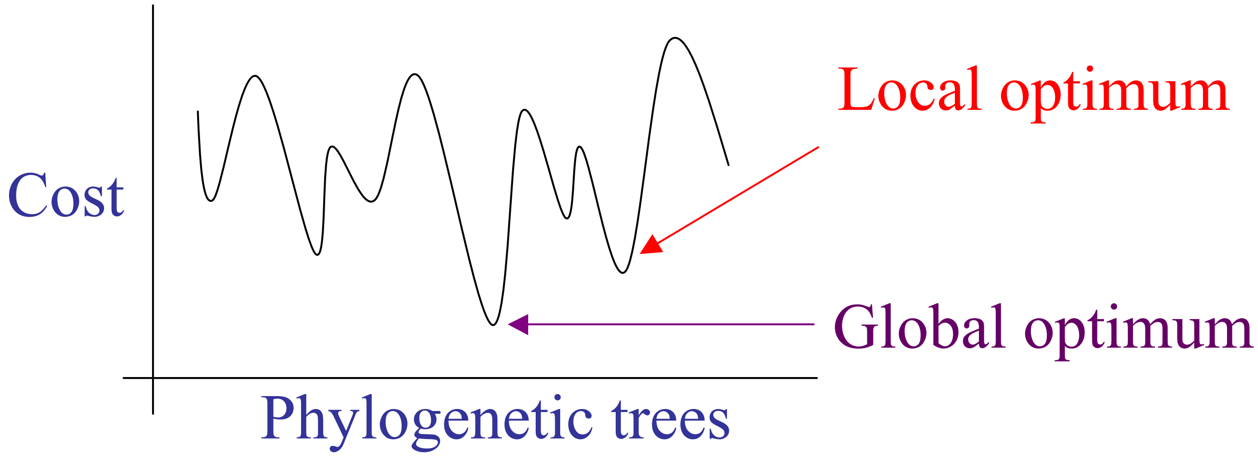
-2 mil yrs

-1 mil yrs

today

Phylogenetic reconstruction methods

1. Heuristics for NP-hard optimization criteria (Maximum Parsimony and Maximum Likelihood)

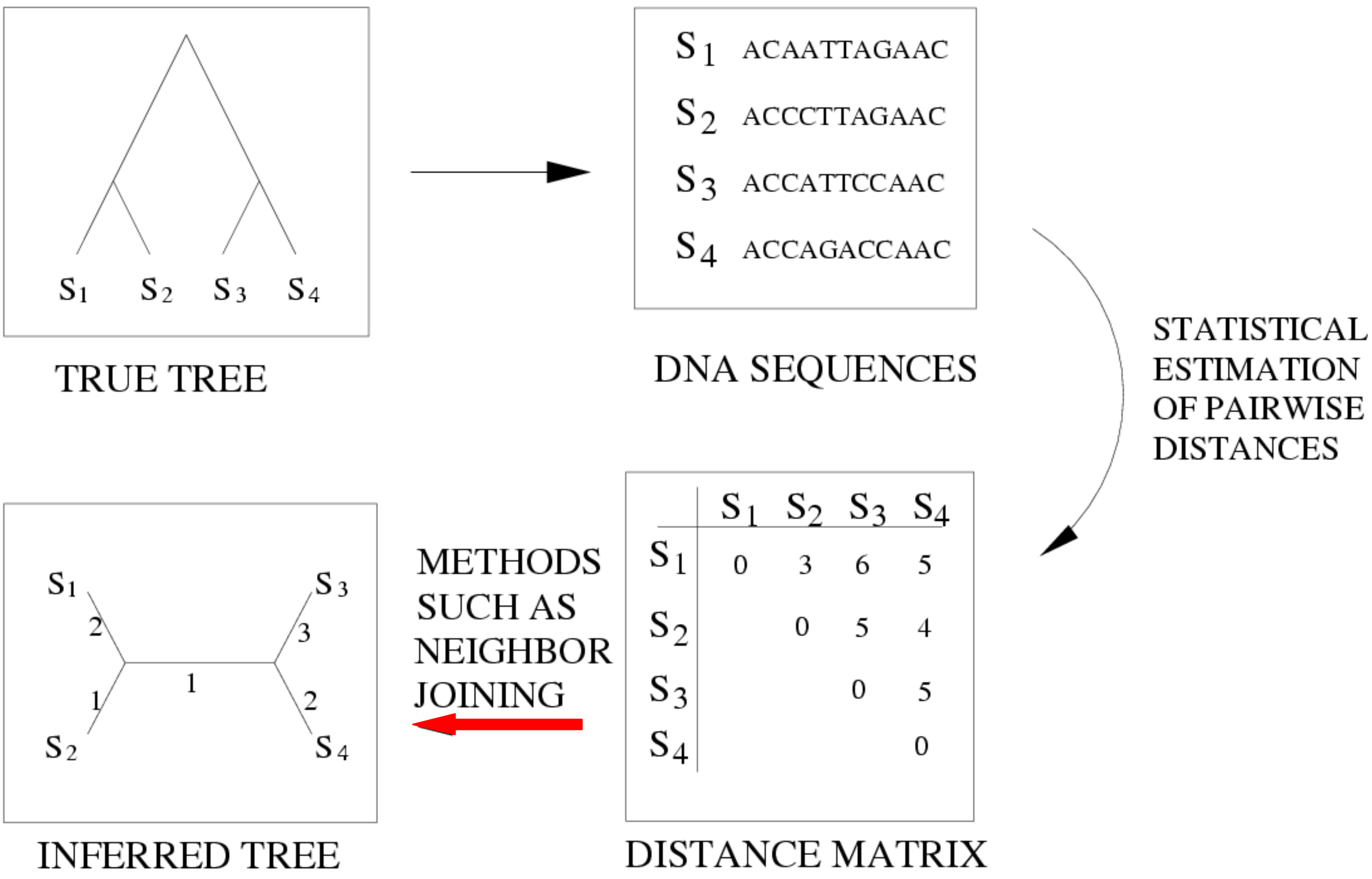


2. Polynomial time distance-based methods: Neighbor Joining, FastME, etc.
3. Bayesian MCMC methods.

Evaluating phylogeny reconstruction methods

- In simulation: how “topologically” accurate are trees reconstructed by the method?
- On real data: how good are the “scores” (typically either maximum parsimony or maximum likelihood) obtained by the method, as a function of time?

Distance-based Phylogenetic Methods



TRUE TREE

S_1 ACAATTAGAAC
S_2 ACCCTTAGAAC
S_3 ACCATTCCAAC
S_4 ACCAGACCAAC

DNA SEQUENCES

STATISTICAL
ESTIMATION
OF PAIRWISE
DISTANCES

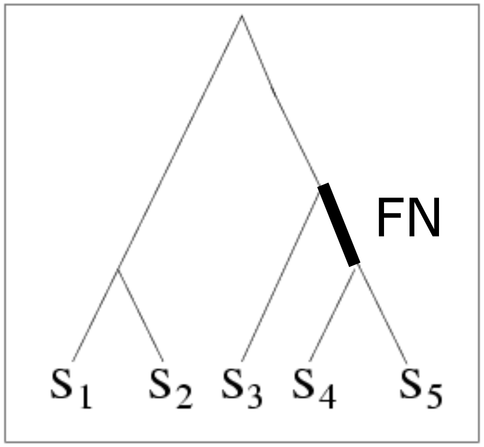
	S_1	S_2	S_3	S_4
S_1	0	3	6	5
S_2		0	5	4
S_3			0	5
S_4				0

DISTANCE MATRIX

METHODS
SUCH AS
NEIGHBOR
JOINING

INFERRED TREE

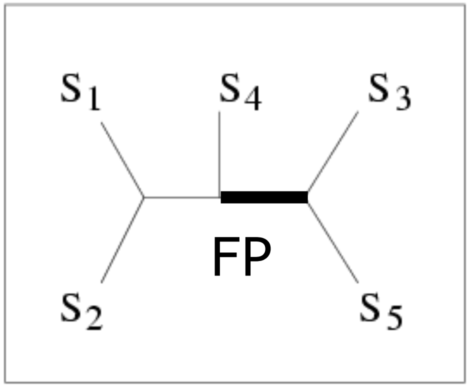
Quantifying Error



TRUE TREE

S_1	ACAATTAGAAC
S_2	ACCCTTAGAAC
S_3	ACCATTCCAAC
S_4	ACCAGACCAAC
S_5	ACCAGACCGGA

DNA SEQUENCES



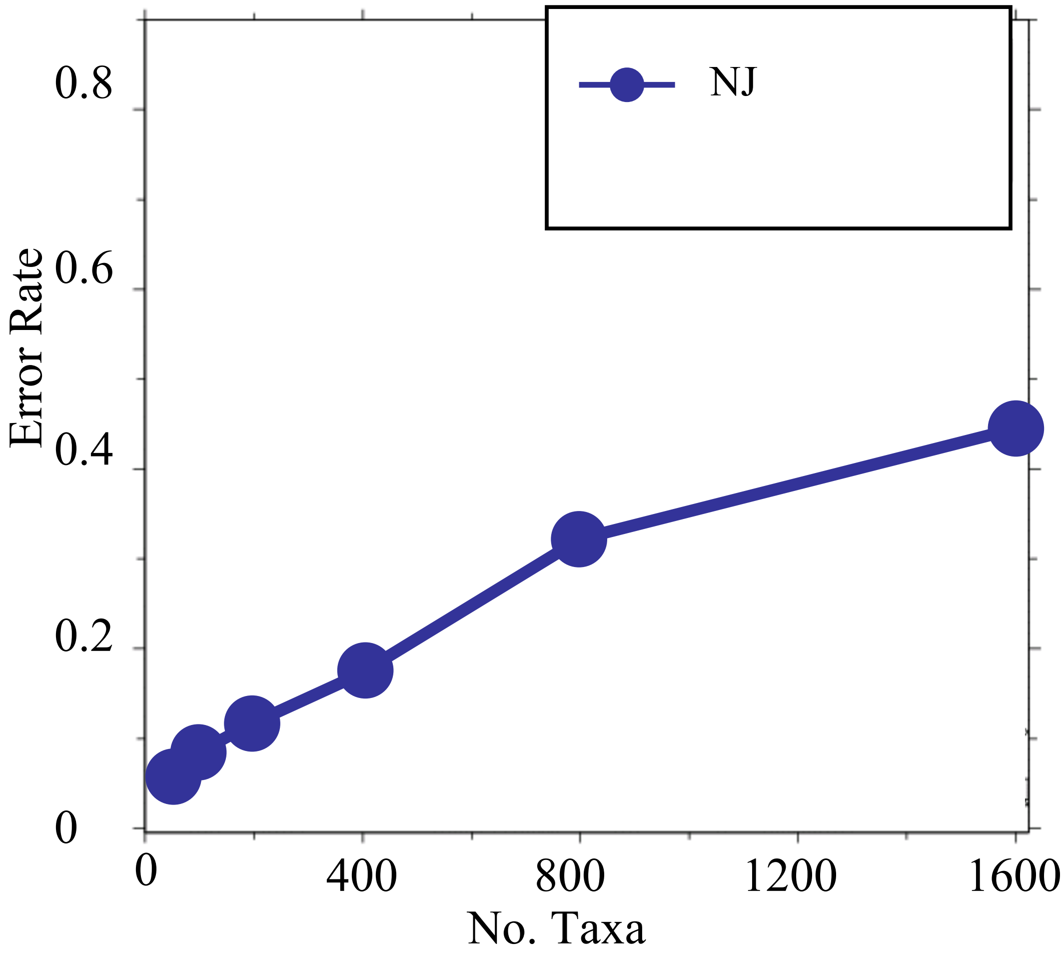
INFERRED TREE

FN: false negative
(missing edge)
FP: false positive
(incorrect edge)

50% error rate

Neighbor joining has poor accuracy on large diameter model trees

[Nakhleh et al. ISMB 2001]



Simulation study based upon fixed edge lengths, K2P model of evolution, sequence lengths fixed to 1000 nucleotides.

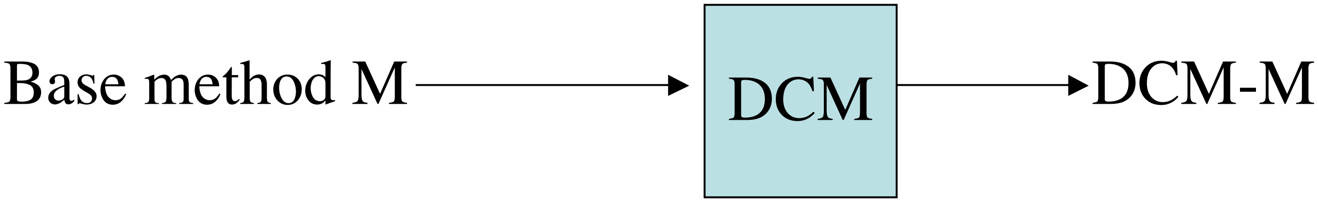
Error rates reflect proportion of incorrect edges in inferred trees.

Neighbor Joining's sequence length requirement is exponential!

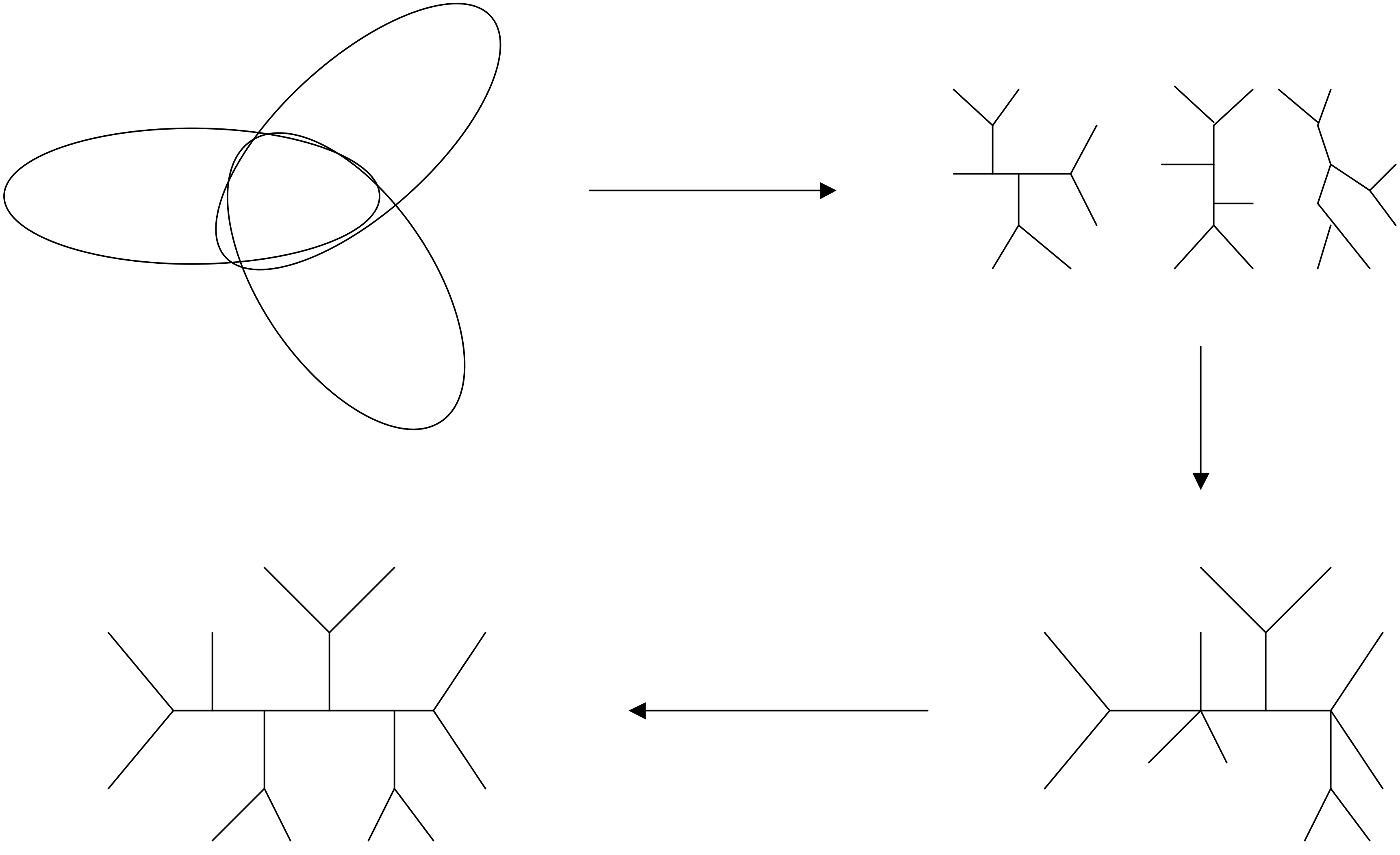
- Atteson: Let T be a General Markov model tree defining additive matrix D. Then Neighbor Joining will reconstruct the true tree with high probability from sequences that are of length at least **$O(\lg n\ e^{\max D_{ij}})$.**

“Boosting” phylogeny reconstruction methods

- DCMs “boost” the performance of phylogeny reconstruction methods.



Divide-and-conquer for phylogeny estimation



Graph-theoretic divide-and-conquer (DCM's)

- Define a **triangulated** graph so that its vertices correspond to the input taxa
- Compute a decomposition of the graph into overlapping subgraphs, thus defining a decomposition of the taxa into overlapping subsets.
- Apply the "base method" to each subset of taxa, to construct a subtree
- Merge the subtrees into a single tree on the full set of taxa.

DCM1 Decompositions

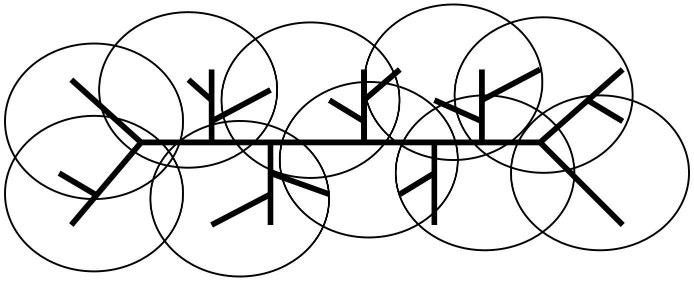
Input: Set S of sequences, distance matrix d, threshold value $q \in \{d_{ij}\}$

1. Compute threshold graph

$$G_q = (V, E), V = S, E = \{(i, j) : d(i, j) \le q\}$$

2. Perform minimum weight triangulation (note: if d is an additive matrix, then the threshold graph is provably **triangulated**).

DCM1 decomposition : Compute maximal cliques

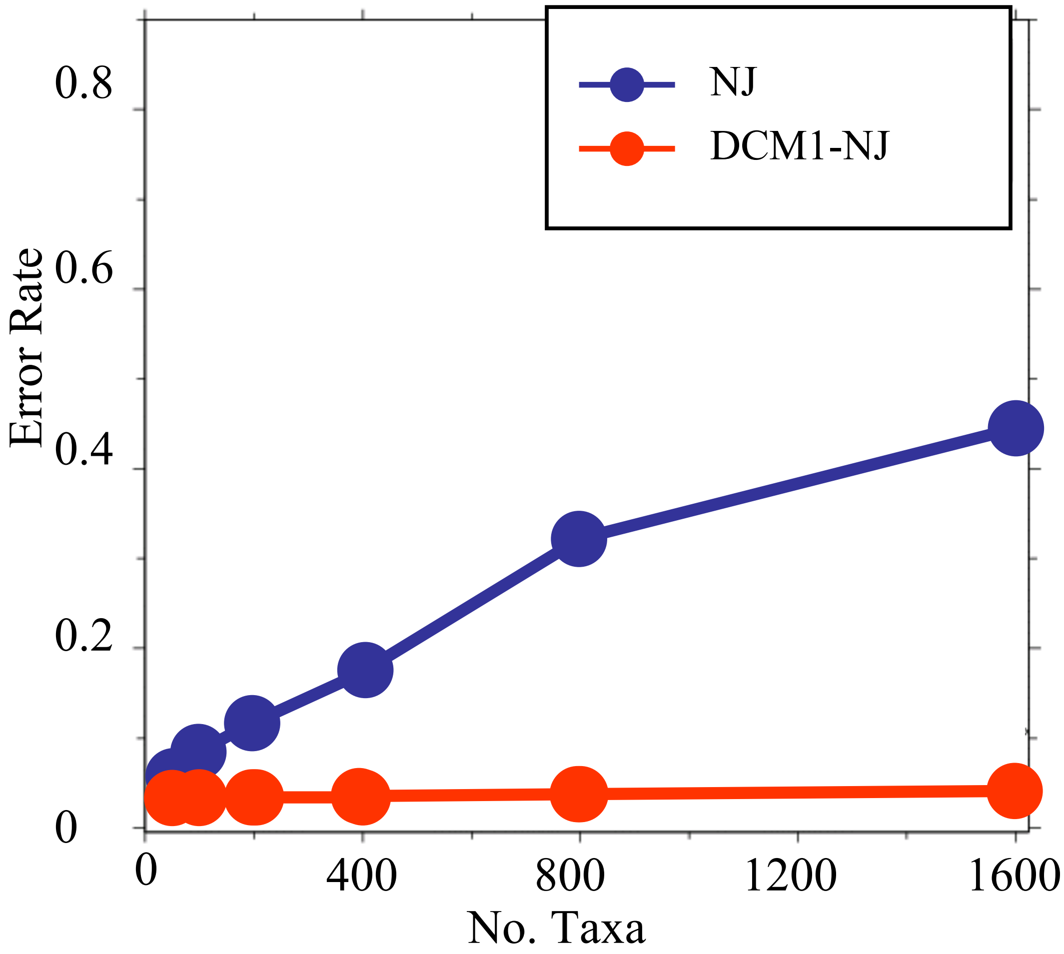


Improving upon NJ

- Construct trees on a number of smaller diameter subproblems, and merge the subtrees into a tree on the full dataset.
- Our approach:
  - Phase I: produce $O(n^2)$ trees (one for each diameter)
  - Phase II: pick the "best" tree from the set.

DCM1-boosting distance-based methods

[Nakhleh et al. ISMB 2001 and Warnow et al. SODA 2001]



Theorem:
DCM1-NJ
converges to the
true tree from
polynomial
length sequences

What about solving MP and ML?

- Maximum Parsimony (MP) and maximum likelihood (ML) are the major phylogeny estimation methods used by systematists.

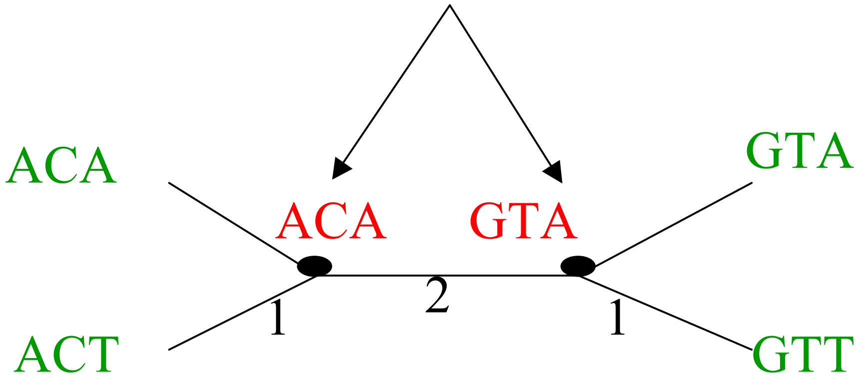
Maximum Parsimony

- **Input**: Set *S* of *n* aligned sequences of length k
- **Output**: A phylogenetic tree *T*
  - leaf-labeled by sequences in *S*
  - additional sequences of length *k* labeling the internal nodes of *T*

such that $\sum_{(i,j)\in E(T)} H(i,j)$ is minimized.

Maximum Parsimony: computational complexity

Optimal labeling can be computed in linear time O(nk)



MP score = 4

Finding the optimal MP tree is **NP-hard**

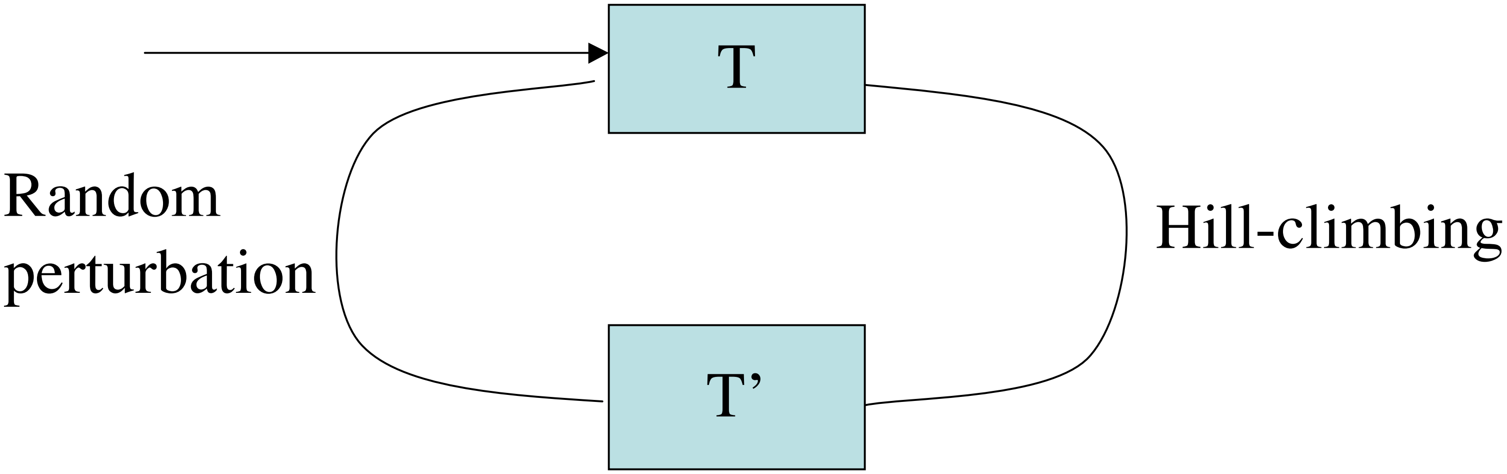
Solving NP-hard problems exactly is … unlikely

- Number of (unrooted) binary trees on *n* leaves is (2n-5)!!
- If each tree on **1000** taxa could be analyzed in **0.001** seconds, we would find the best tree in

  2890 millennia

#leaves	#trees
4	3
5	15
6	105
7	945
8	10395
9	135135
10	2027025
20	2.2×10^{20}
100	4.5×10^{190}
1000	2.7×10^{2900}

Standard heuristic search



T

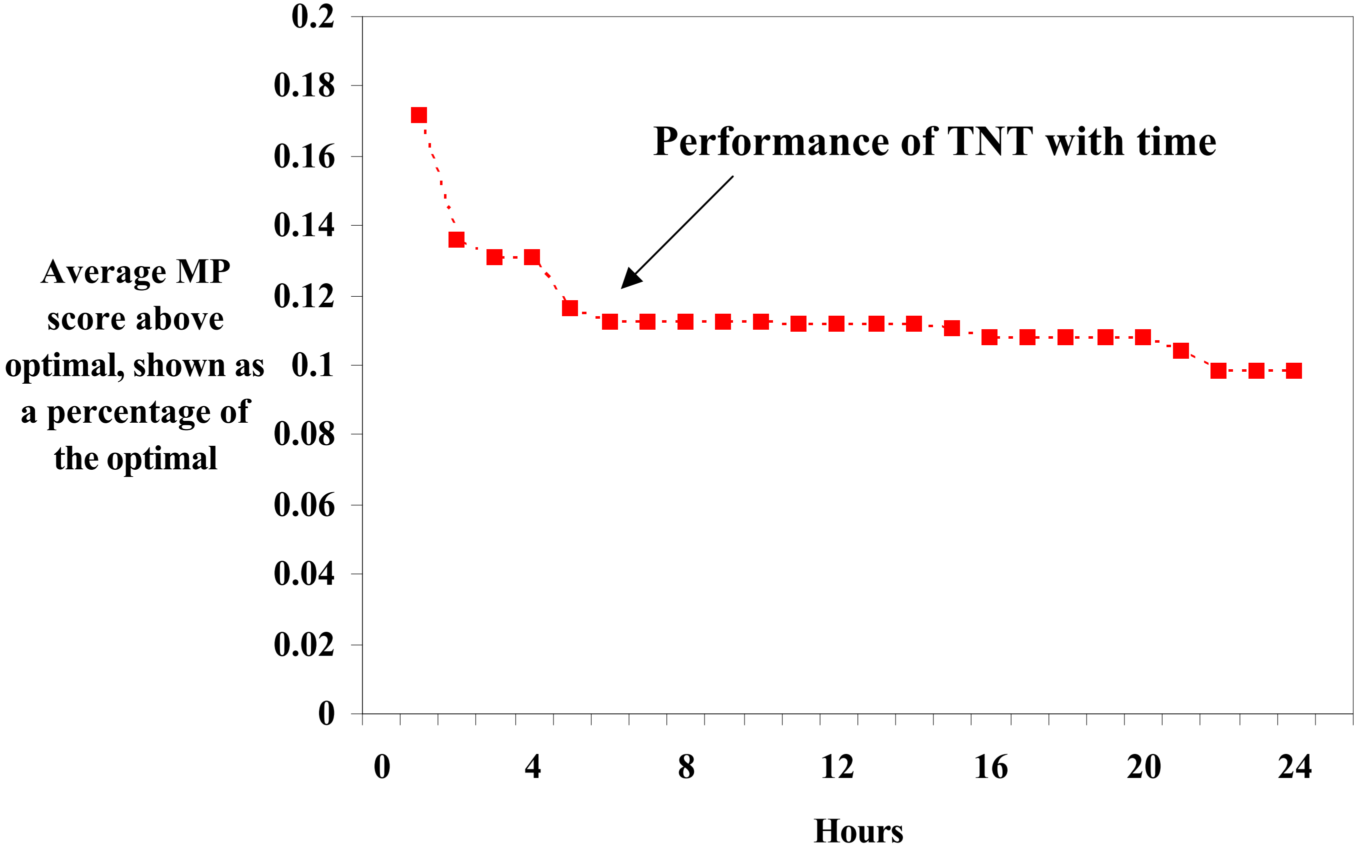
Random perturbation

Hill-climbing

T’

Problems with current techniques for MP

Shown here is the performance of the TNT software for maximum parsimony on a real dataset of almost 14,000 sequences. The required level of accuracy with respect to MP score is no more than **0.01% error** (otherwise high topological error results). ("Optimal" here means best score to date, using any method for any amount of time.)

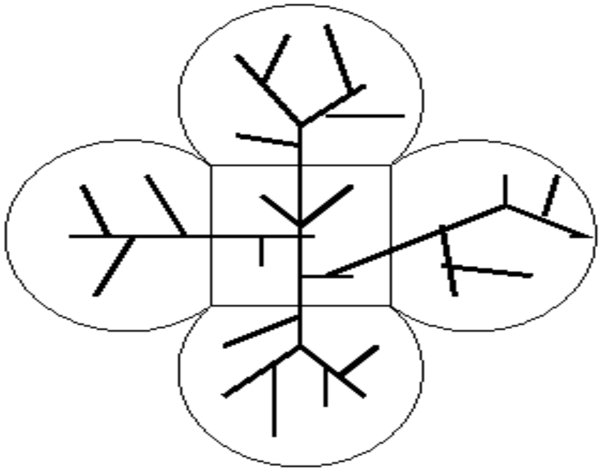


New DCM3 decomposition

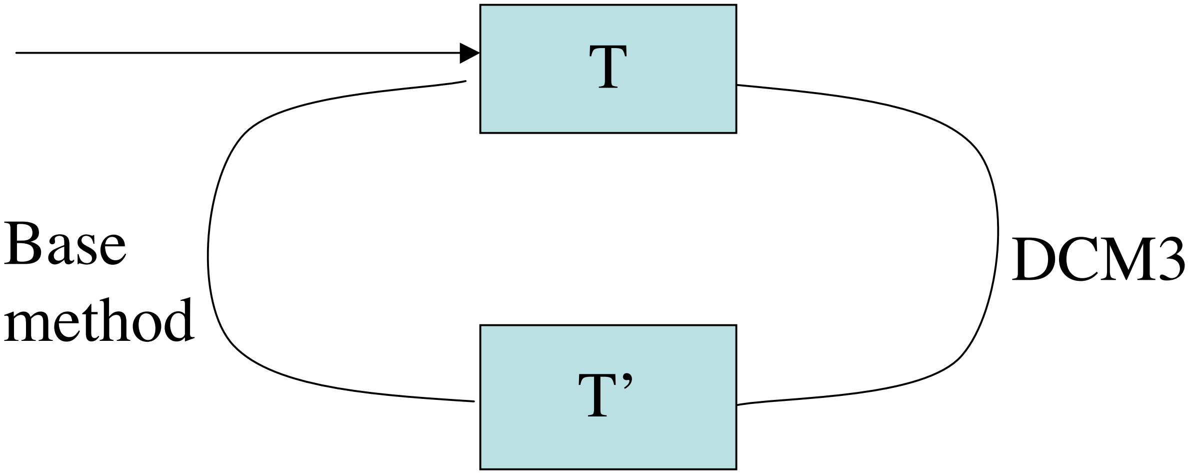
Input: Set *S* of sequences, and guide-tree *T*

1. We use a new graph ("*short subtree* graph") *G(S,T))*
   *Note: G(S,T) is **triangulated**!*
2. Find clique separator in *G(S,T)* and form subproblems

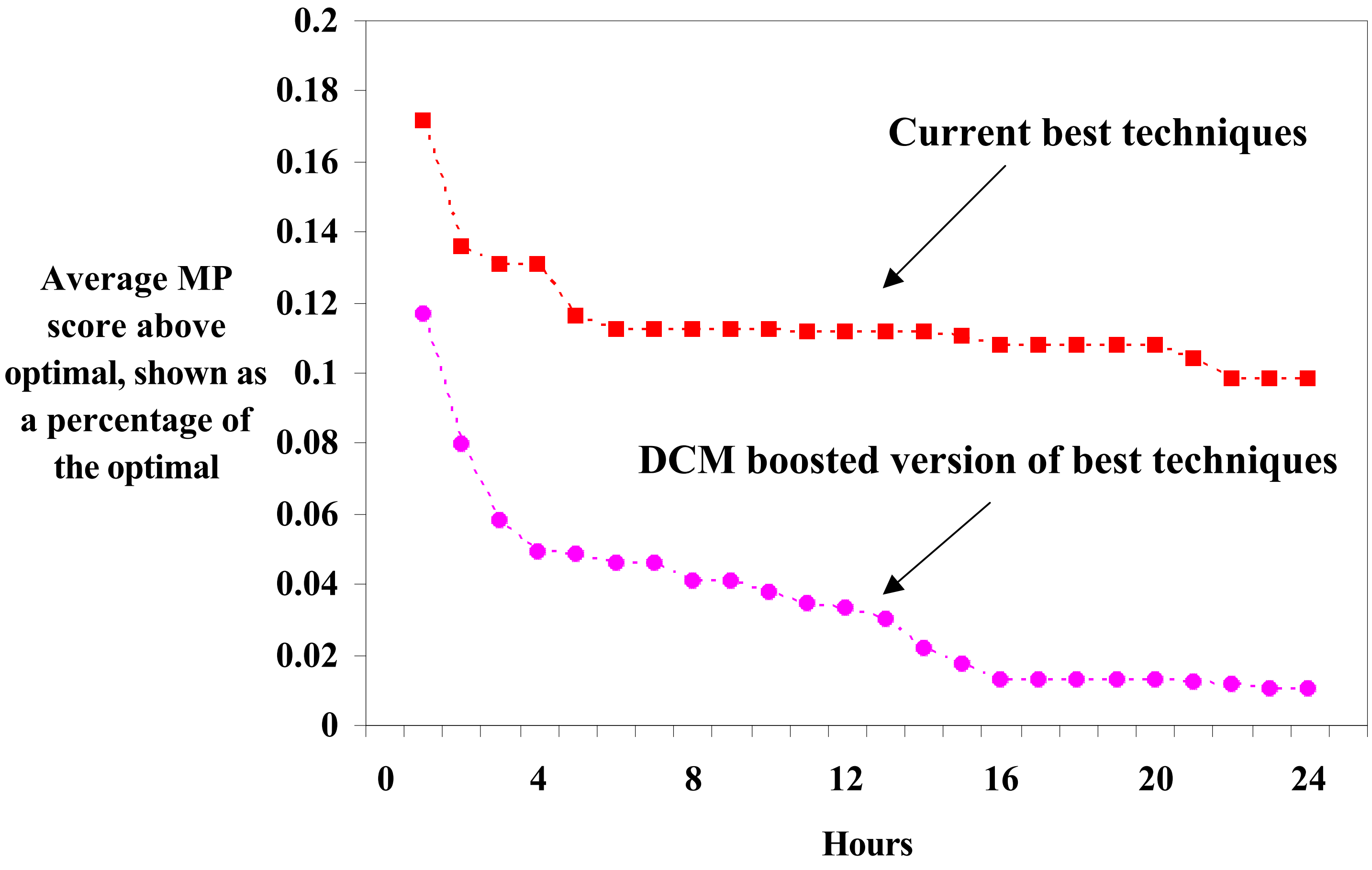
DCM3 decompositions
(1) can be obtained in **O(n)** time
(2) yield small subproblems
(3) can be used iteratively



Iterative-DCM3



Rec-I-DCM3 significantly improves performance



Comparison of TNT to Rec-I-DCM3(TNT) on one large dataset

Summary

- NP-hard optimization problems abound in phylogeny reconstruction, and in computational biology in general, and need very accurate solutions.
- Many real problems have beautiful and natural combinatorial and graph-theoretic formulations.

Acknowledgments

- The CIPRES project www.phylo.org (and the US National Science Foundation more generally)
- The David and Lucile Packard Foundation
- The Program for Evolutionary Dynamics at Harvard, The Radcliffe Institute for Advanced Research, and the Institute for Cellular and Molecular Biology at UT-Austin
- Collaborators: Bernard Moret, Usman Roshan, Tiffani Williams, Daniel Huson, and Donald Ringe.