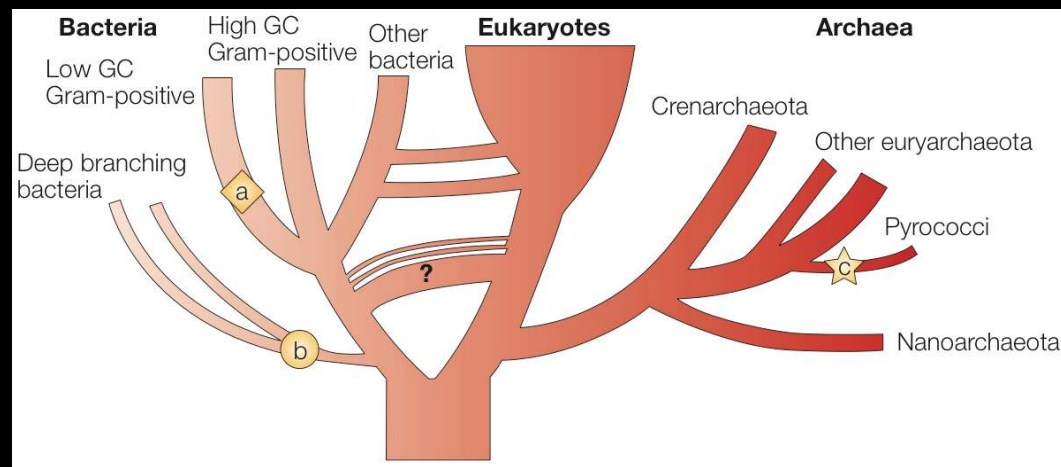


Phylogenomics

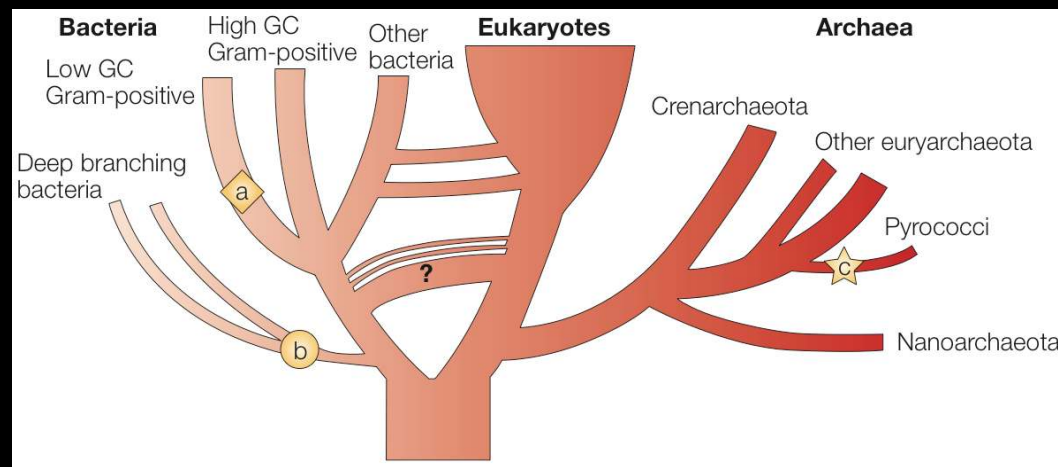
Jeffrey P. Townsend
Department of Ecology and Evolutionary Biology
Yale University

How may we improve our inferences?

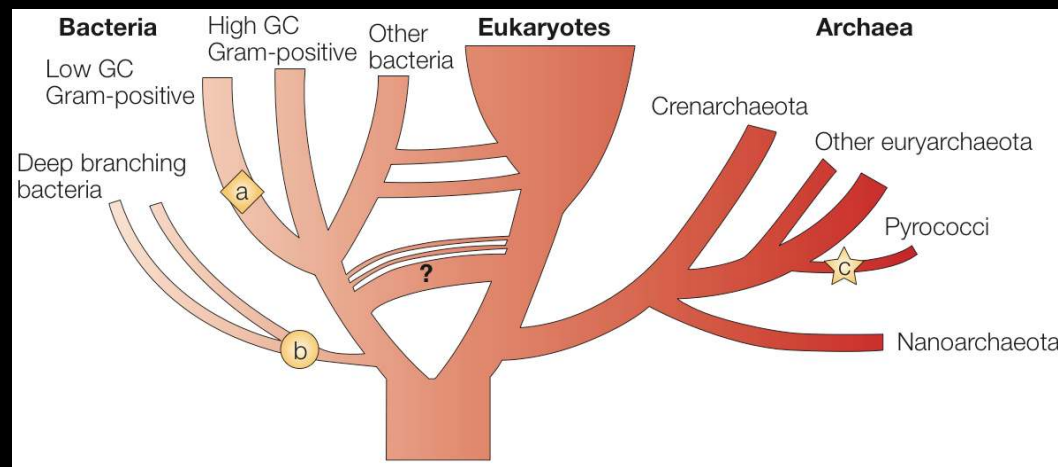


How may we improve our inferences?

- Inferences I Data

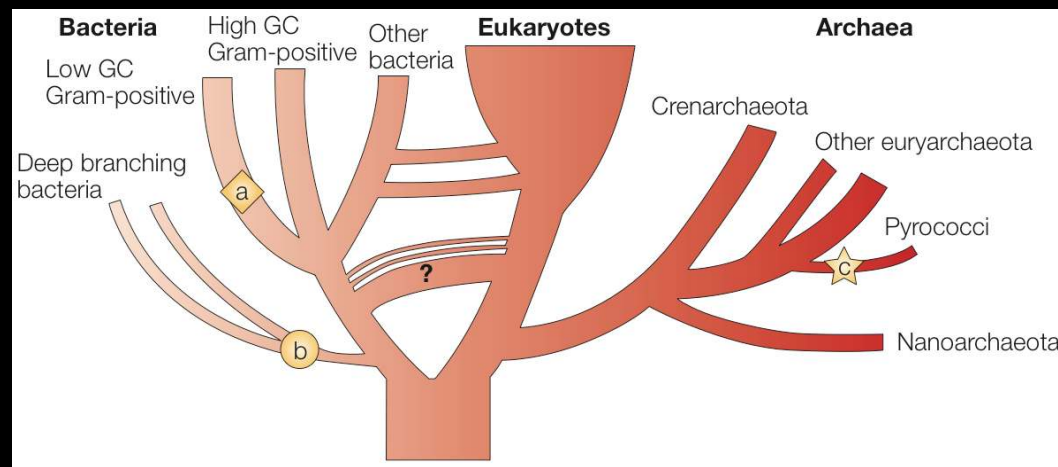


How may we improve our inferences?



- Inferences | Data
- Data | Experimental Design

How may we improve our inferences?

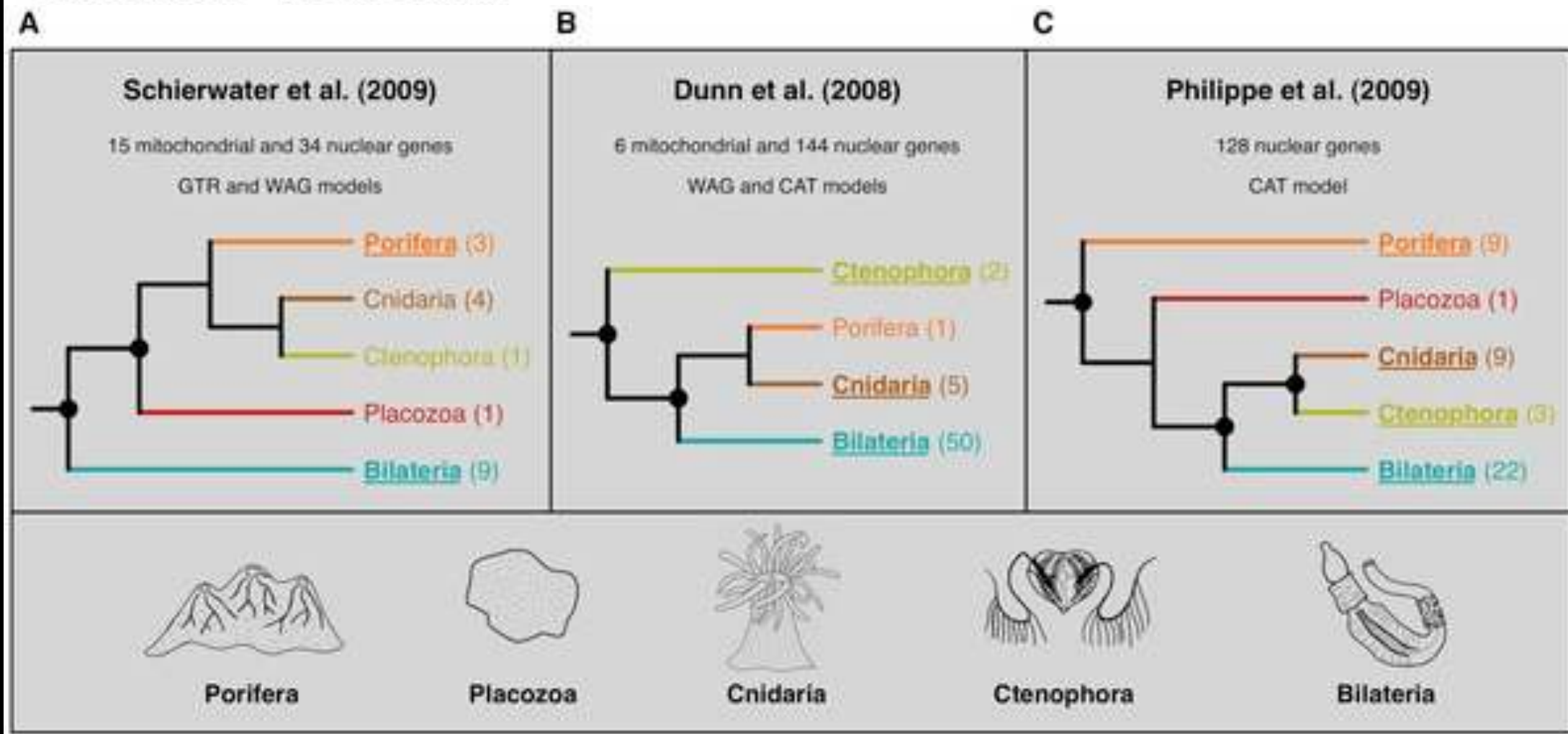


- Inferences | Data
- Data | Experimental Design
- Experimental Design | Prior Knowledge

Perspective

Resolving Difficult Phylogenetic Questions: Why More Sequences Are Not Enough

Hervé Philippe^{1*}, Henner Brinkmann¹, Dennis V. Lavrov², D. Timothy J. Littlewood³, Michael Manuel⁴, Gert Wörheide^{5,6}, Denis Baurain⁷



Phylogenetic experimental design has a diffuse history

- Which types of characters are most informative? (Collins et al., 2005; Dequeiroz and Wimberger, 1993; Graybeal, 1994; Naylor and Brown, 1997; Rokas and Holland, 2000; Wiens and Servedio, 1997; Yang, 1998; Zwickl and Hillis, 2002)
- Would increased taxonomic or character sampling be more informative? (Graybeal, 1998; Hillis, 1998; Kim, 1996, 1998; Poe, 1998; Pollock et al., 2002; Rannala et al., 1998; Rokas and Carroll, 2005; Rosenberg and Kumar, 2001, 2003; Sullivan et al., 1999)
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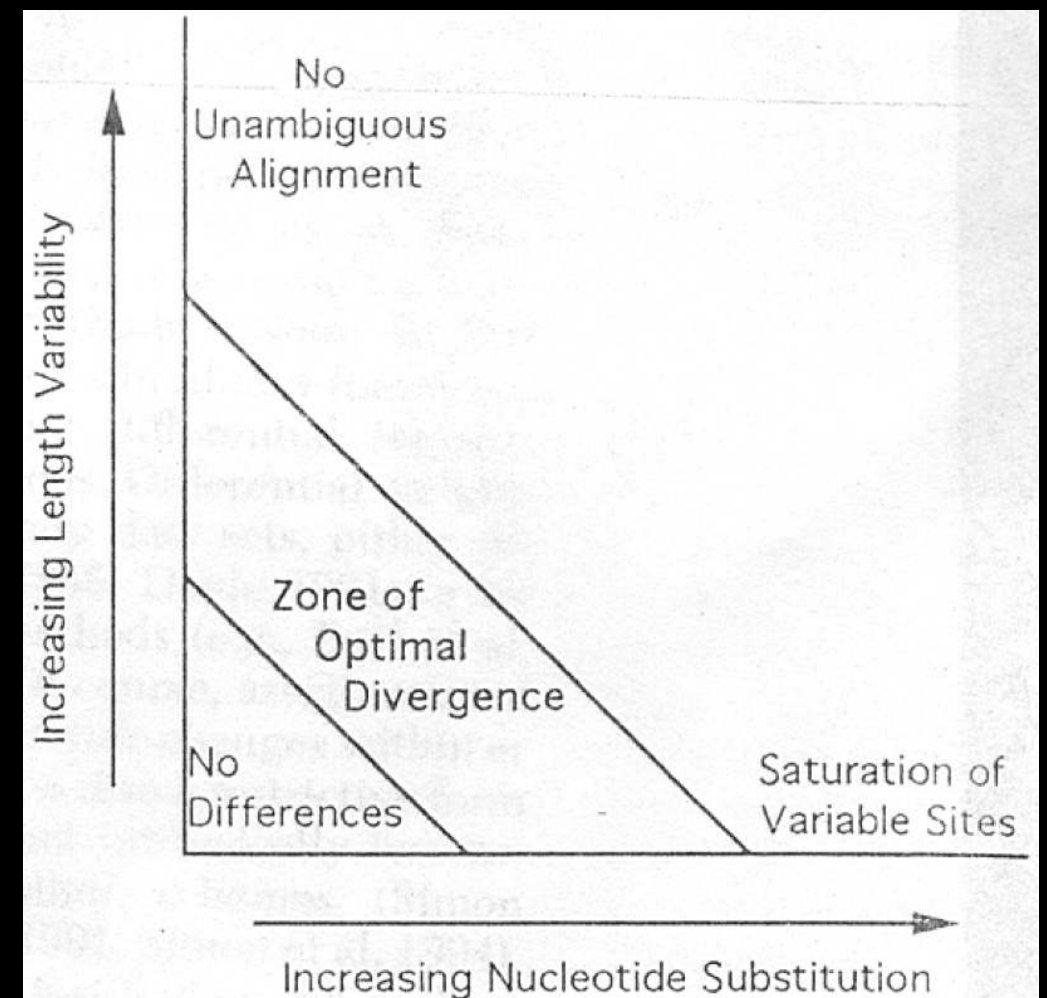
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Which types of characters are most informative?

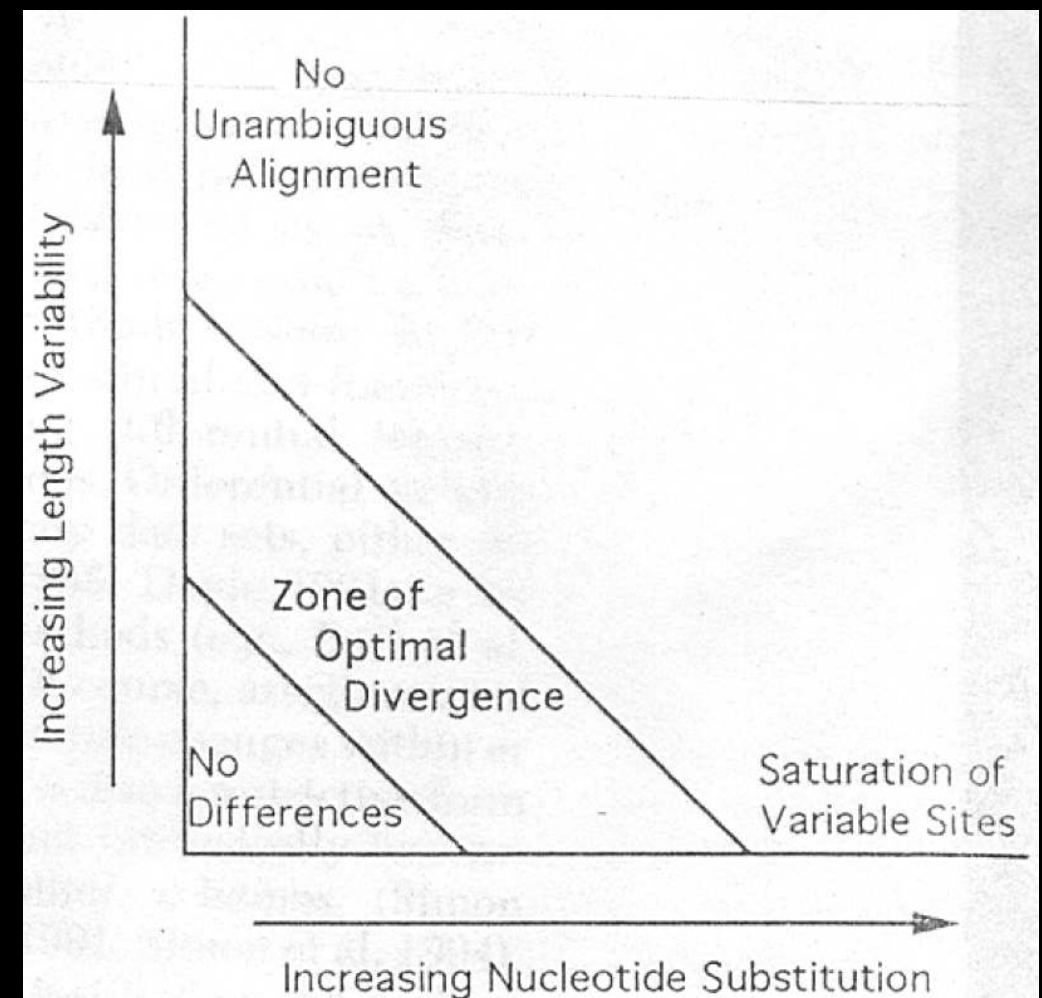
Ancient utility	Recent utility	Reference
Morphological	Behavioral	(Dequieroz & Wimberger, 1993)
Polymorphic	Fixed	(Wiens & Servedio, 1997)
Nonsynonymous	Synonymous	(Graybeal, 1994; Naylor & Brown, 1997)
Amino acids	Nucleotides	(Russo et al. 1996, Gissi et al. 2006)
Rarely changing	characters are best	(many; Rokas & Holland, 2000)

Can we visualize phylogenetic informativeness?



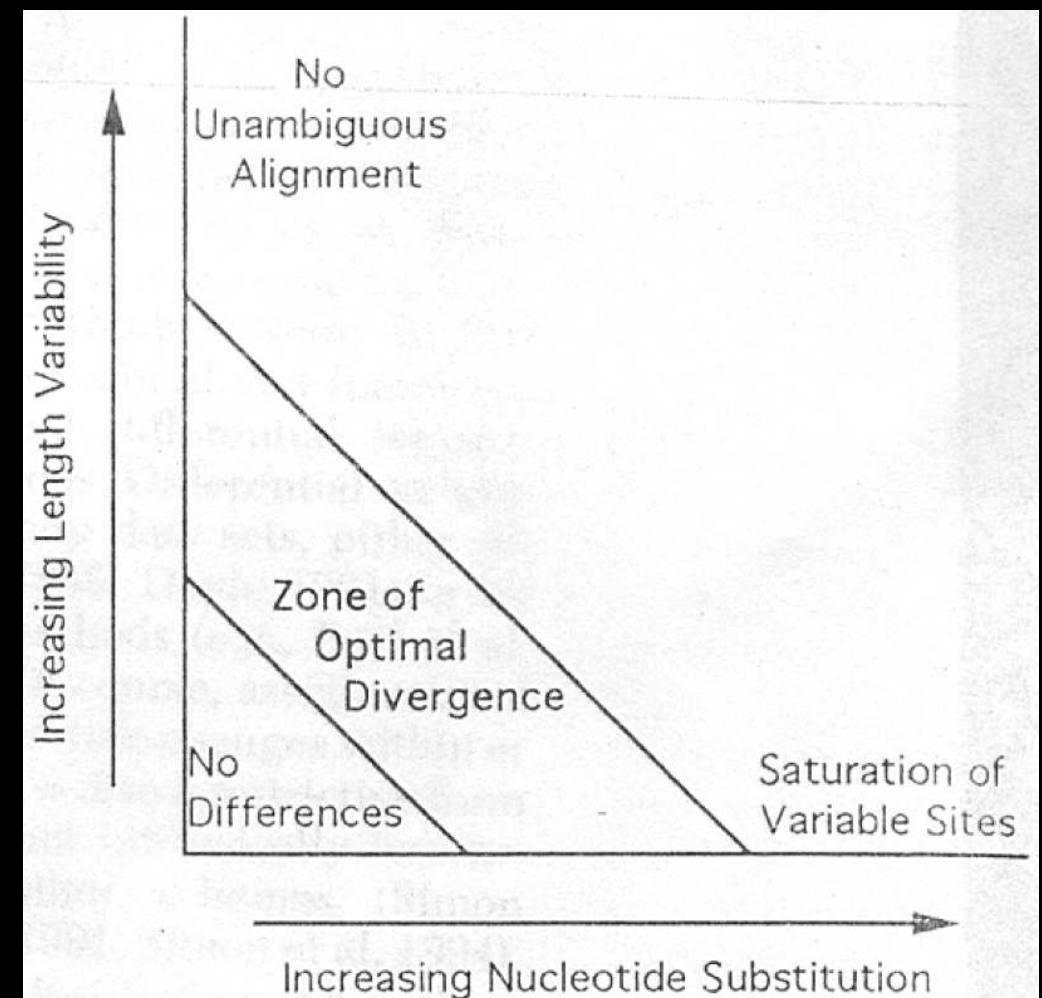
Can we visualize phylogenetic informativeness?

- Characters with no differences across taxa are useless



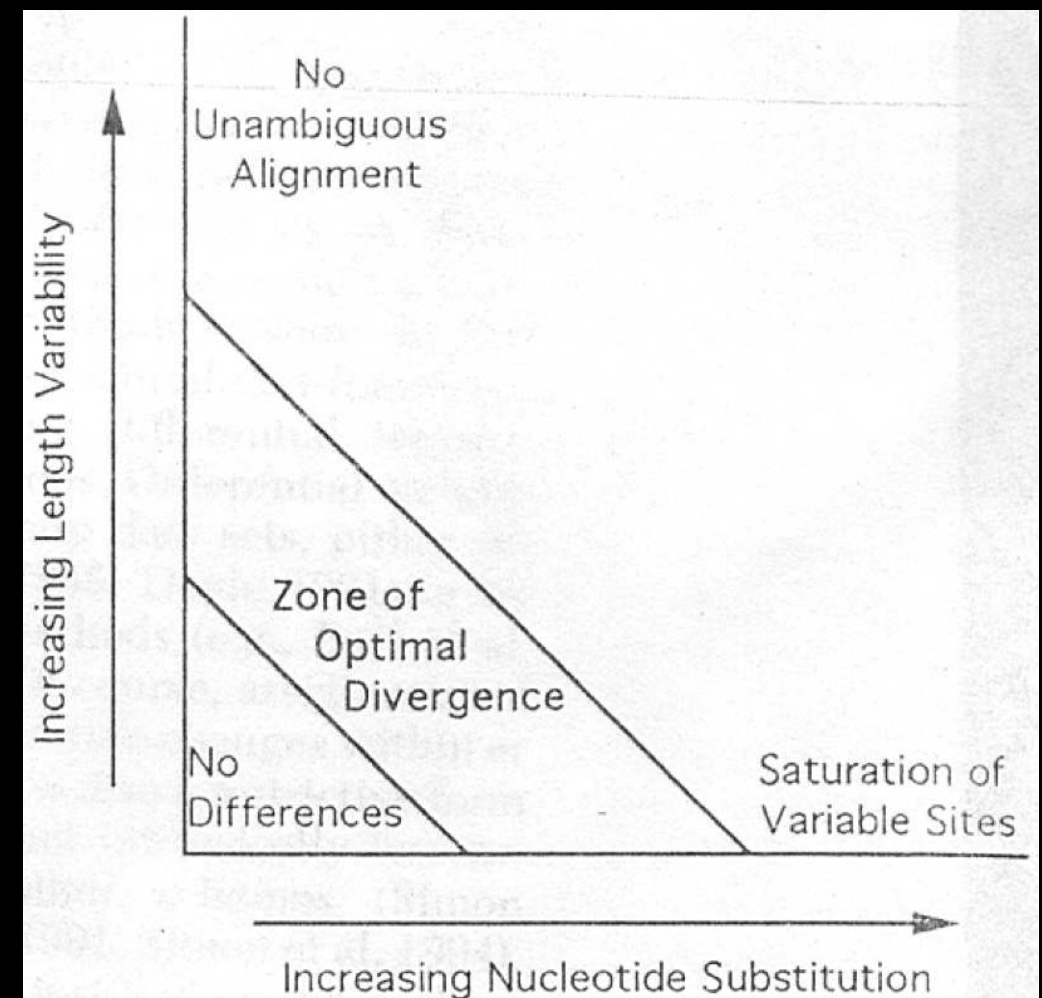
Can we visualize phylogenetic informativeness?

- Characters with no differences across taxa are useless
- Characters that are saturated with mutations across taxa are misleading



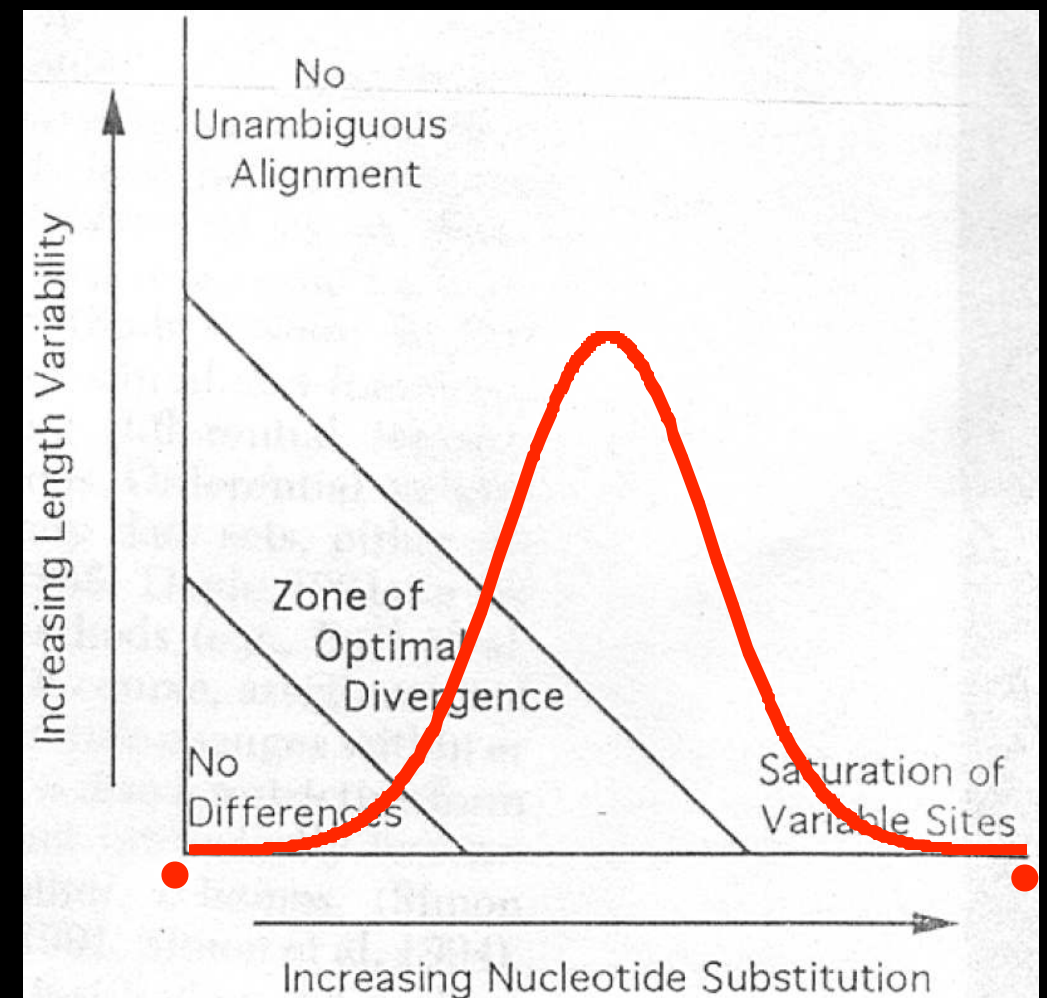
Can we visualize phylogenetic informativeness?

- Characters with no differences across taxa are useless
- Characters that are saturated with mutations across taxa are misleading
- There exists a happy medium



Can we visualize phylogenetic informativeness?

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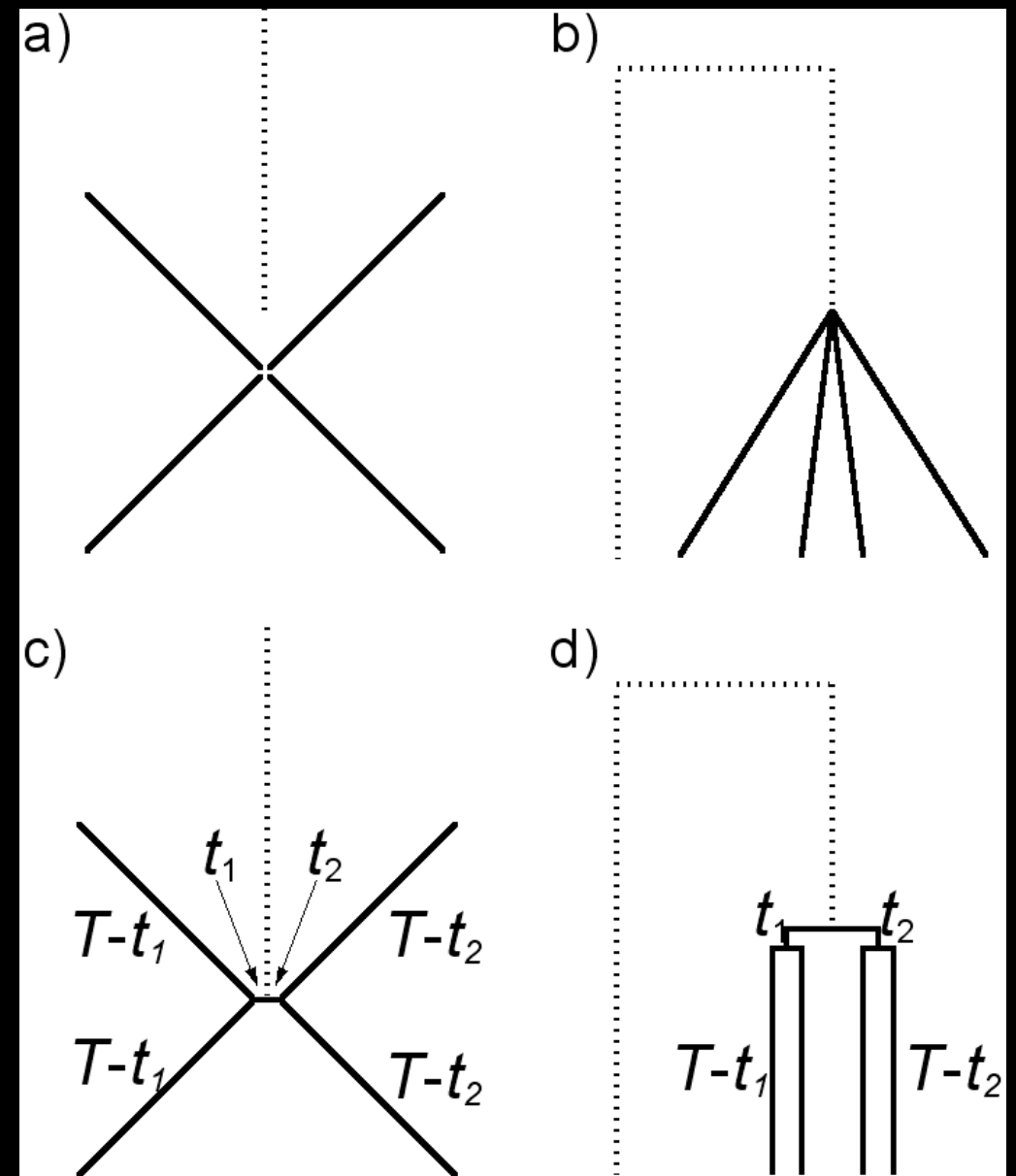


Deriving phylogenetic informativeness

- Calculate the probability of a site being informative, given a rate of evolution, λ , and letting $t_1 + t_2 \rightarrow 0$.

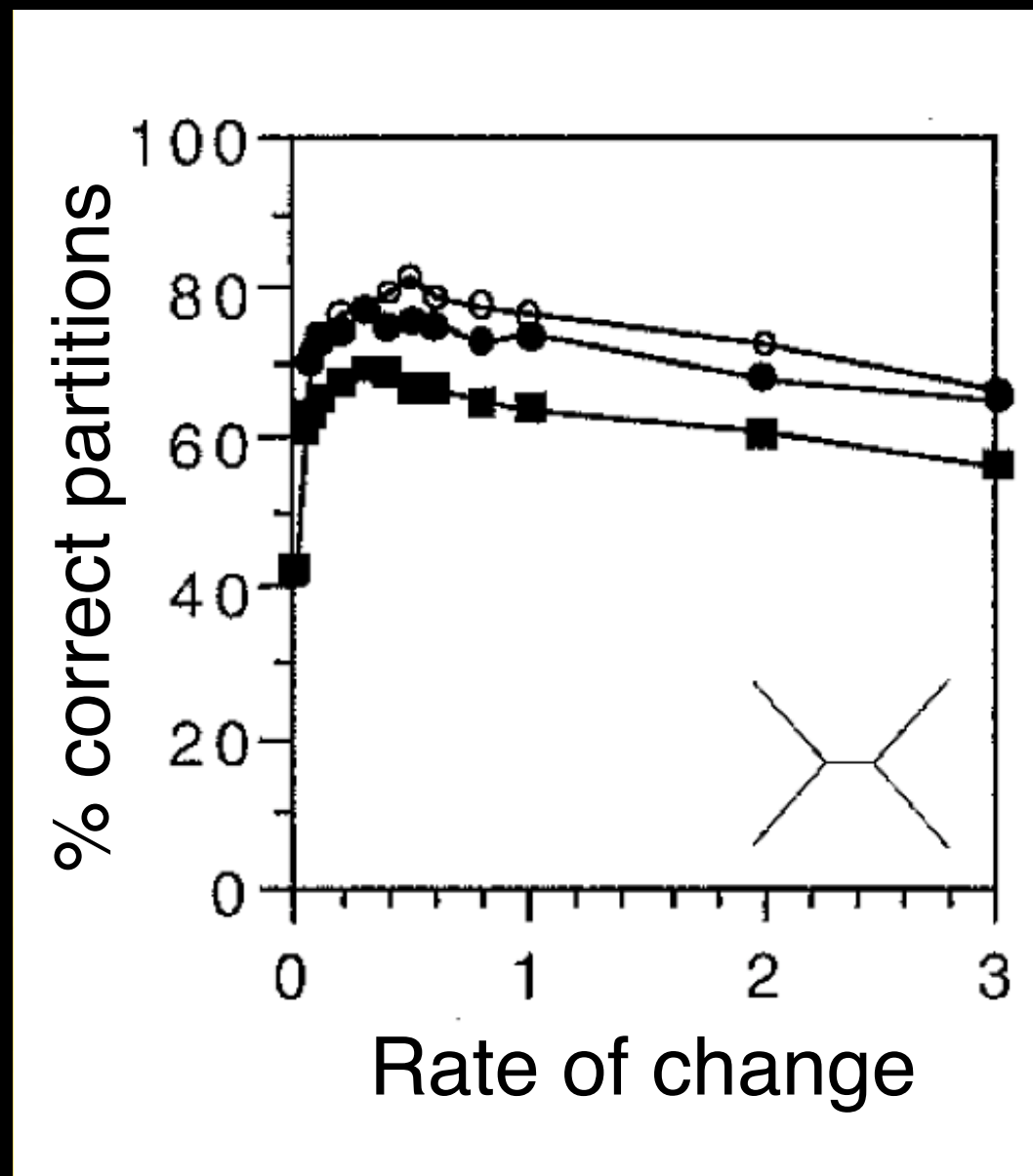
- $\hat{\lambda} = \frac{1}{4}T$

-



Townsend, 2007, *Systematic Biology* 56:222-231

Simulations demonstrate a $1/4T$ optimal rate of character change



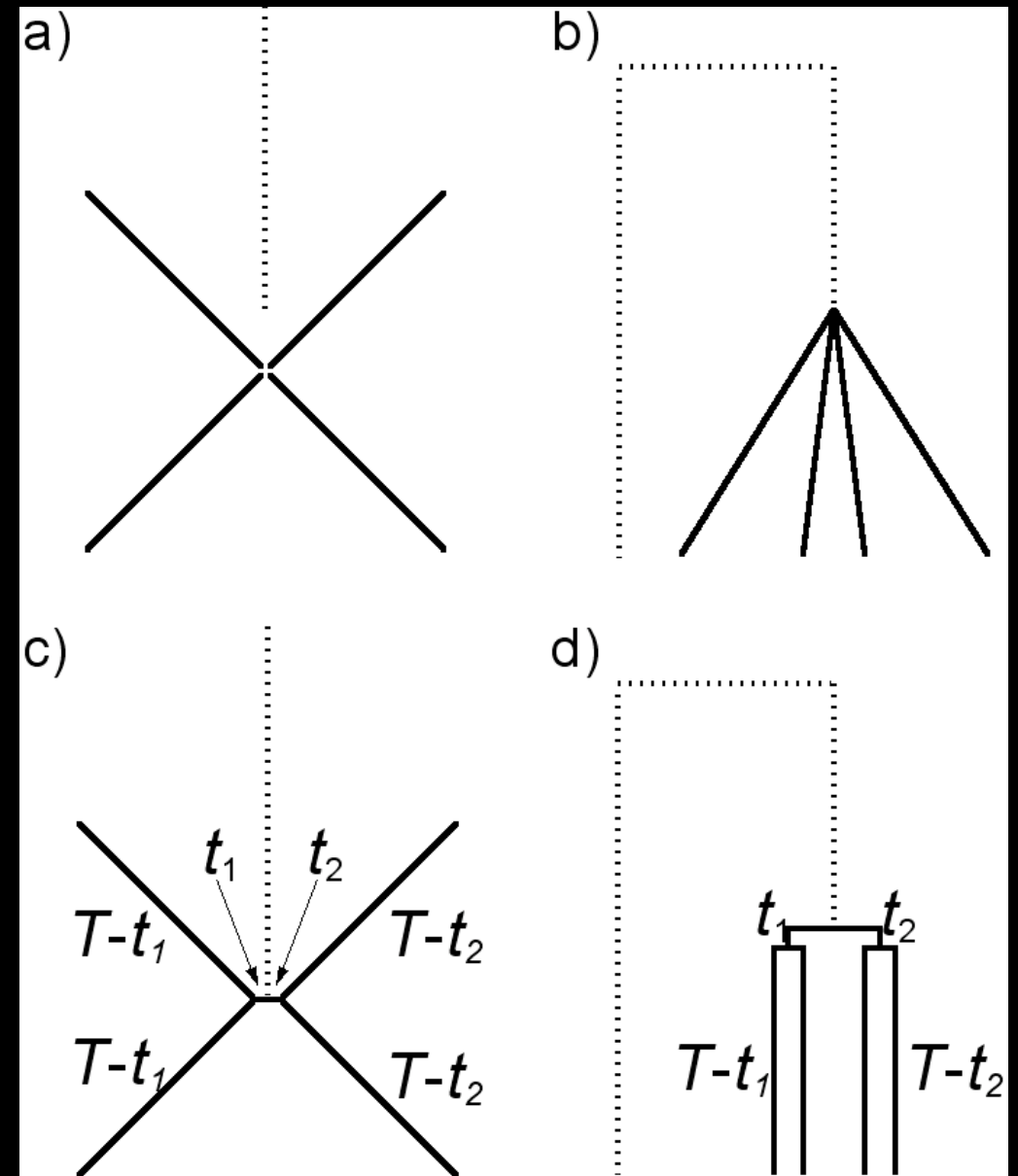
Yang, *Systematic Biology* (1998)

Deriving phylogenetic informativeness

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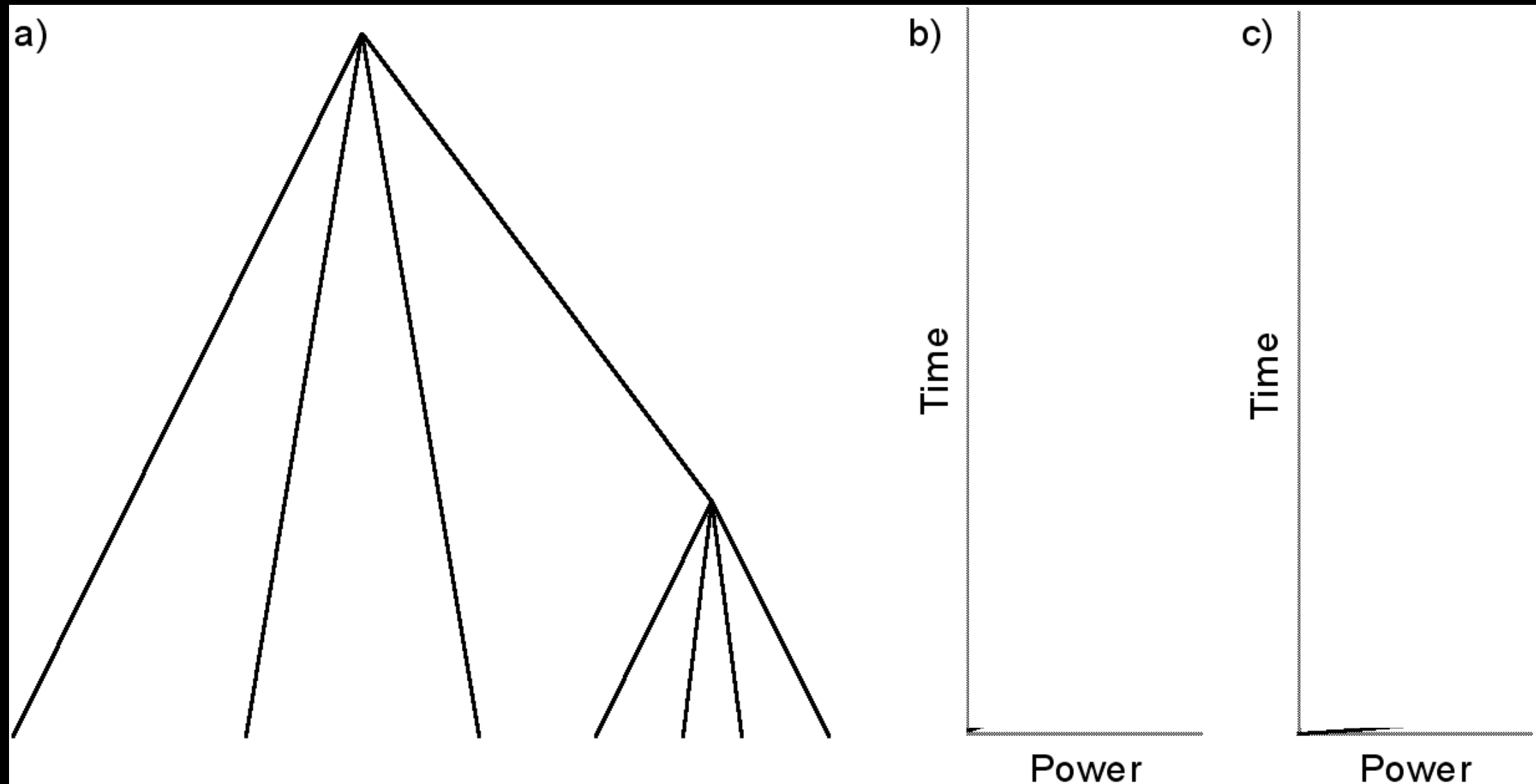
- $\hat{\lambda} = \frac{1}{4}T$

- $\rho(T; \lambda_1, \dots, \lambda_n) = \sum_{i=1}^n 16\lambda_i^2 T e^{-4\lambda_i T}$



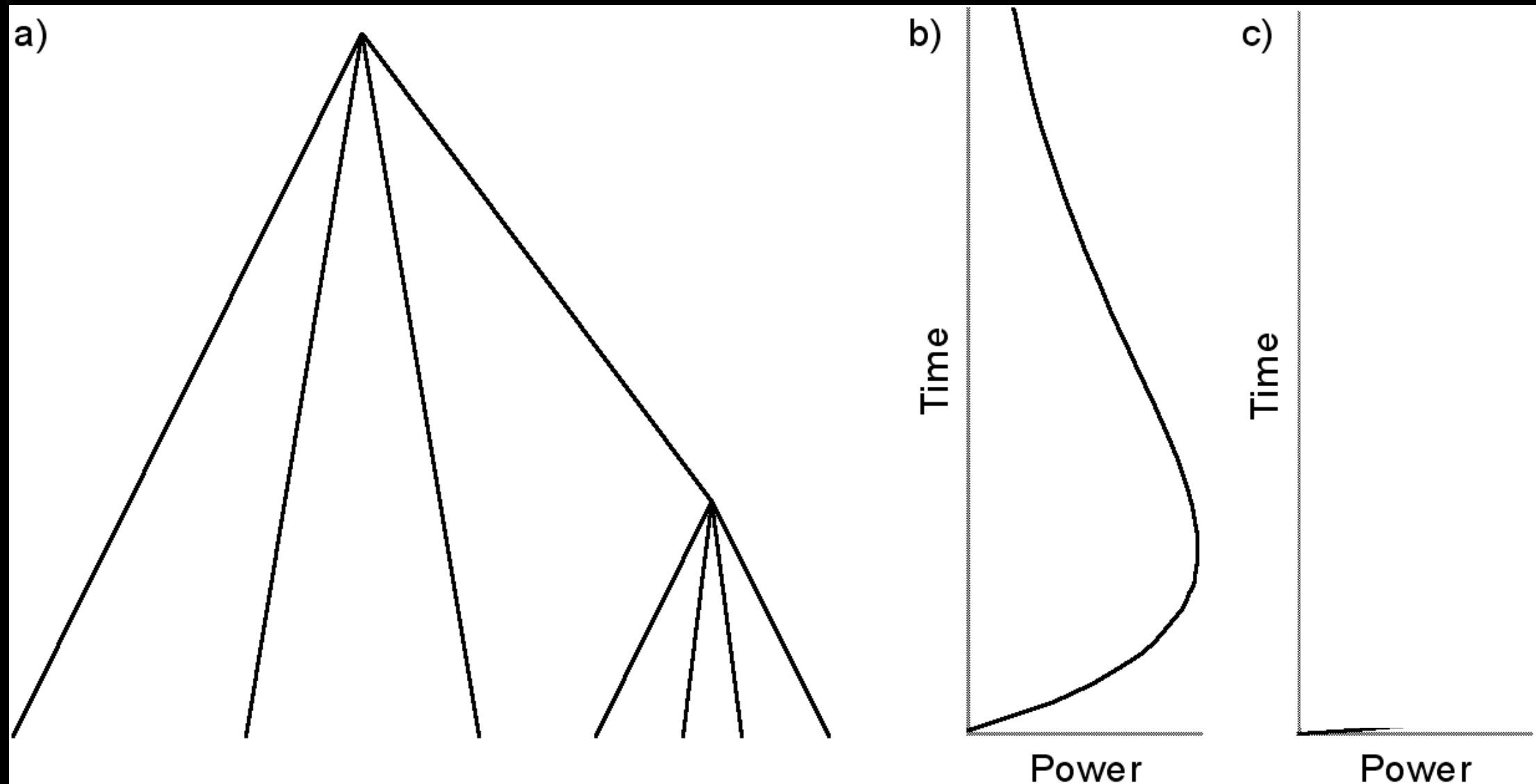
Townsend, 2007, *Systematic Biology* 56:222-231

Informativeness is not obvious



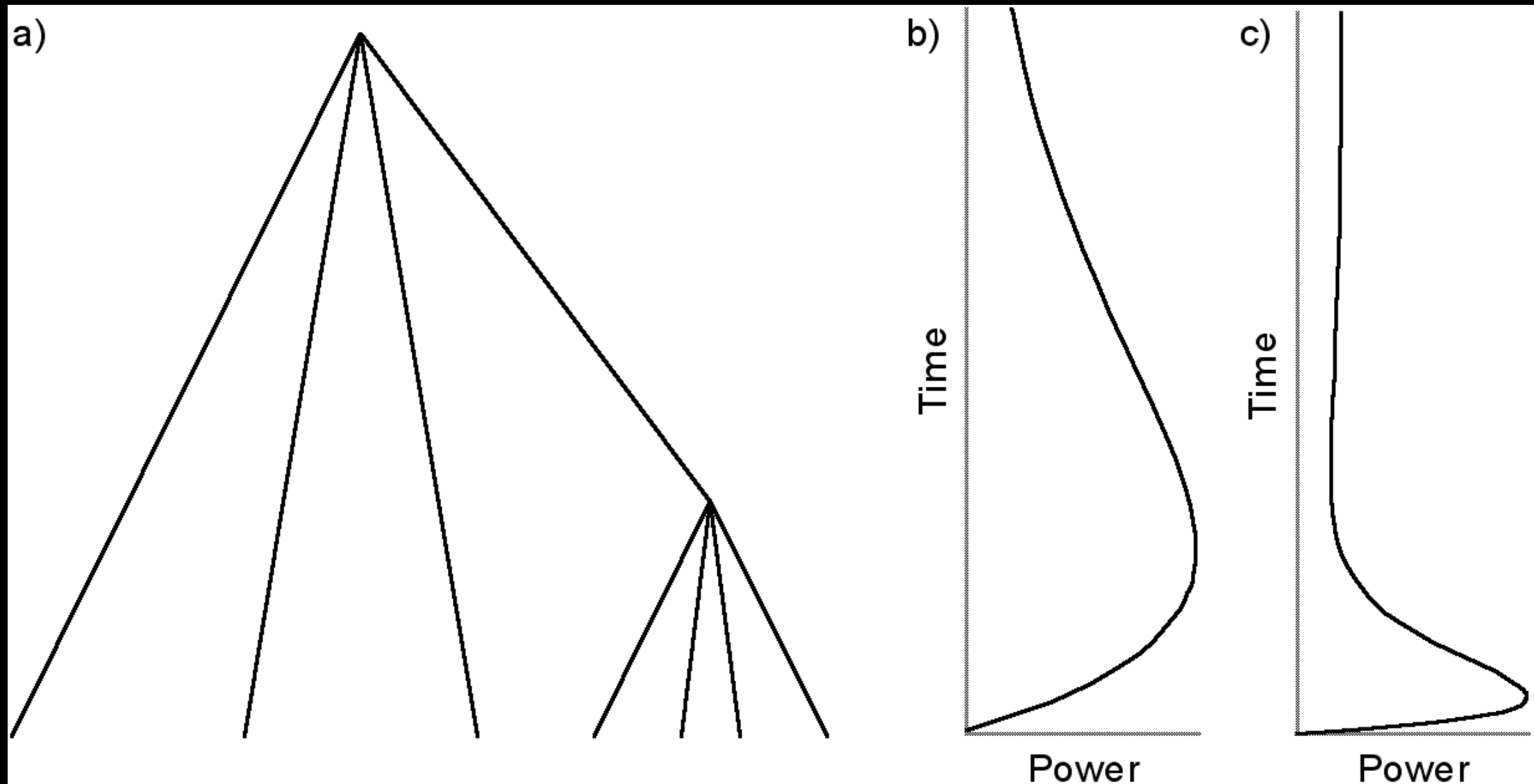
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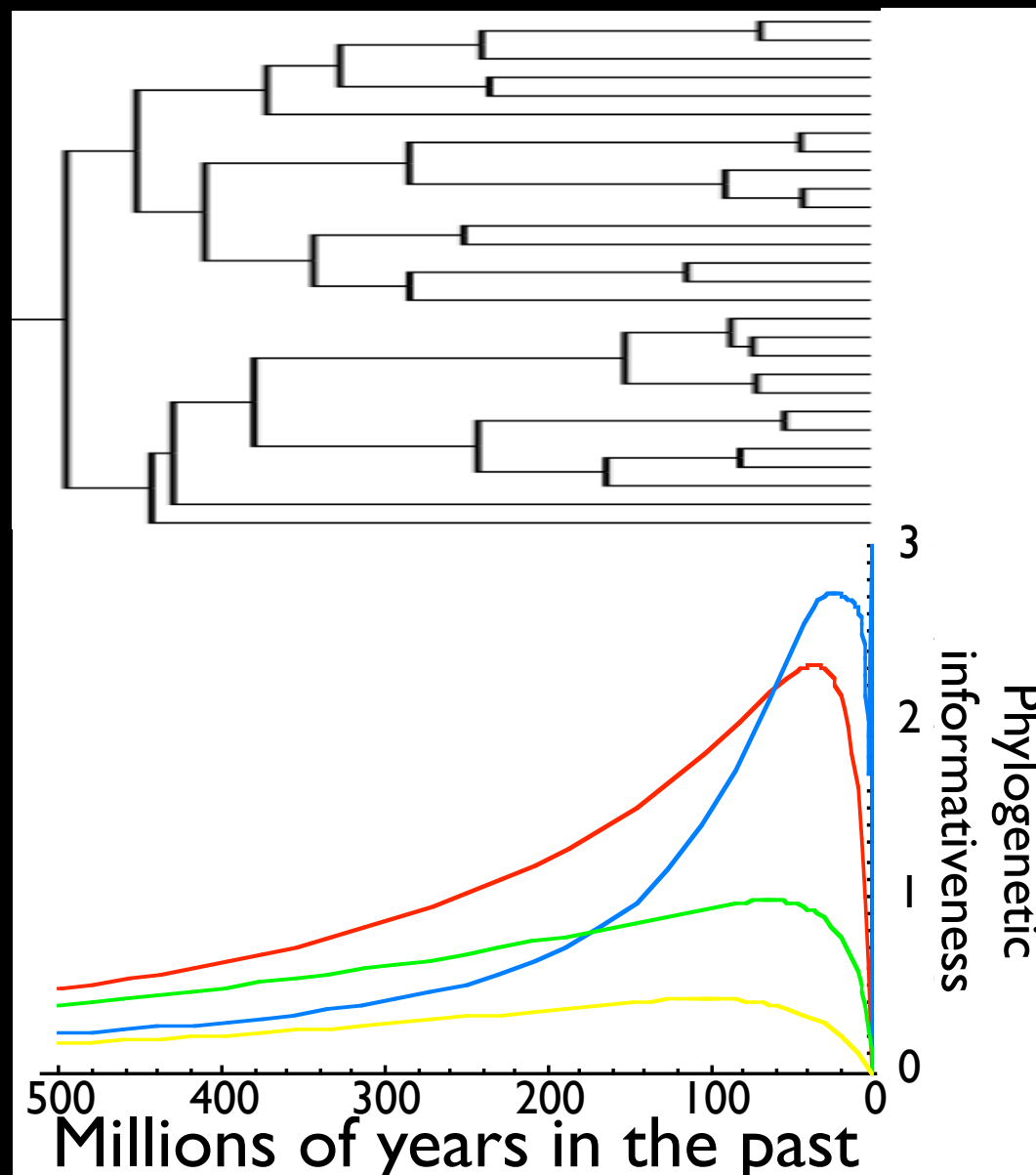
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Townsend, 2007, *Systematic Biology* 56:222-231

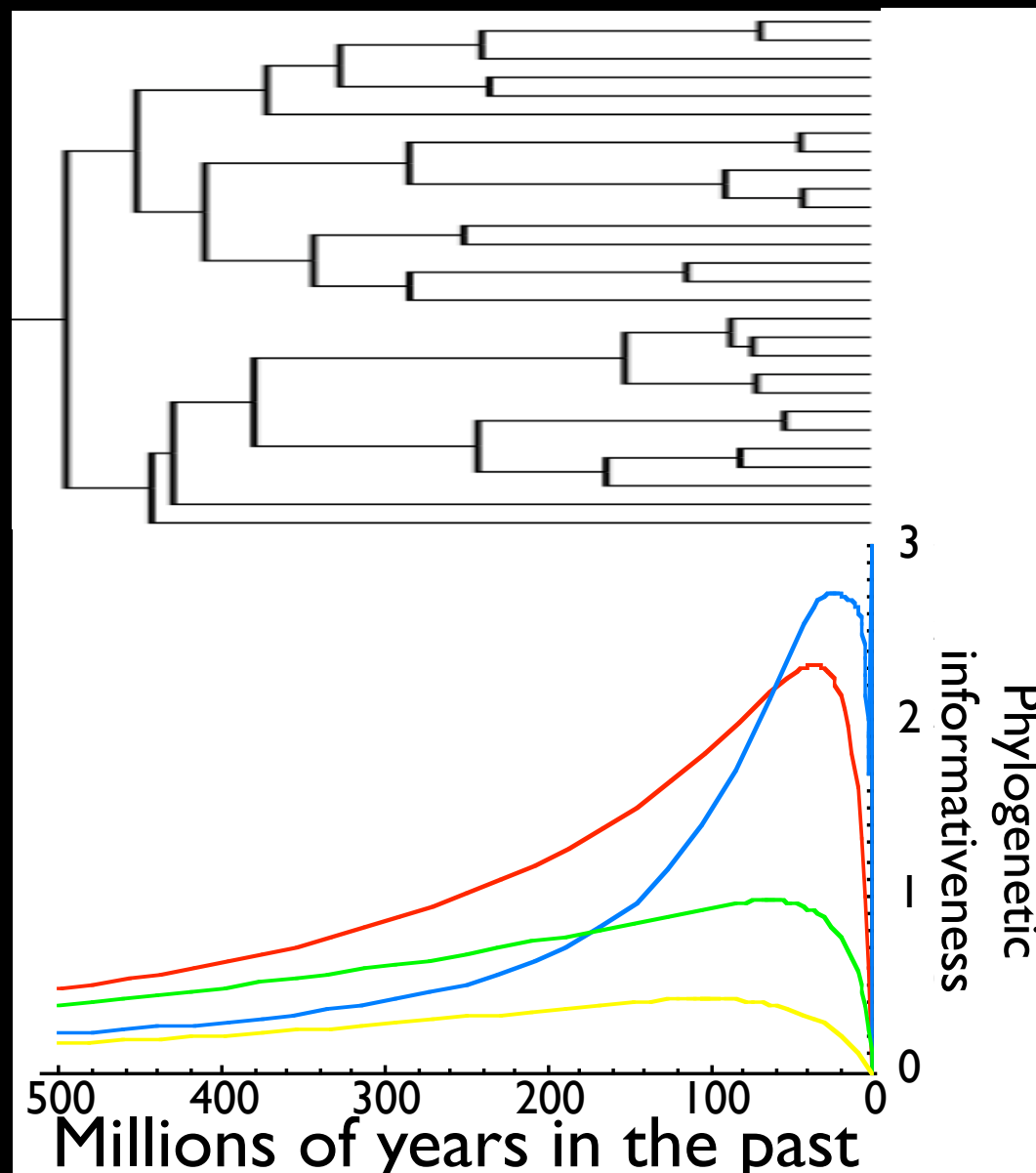
Phylogenetic informativeness yields predictions of relative performance



- Generally, higher phylogenetic informativeness of a gene indicates a higher ability to resolve the corresponding node.

Townsend et al., 2008, *JME* 67: 222-231

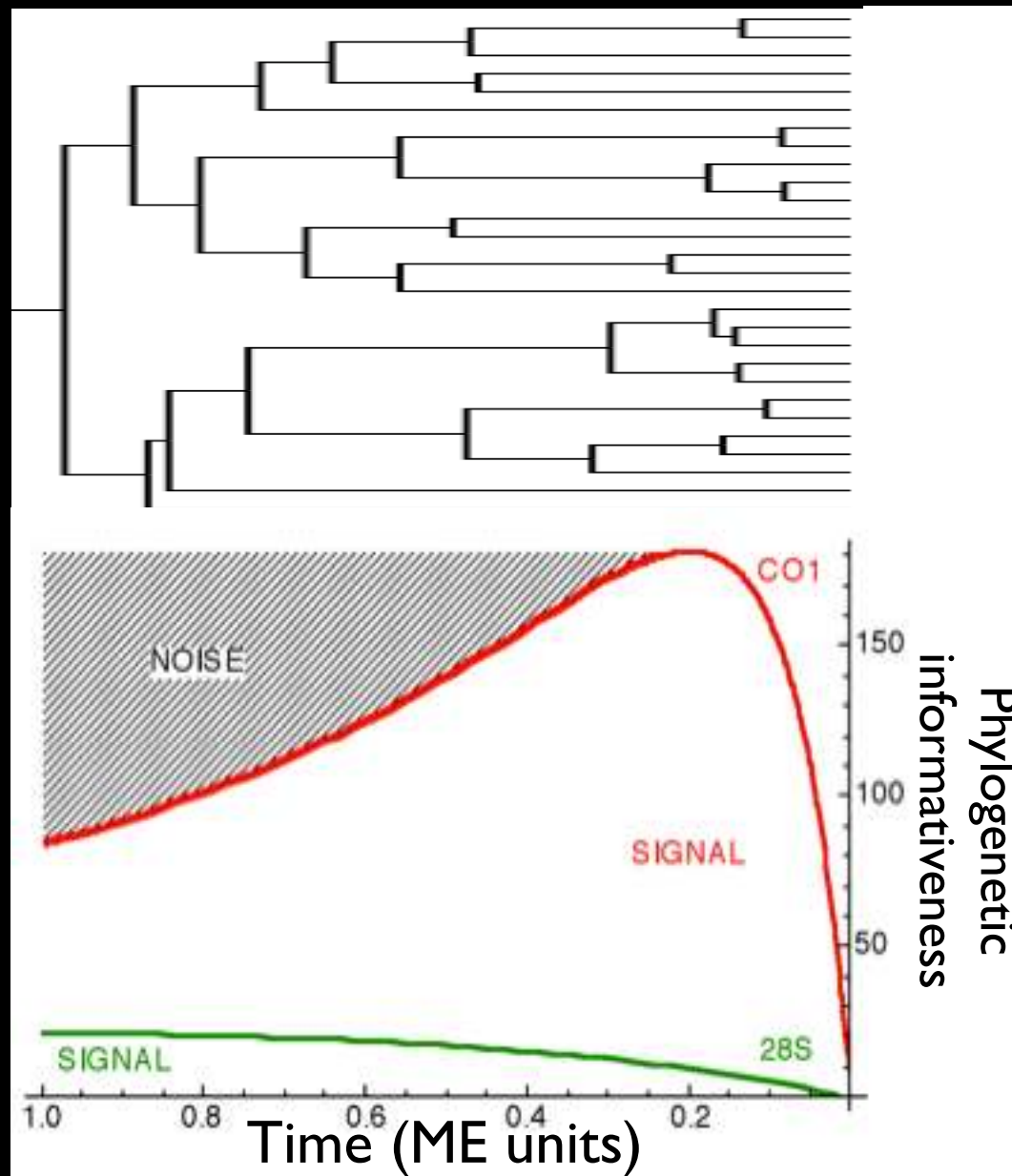
Phylogenetic informativeness must be considered with caveats



- Informativeness profiles provide no clear expectation of performance for specific nodes
- No reason to expect an x-fold difference in informativeness would result in an X-fold difference in the number of nodes resolved
- Profiles of informativeness predict signal but not the misleading effect of noise (convergence or parallelism)

Townsend et al., 2008, *JME* 67: 222-231

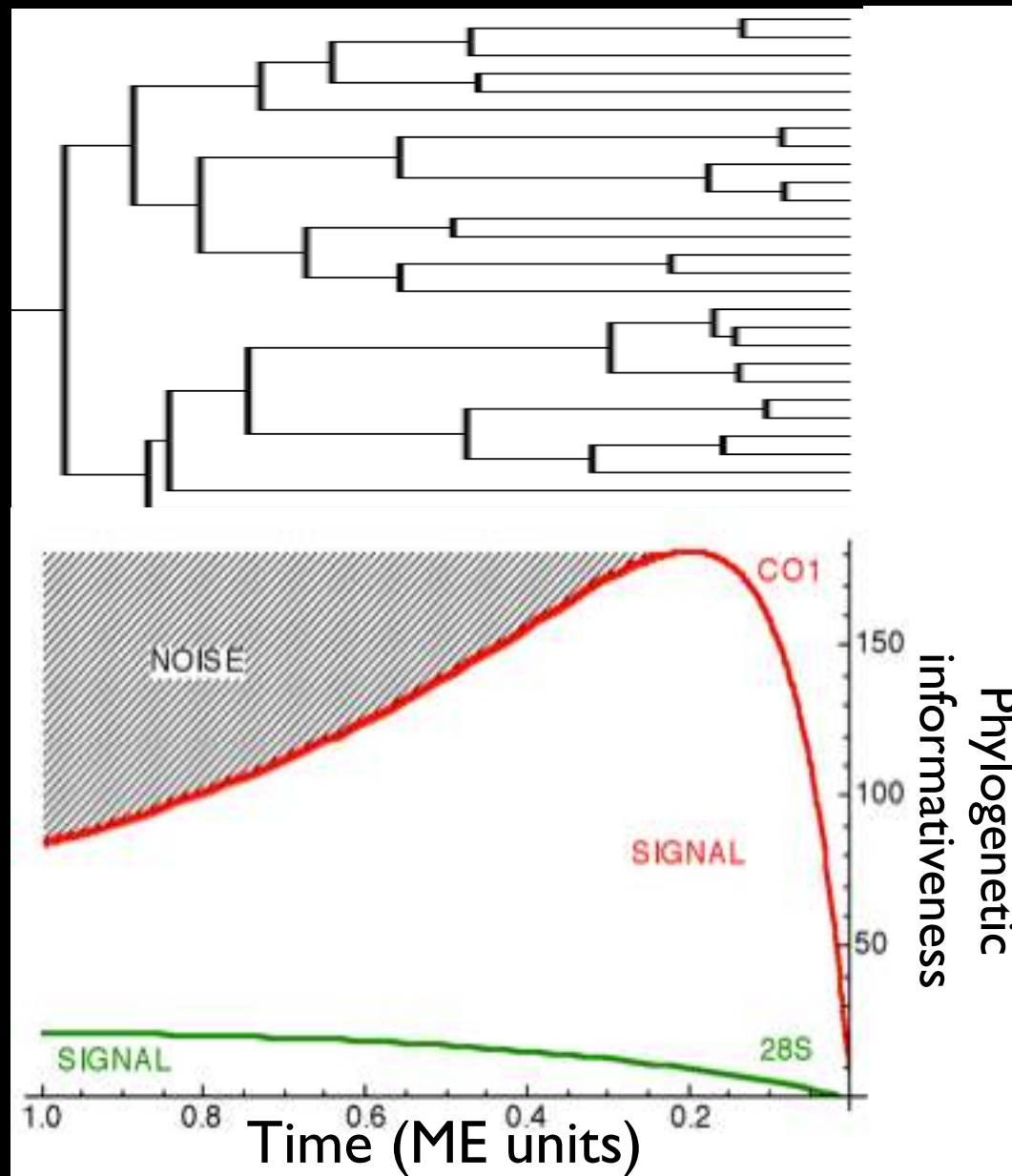
With profiles alone, the effect of noise can be depicted, but not quantified



- Informativeness profiles do not account for misleading effects of noise (convergence or parallelism)
- No quantitative rule, but as a rule of thumb, selecting genes that peak deeper than the time interval of interest will minimize the influence of noise

Townsend et al., 2008, *JME* 67: 222-231

Large data sets lead to both signal and noise



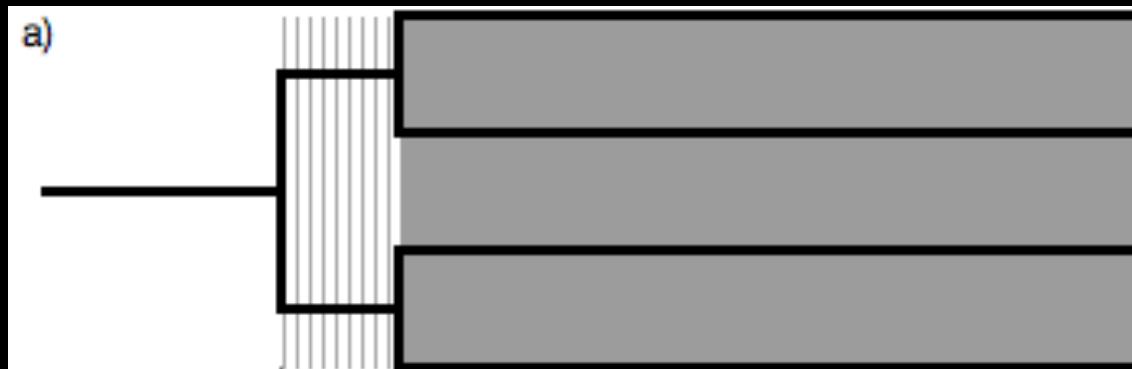
- Gathering large data sets may enable signal to outweigh noise...
- ...but signal *and* noise are contributed by larger datasets.
- Thus, large datasets can lead to spurious resolutions of deep polytomies.
- Deep time and short internodes exacerbate this issue.

Townsend et al., 2008, *JME* 67: 222-231

Matrix methods quantify signal and noise

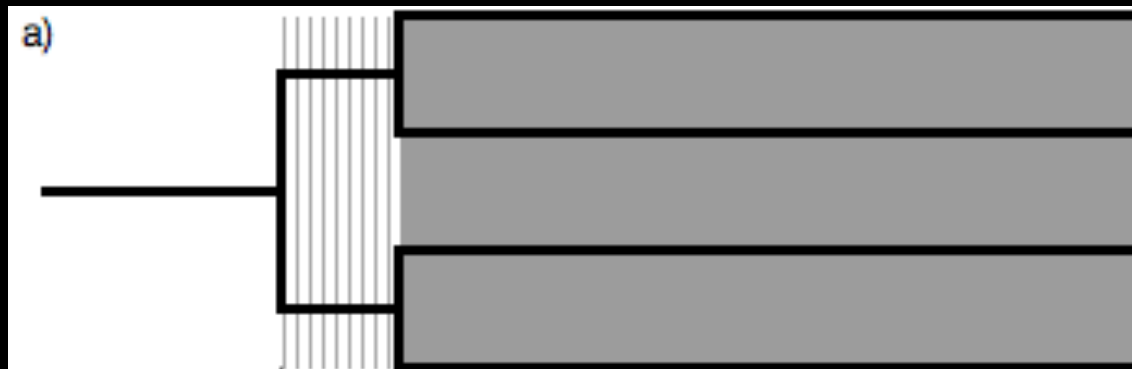
Townsend et al., 2012, *Systematic Biology*

Matrix methods quantify signal and noise



Townsend et al., 2012, *Systematic Biology*

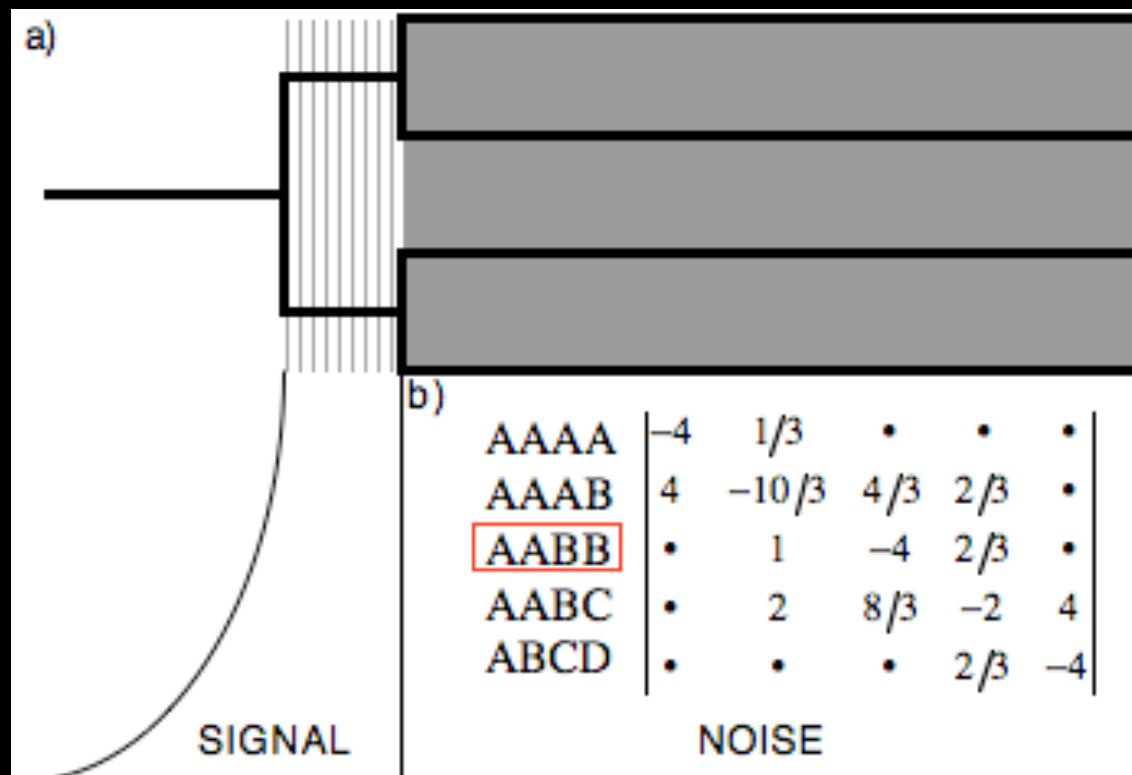
Matrix methods quantify signal and noise



- Begin with a four taxon tree, branches to time T , internode t_0

Townsend et al., 2012, *Systematic Biology*

Matrix methods quantify signal and noise

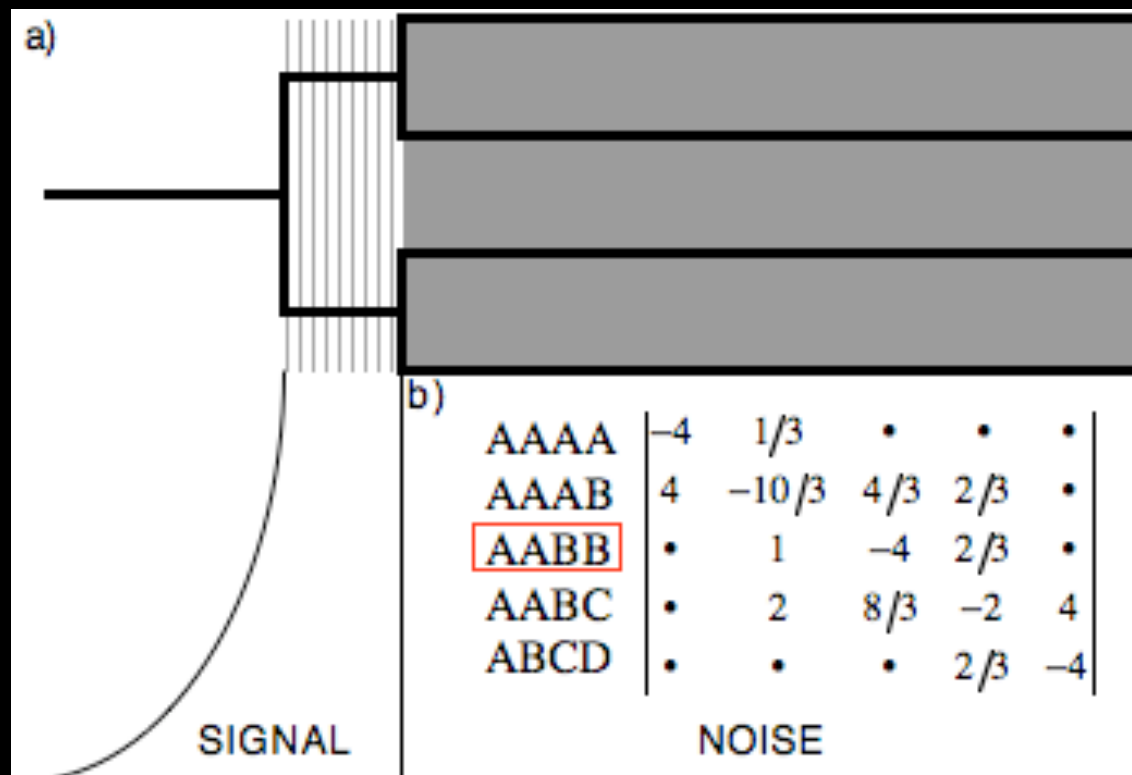


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Matrix methods

quantify signal and noise

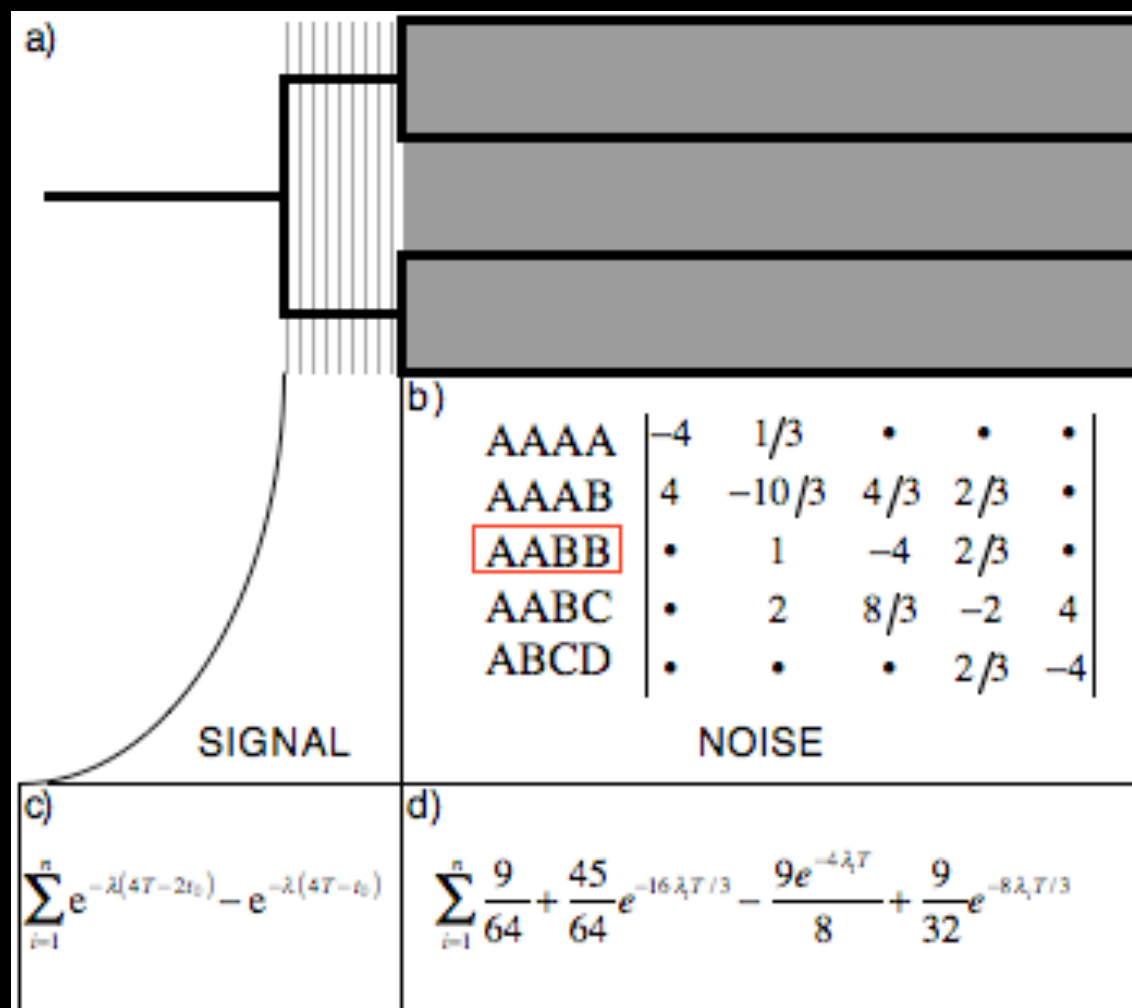


- Begin with a four taxon tree, branches to time T , internode t_0
- Derive transition matrix for the site patterns for the four species: AAAA, AAAB, AABB, AABC, ABCD

Townsend et al., 2012, *Systematic Biology*

Matrix methods

quantify signal and noise

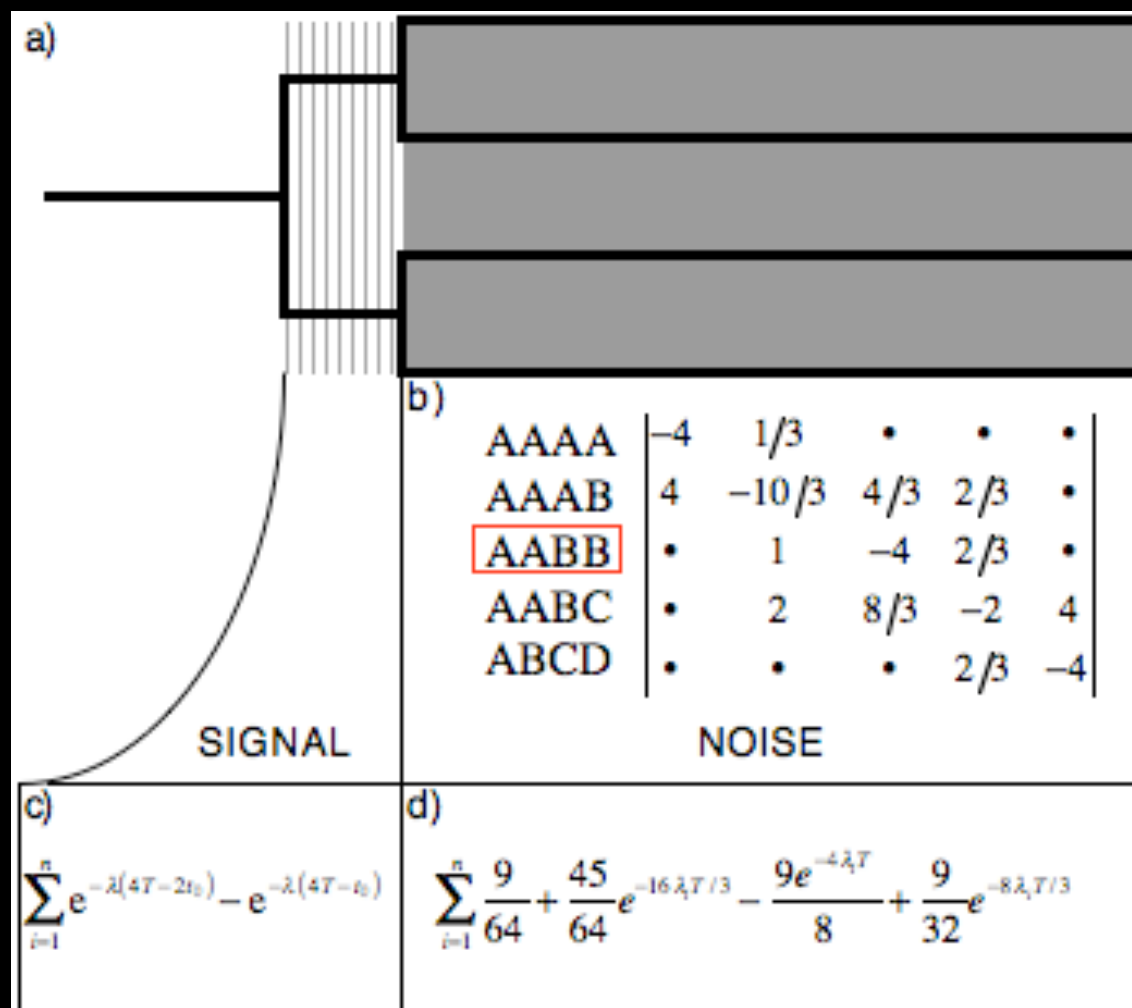


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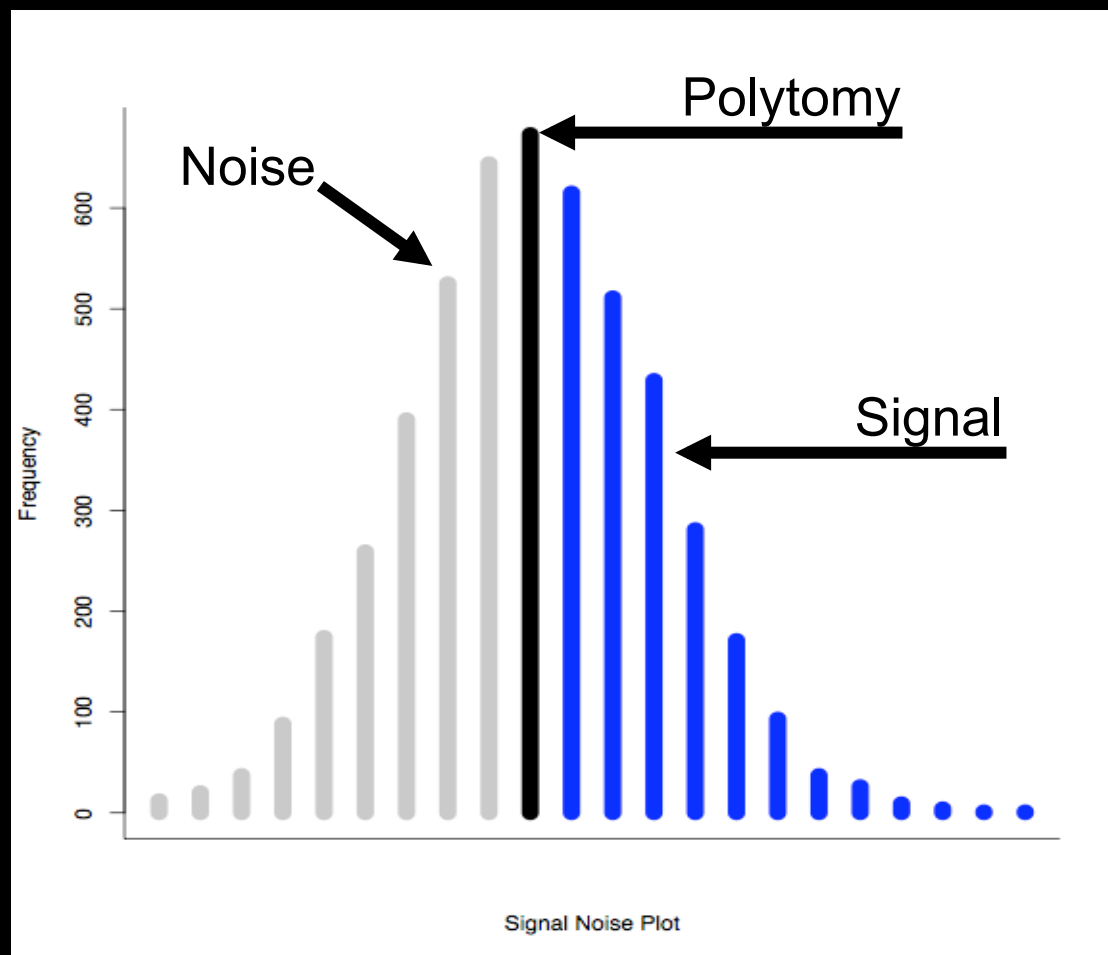
quantify signal and noise



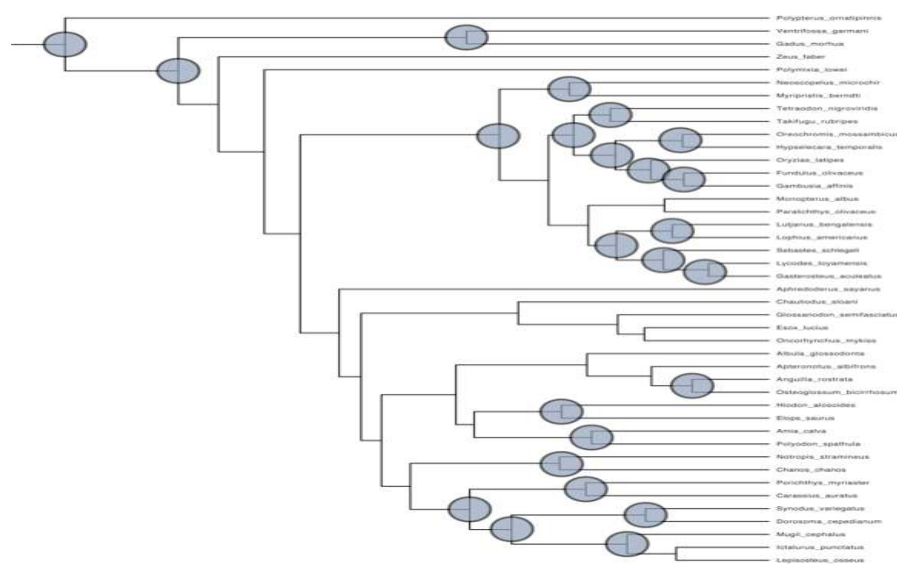
- Begin with a four taxon tree, branches to time T , internode t_0
- Derive transition matrix for the site patterns for the four species: AAAA, AAAB, AABB, AABC, ABCD
- Power to resolve a node can then be reduced to a biased random walk problem, with each site representing a “step.”

Townsend et al., 2012, *Systematic Biology*

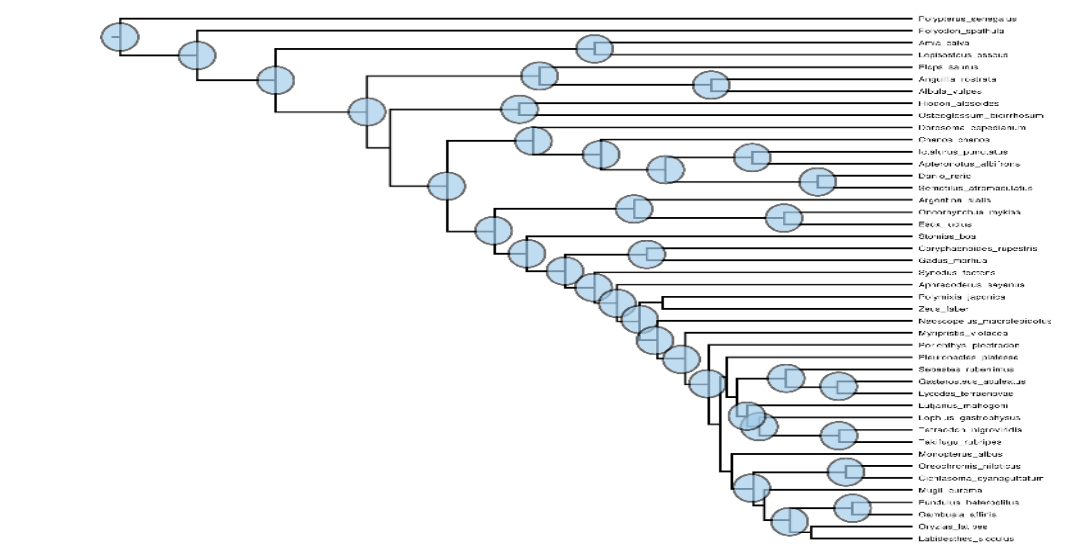
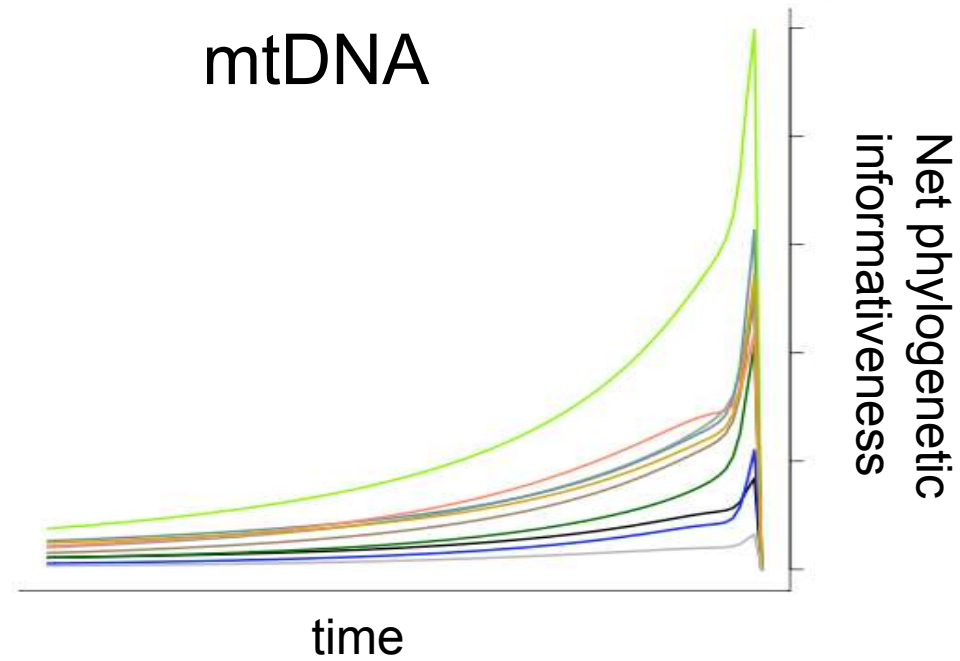
Each site contributes to the probability of correct resolution, incorrect resolution, or polytomy



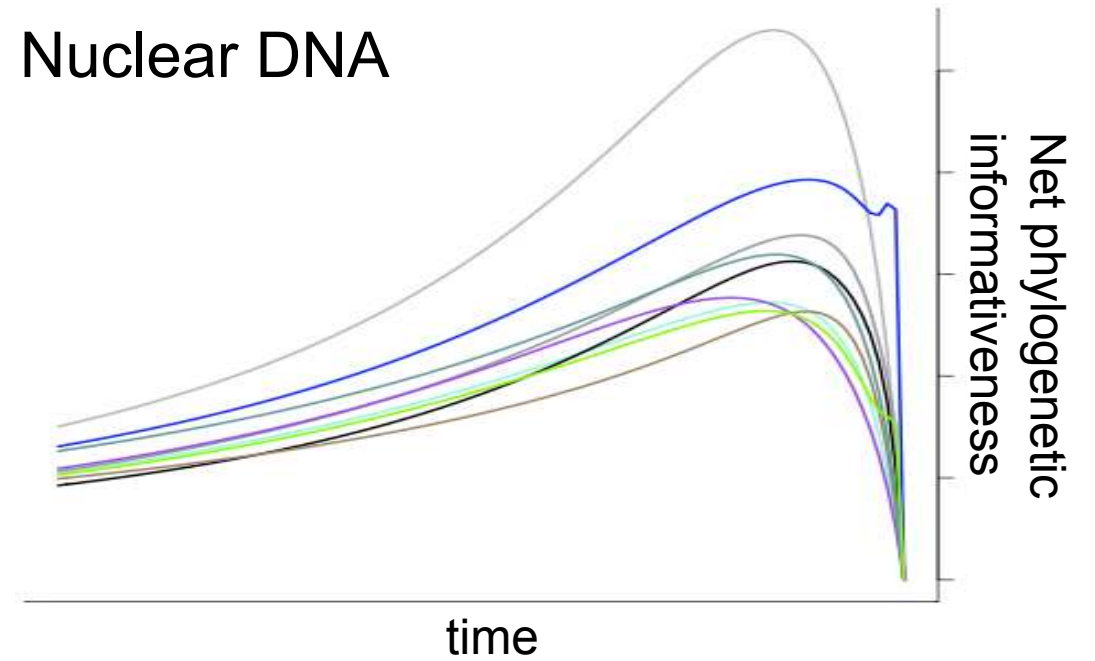
- Probability signal 0.43
- Probability polytomy 0.14
- Probability noise 0.43



mtDNA



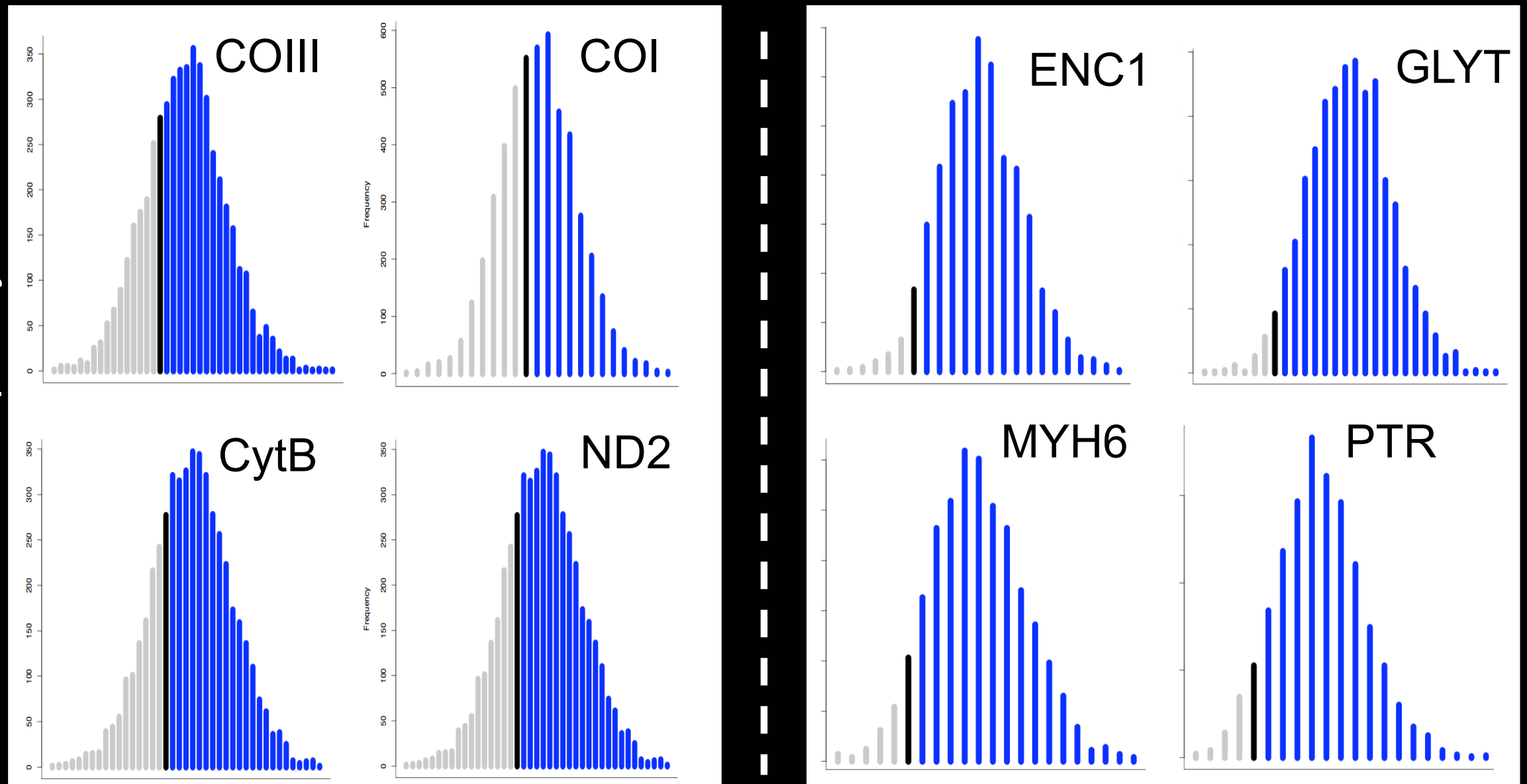
Nuclear DNA



Dornburg et al., in revision



Frequency



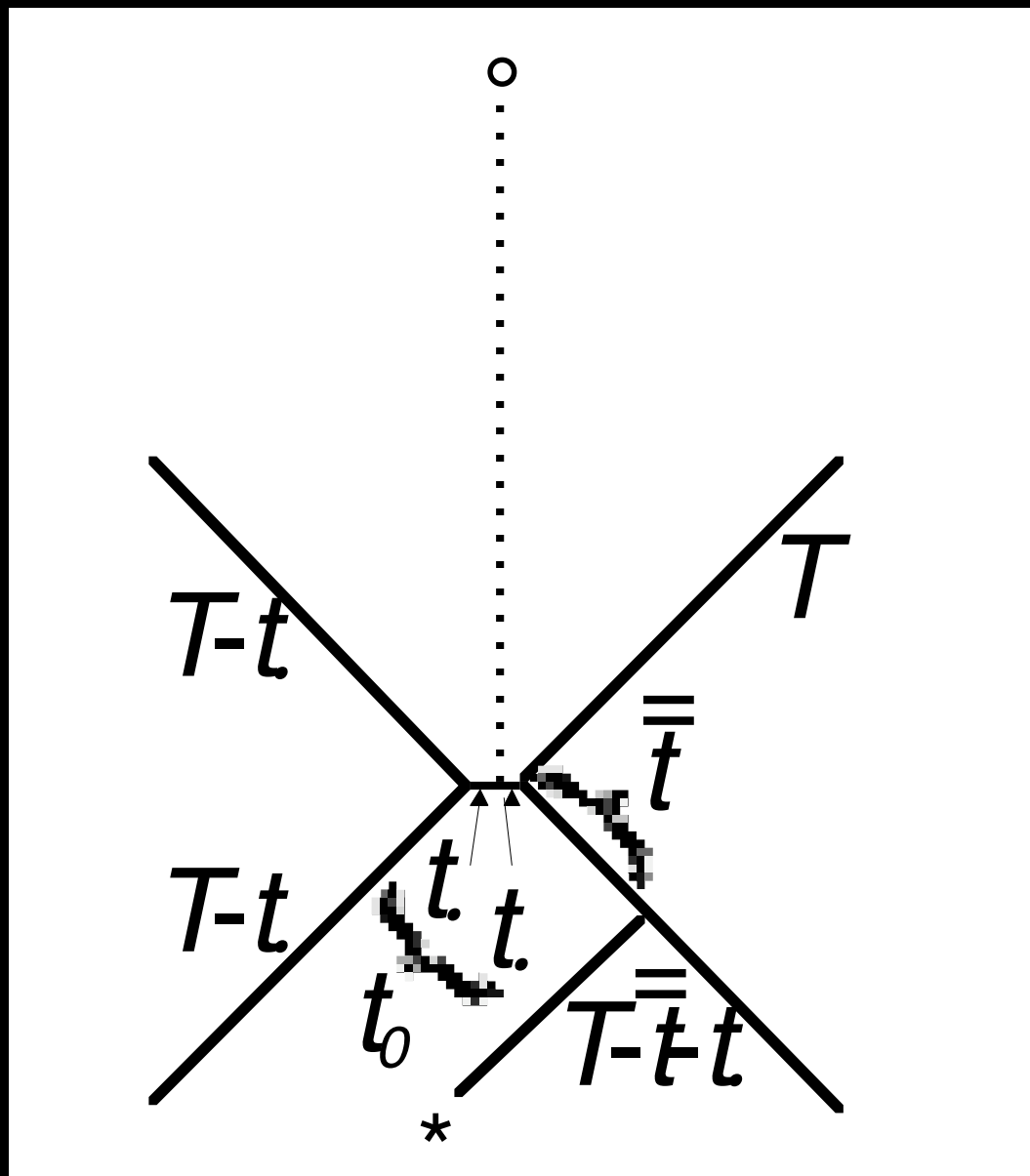
Noise/Polytomy/Signal

Dornburg et al., in revision

Phylogenetic experimental design has a diffuse history

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Phylogenetic informativeness can be modified to optimize taxon sampling

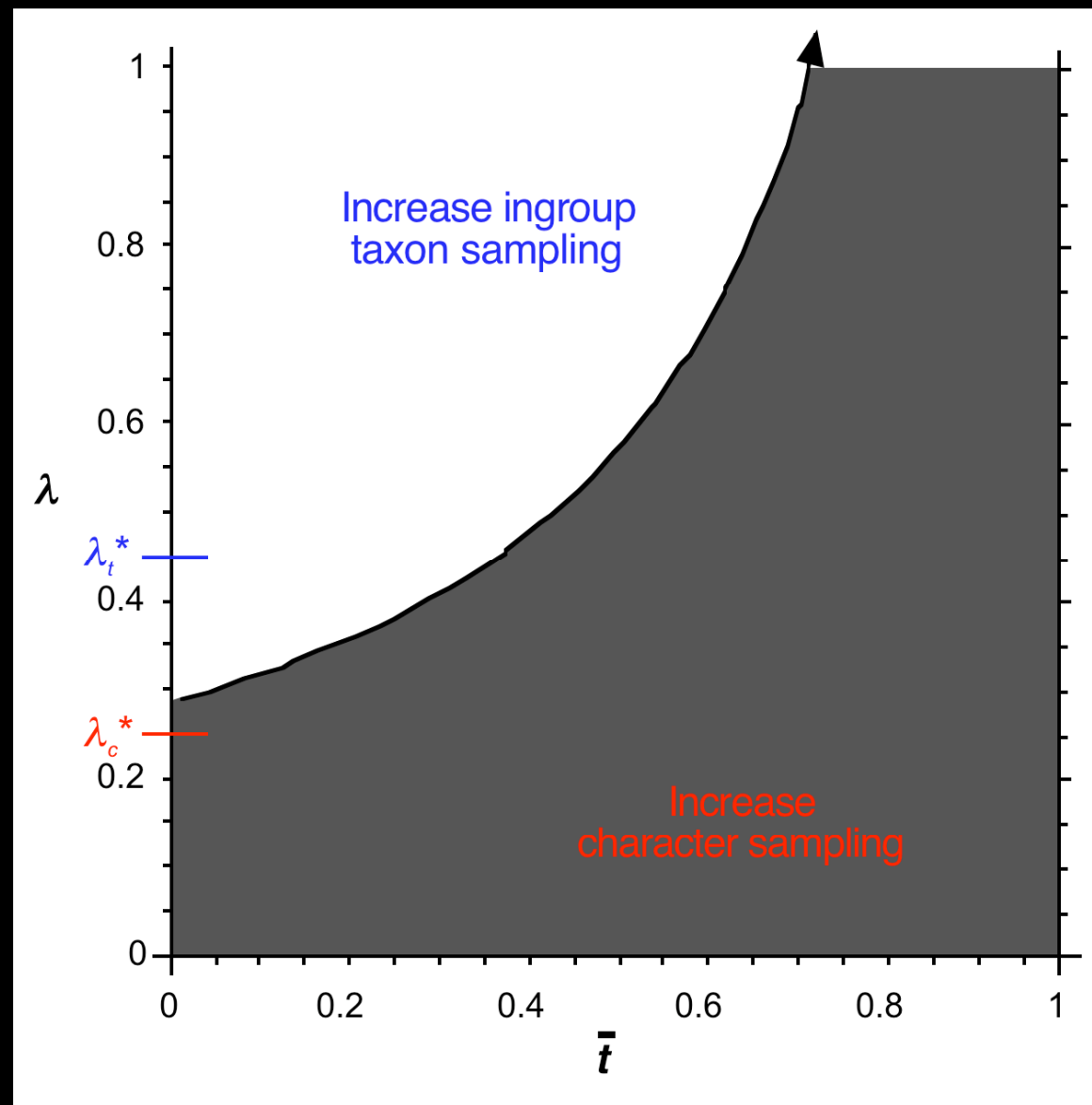


- $\Pr\{\text{inf}\} = e^{-4T\lambda} (1 - e^{-t_0\lambda}) (1 - e^{-(T-\bar{t})\lambda})$

$$\hat{\lambda}_t \approx \frac{1}{(2.2)T}$$

Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

Increase taxon sampling with fast-evolving characters, increase character sampling with slow-evolving characters



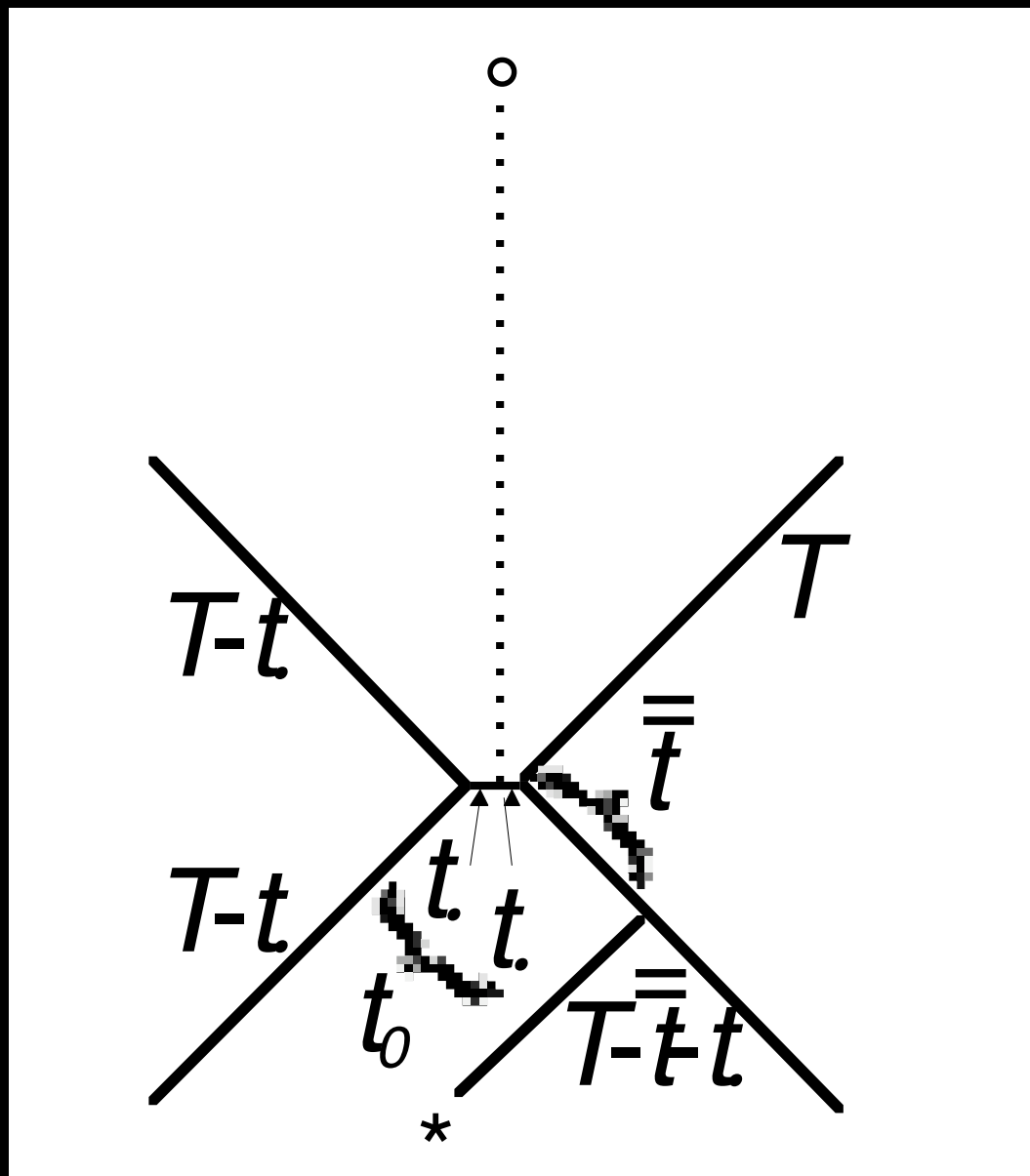
- Optimal choice of taxon and gene depends on rate of character evolution and ingroup divergence time

Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

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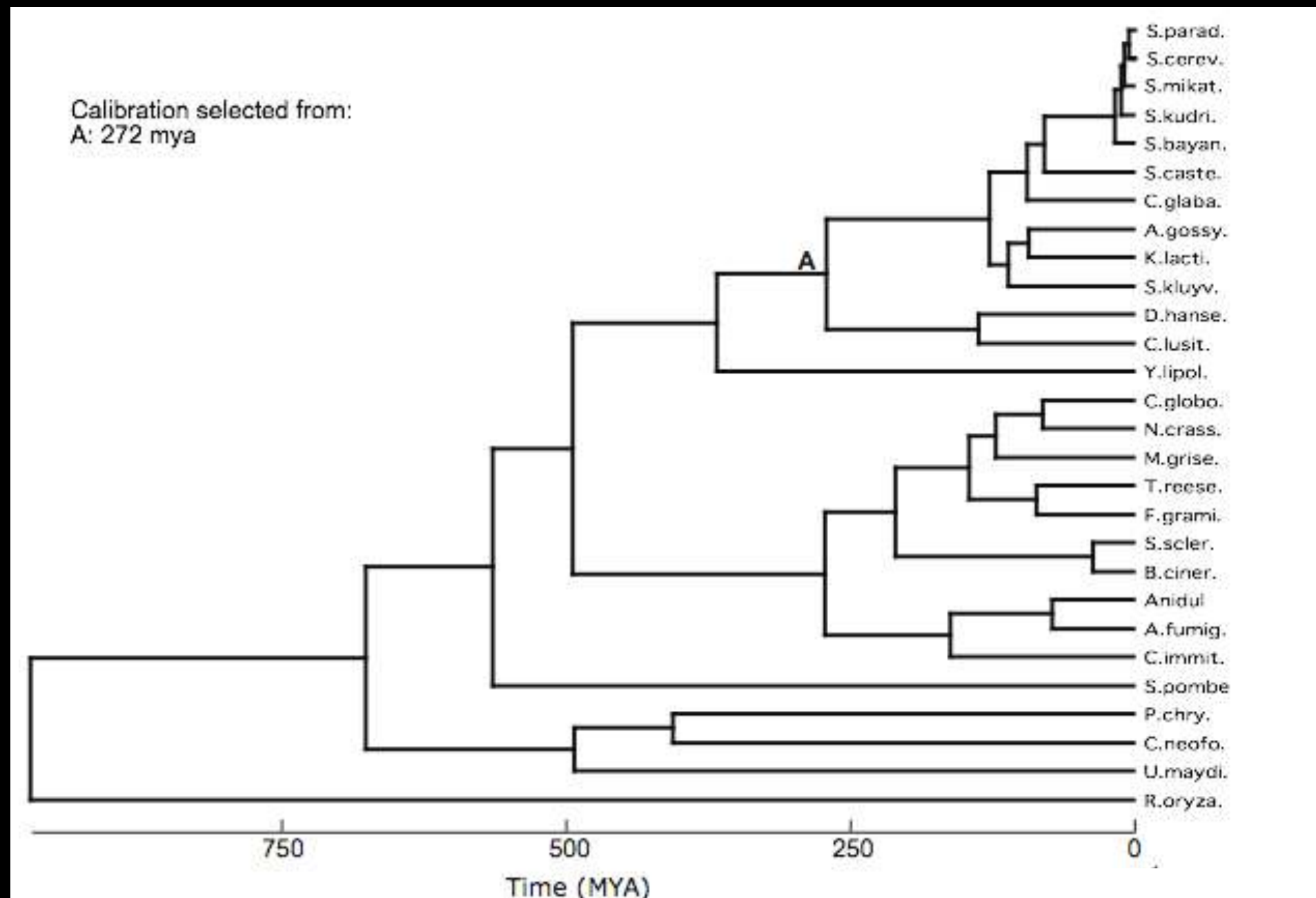


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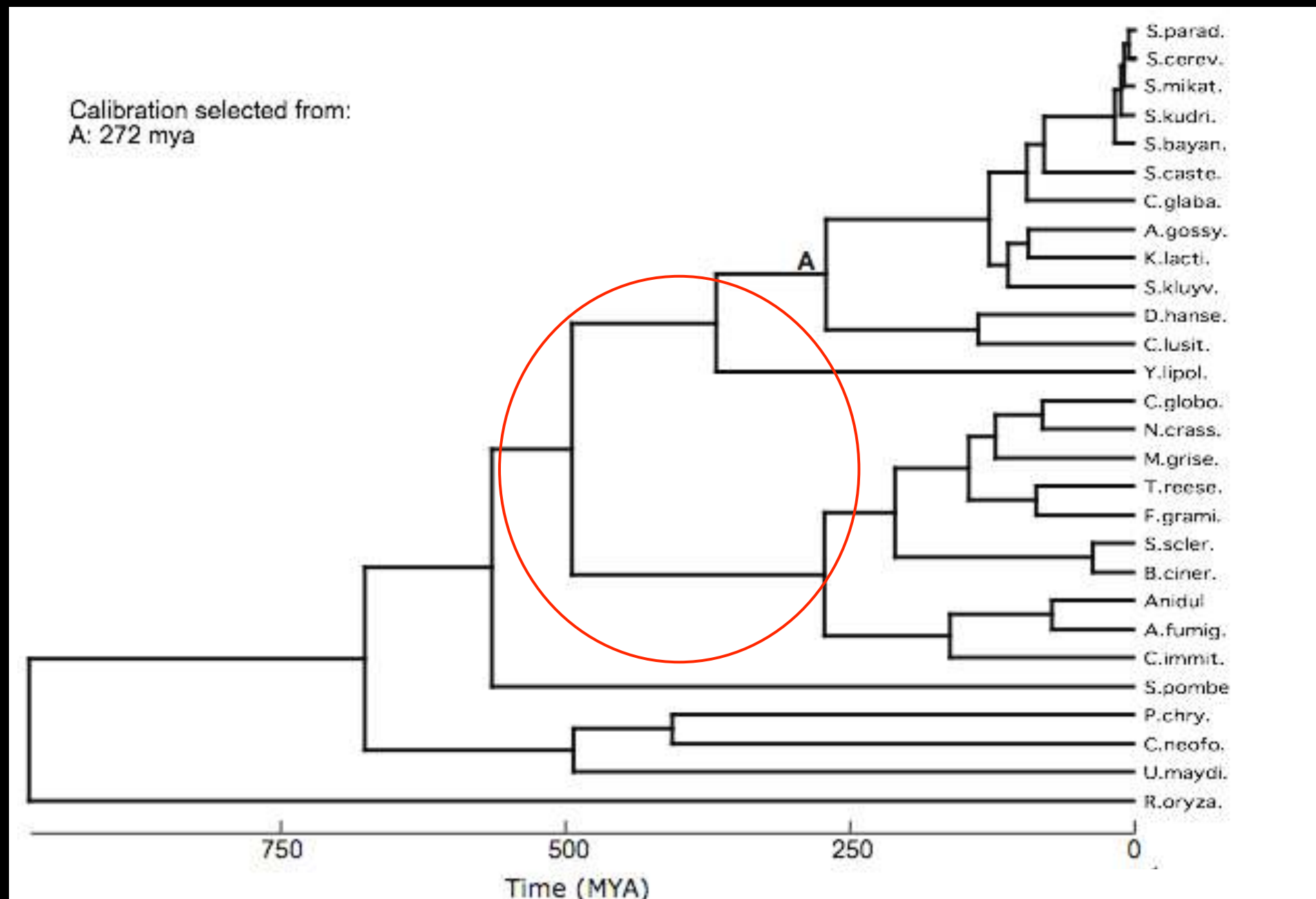
Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

Four taxa and their ingroups were used to evaluate PITA



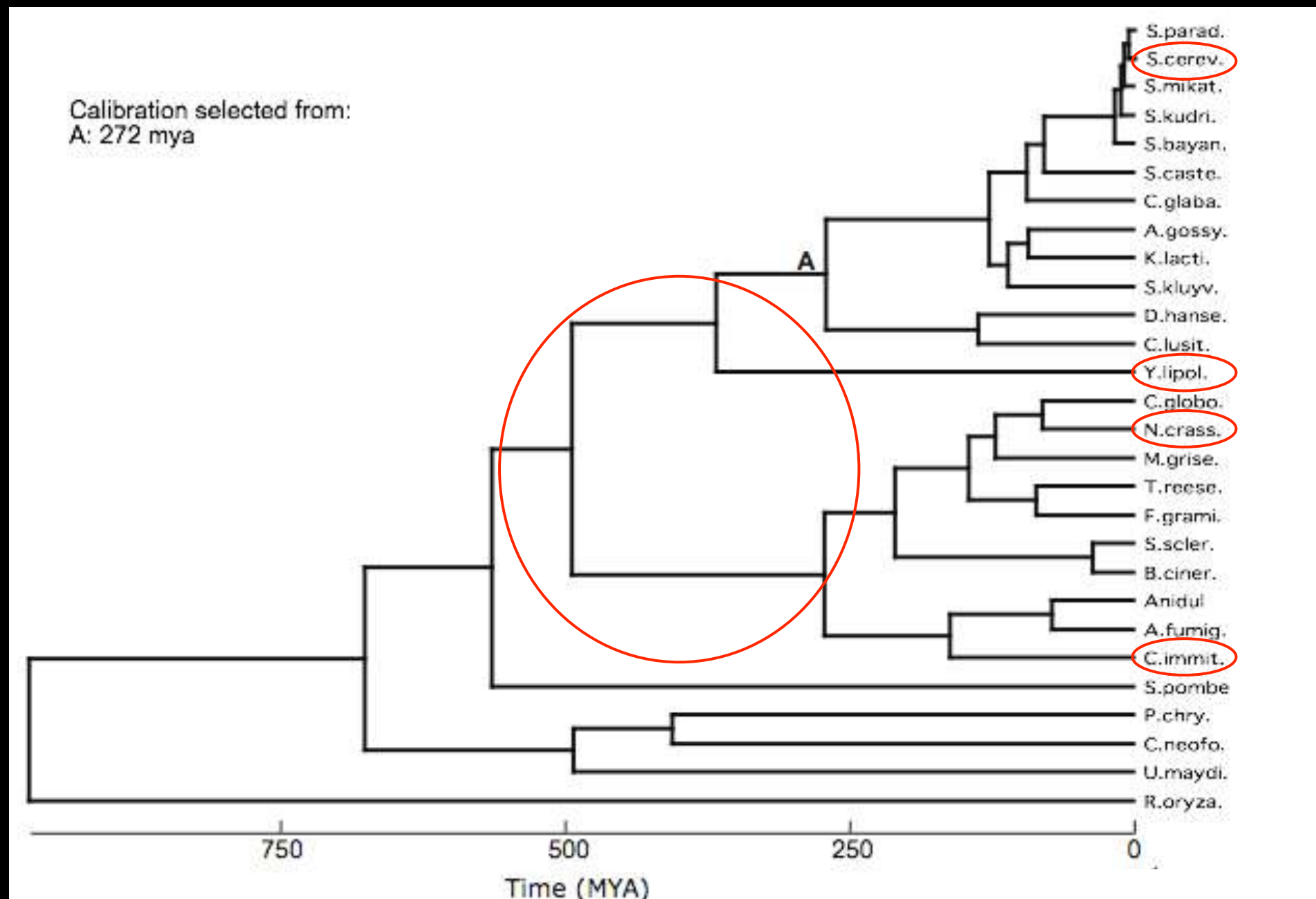
Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

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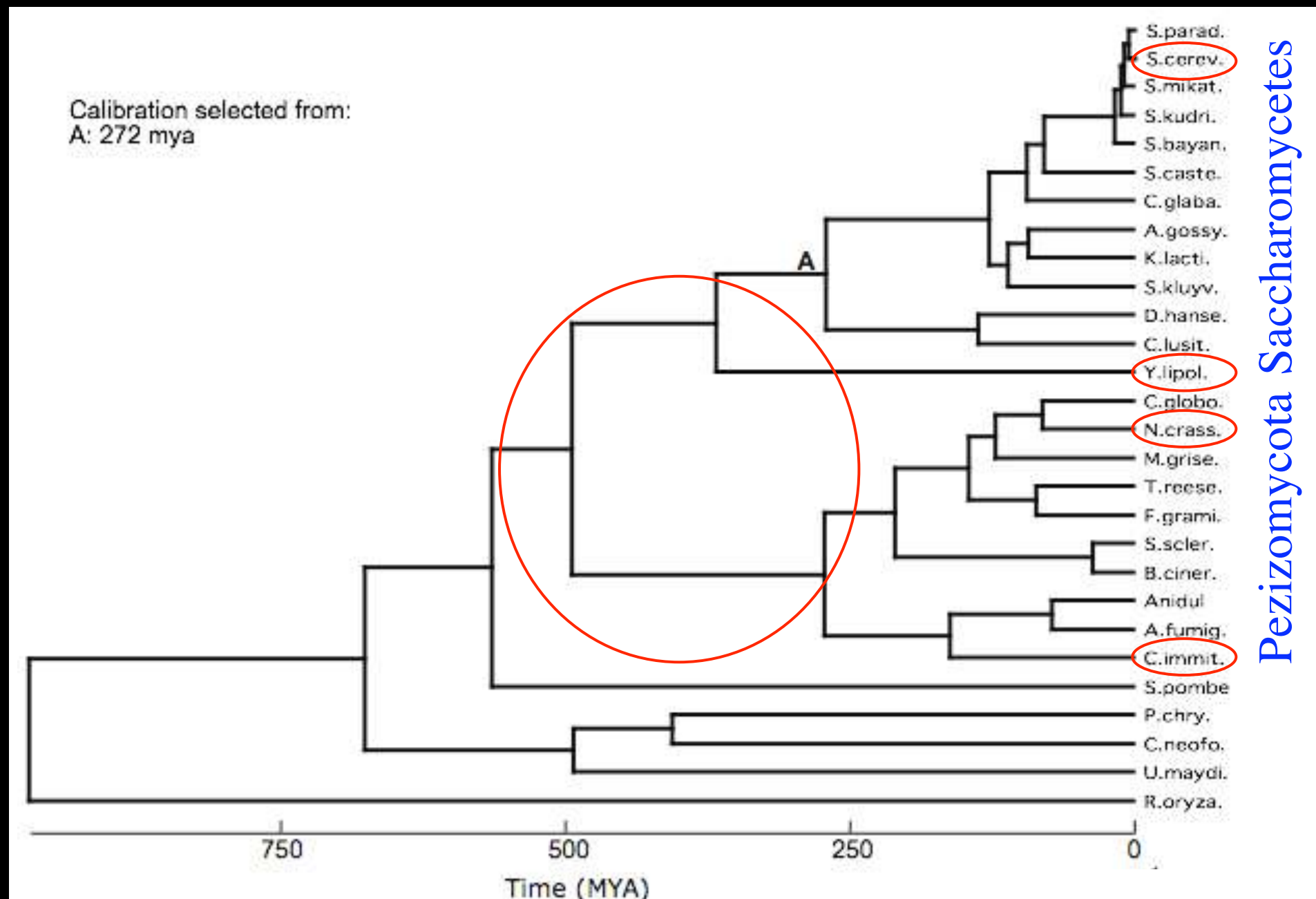
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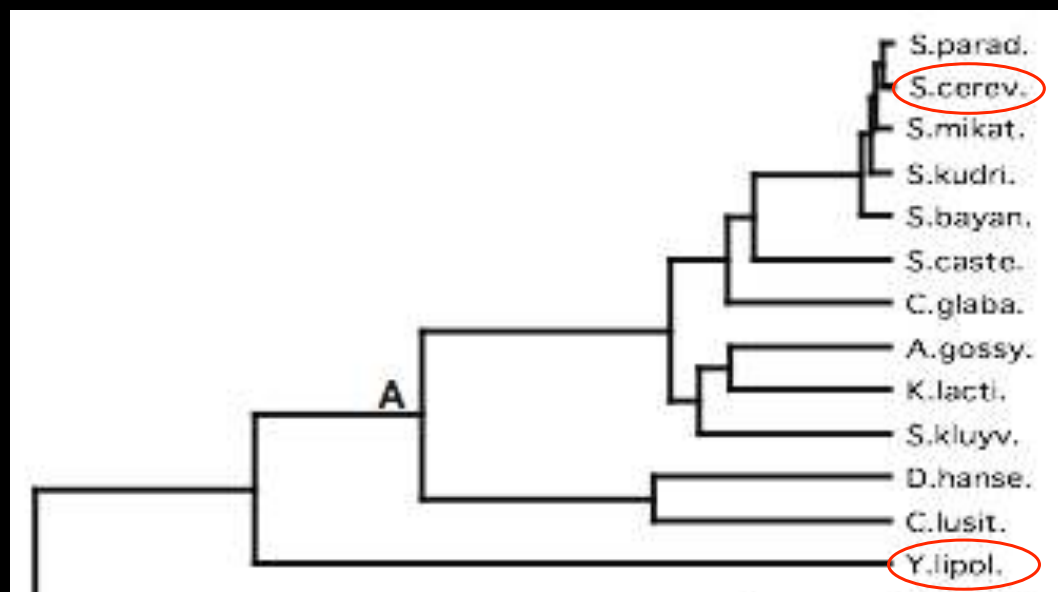
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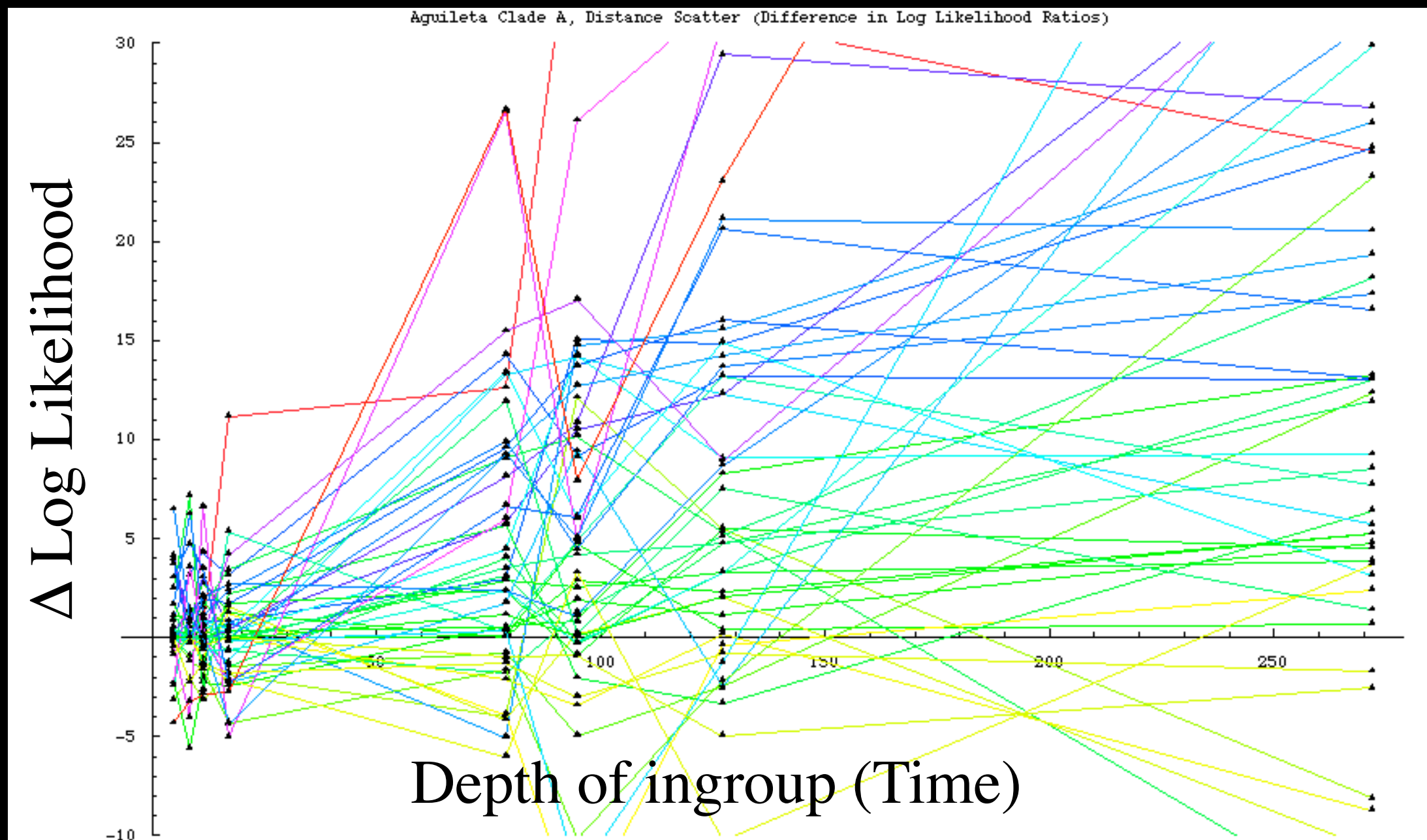
Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

The Saccharomycetes chronogram features



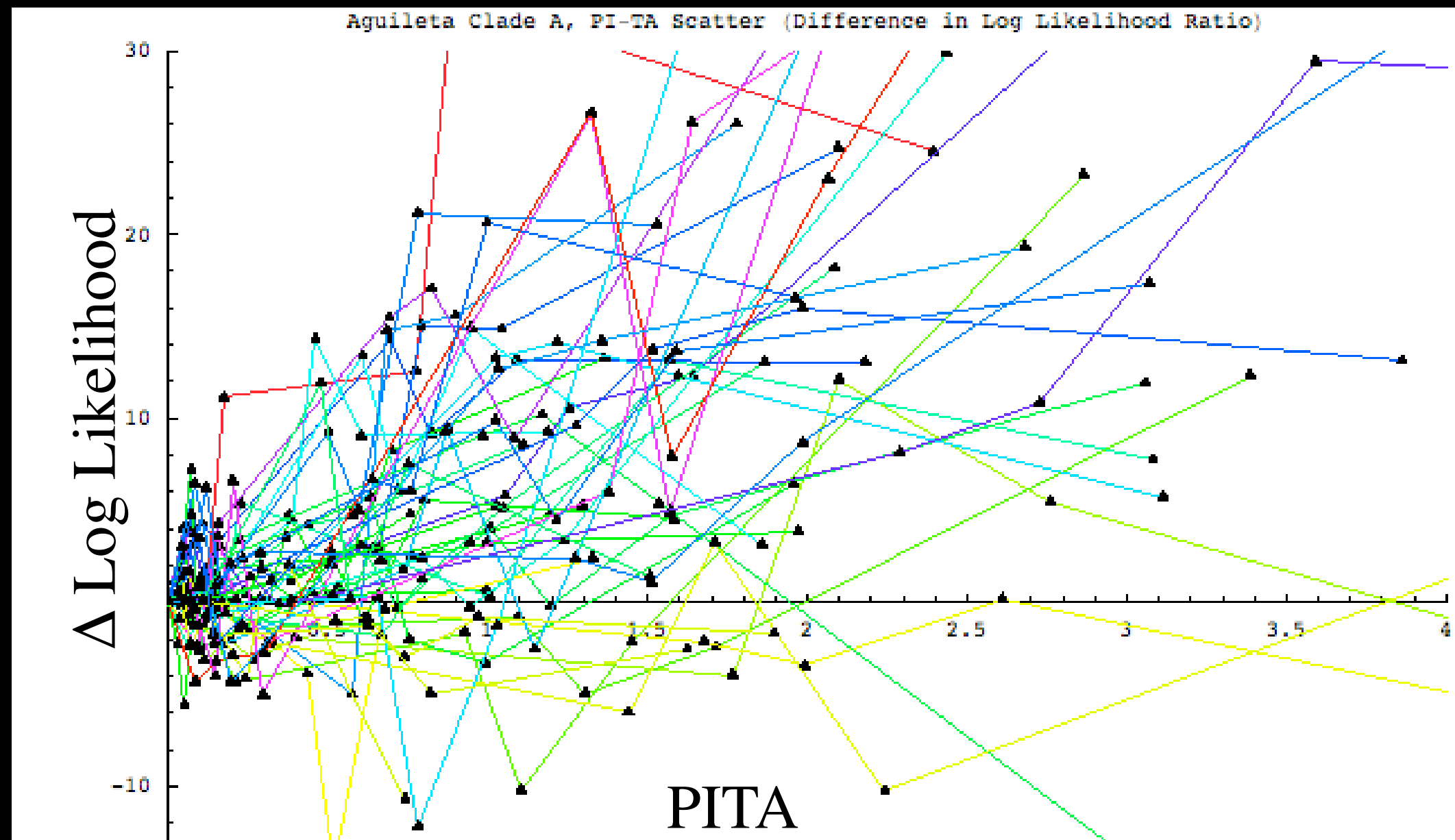
- four tip lineages in the genus *Saccharomyces*, closely related to *S. cerevisiae*, and
- a range of ingroup taxa at other depths

Sampling the deepest ingroups typically yields the greatest resolution



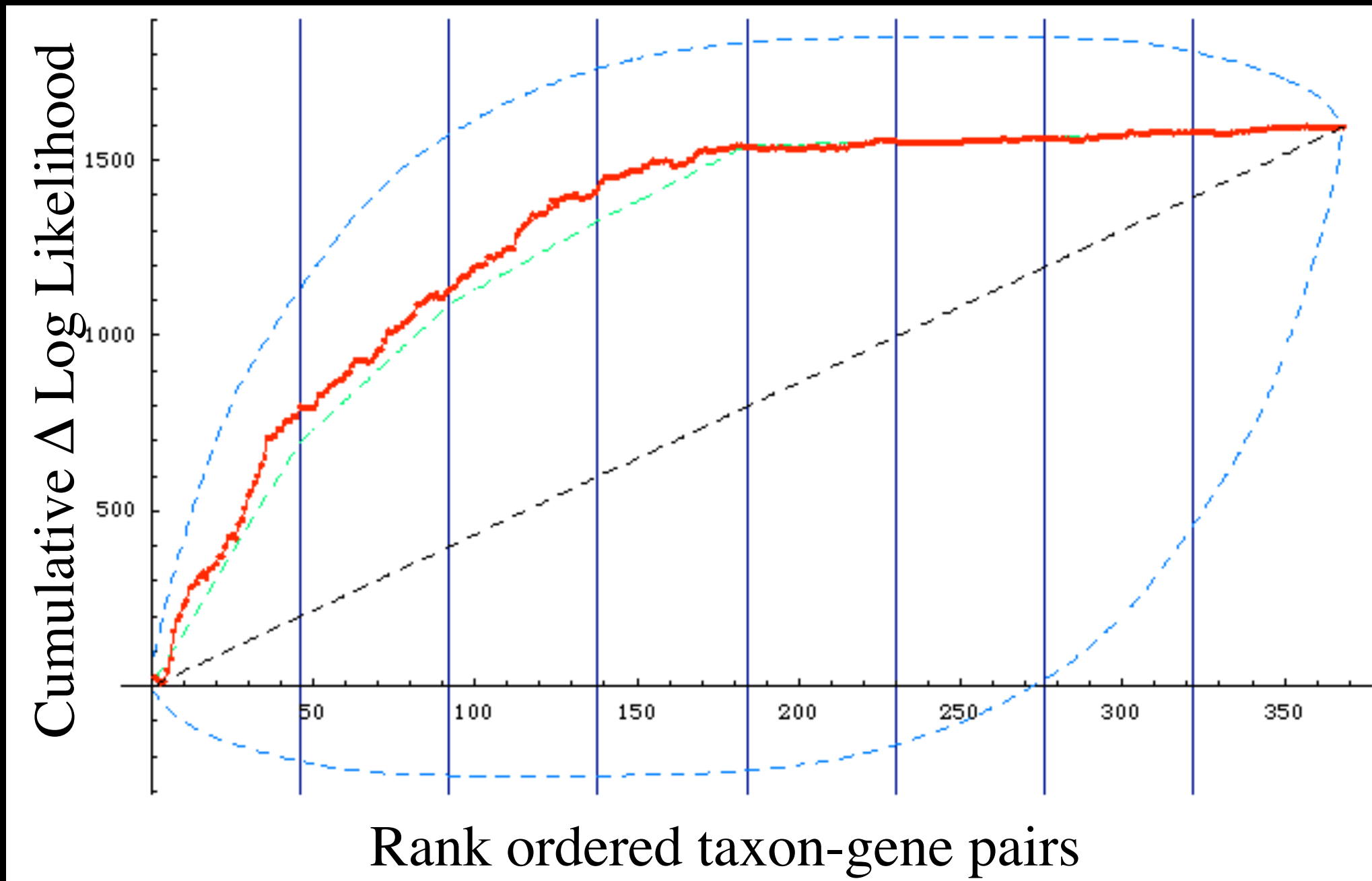
Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

Sampling using PITA is correlated with support



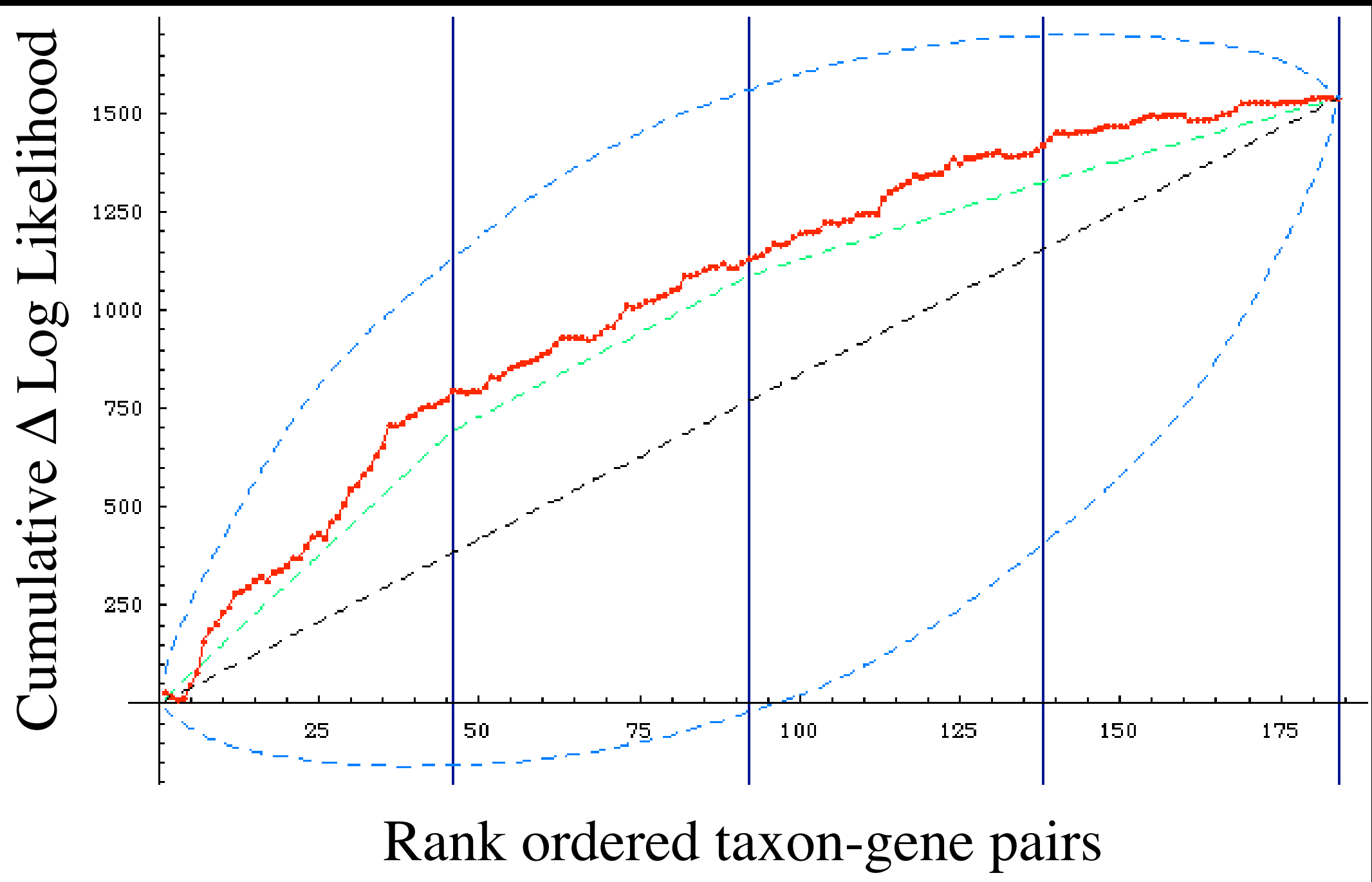
Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

Saccharomycete clade: PITA performs best



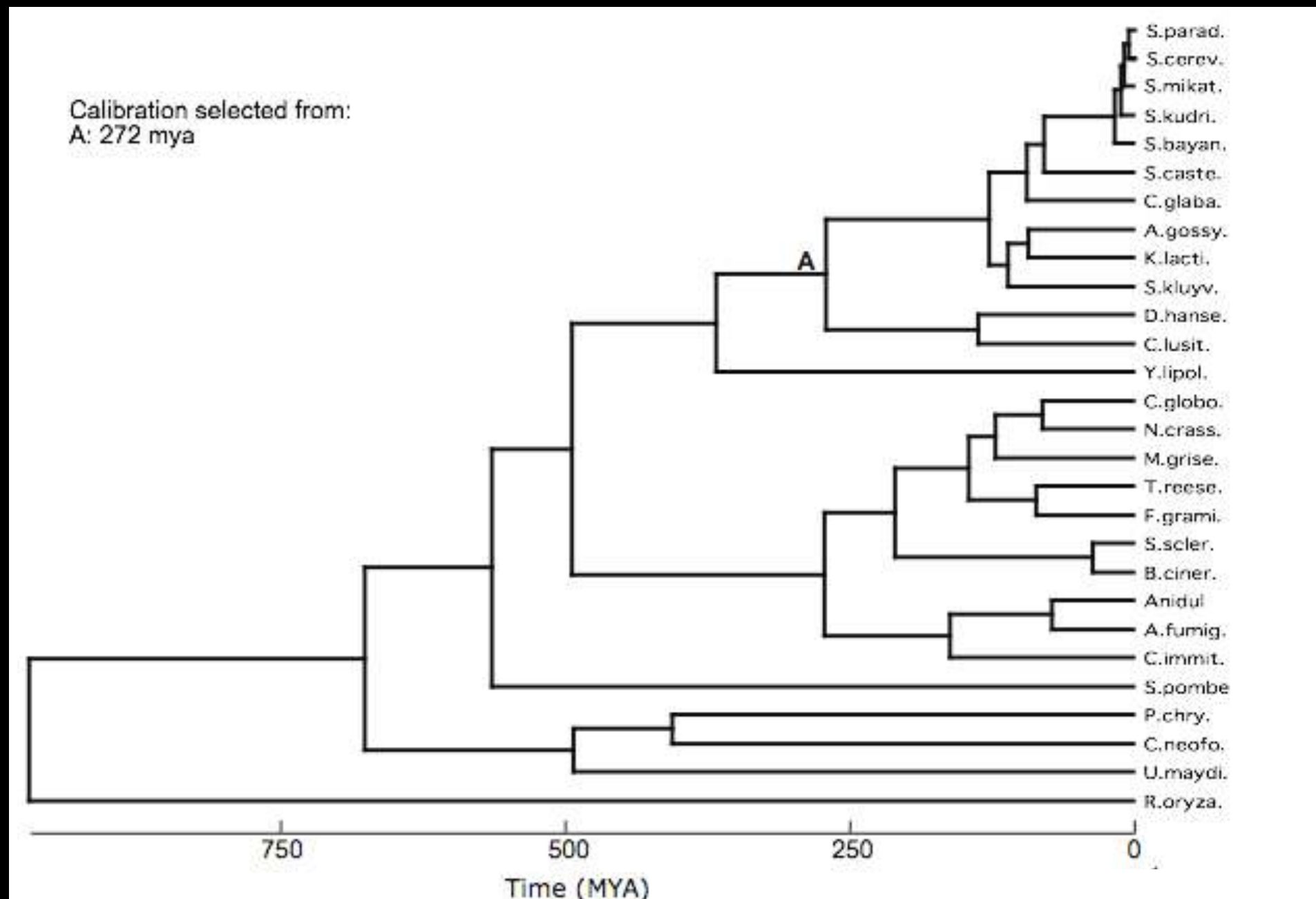
Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

Deep Saccharomycete clade: PITA performs best

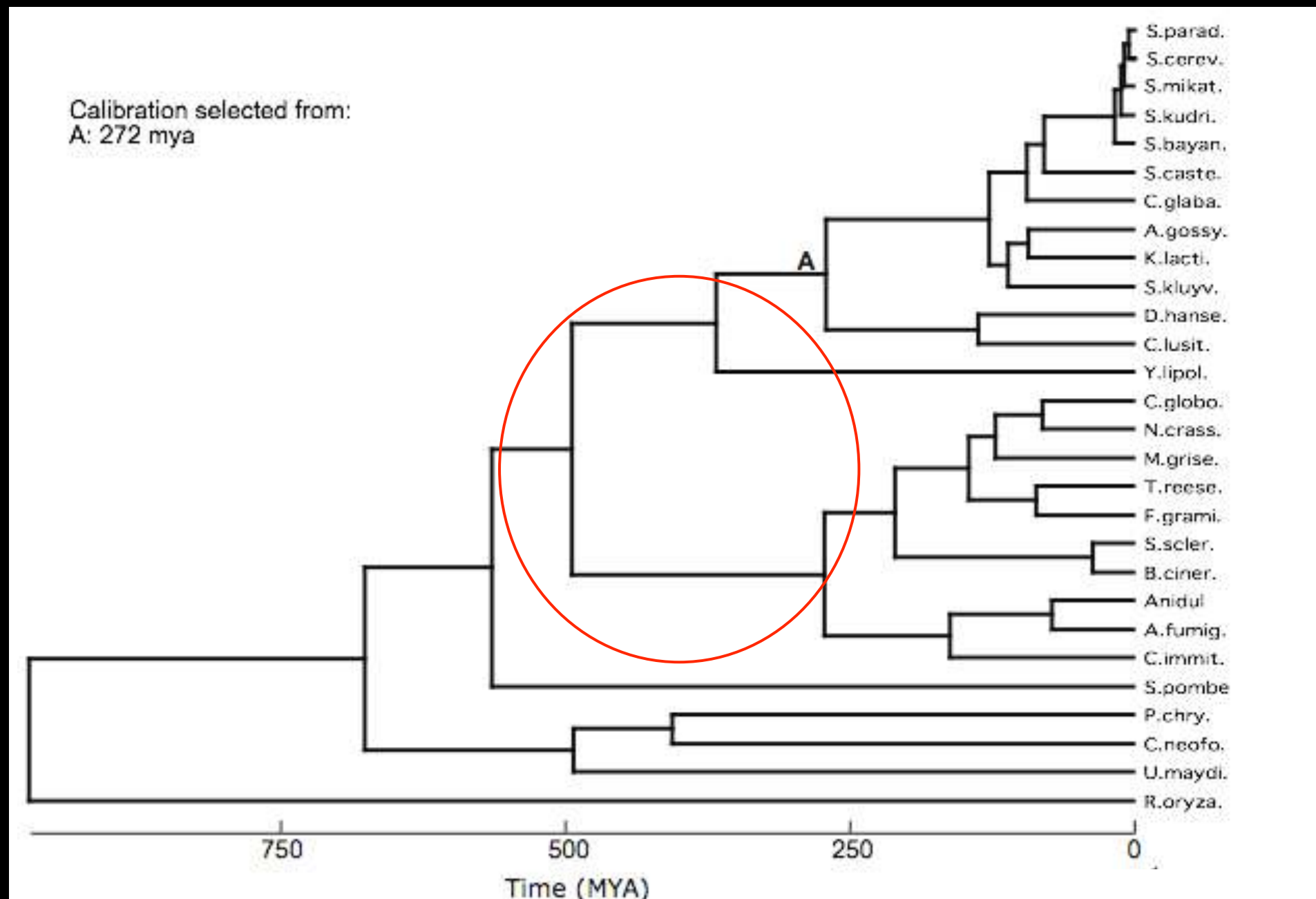


Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

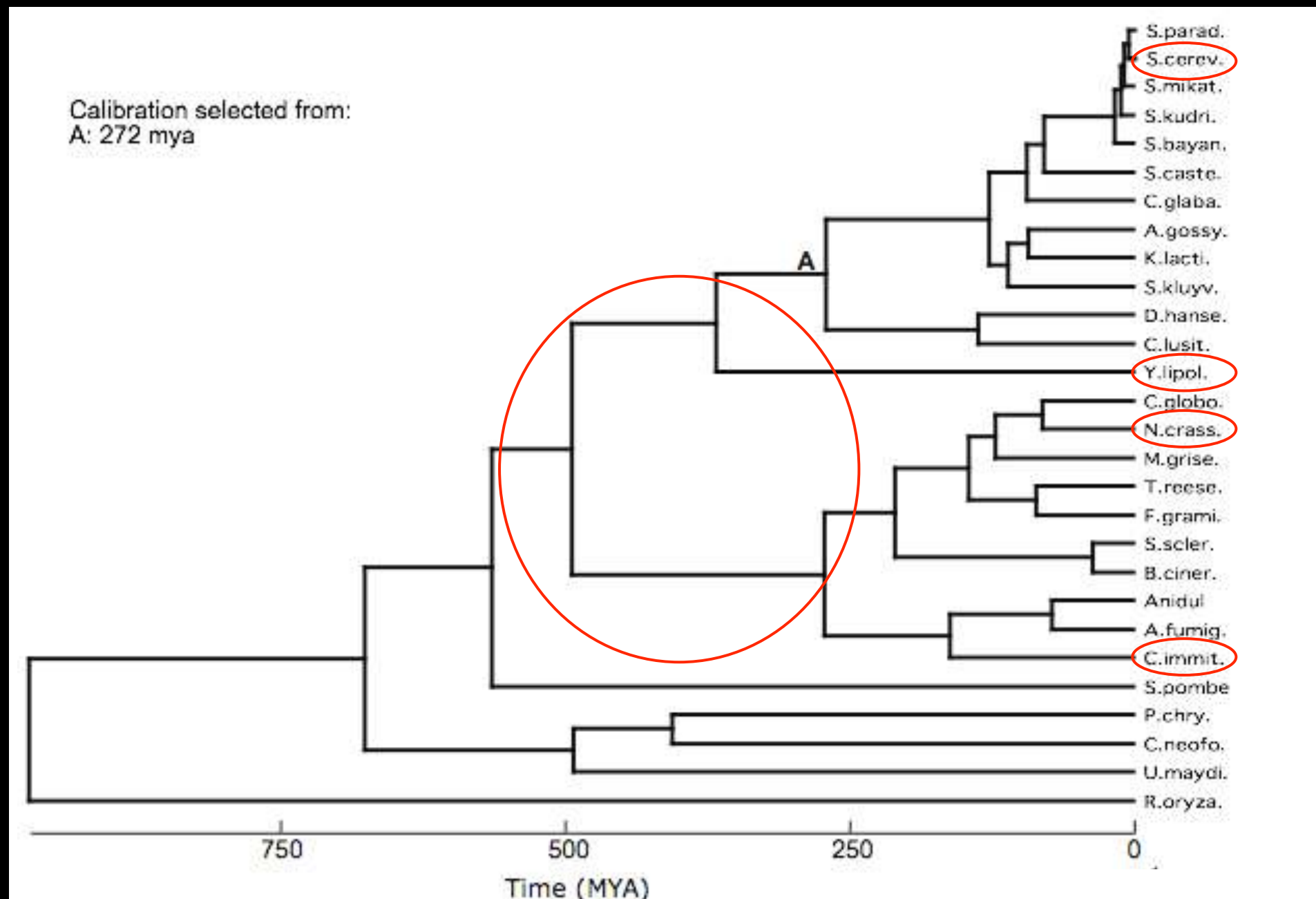
Does the other ingroup clade show the same patterns?



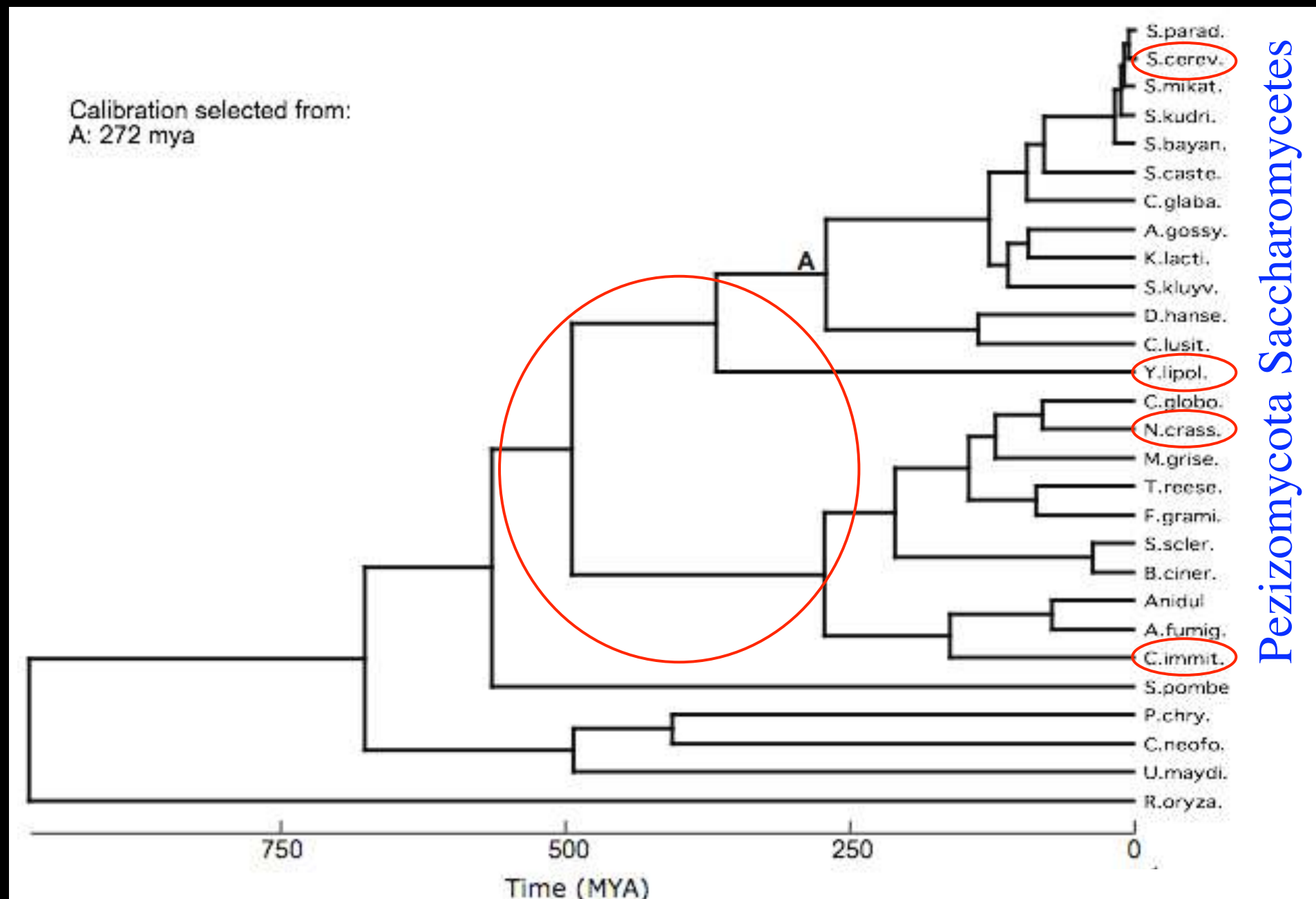
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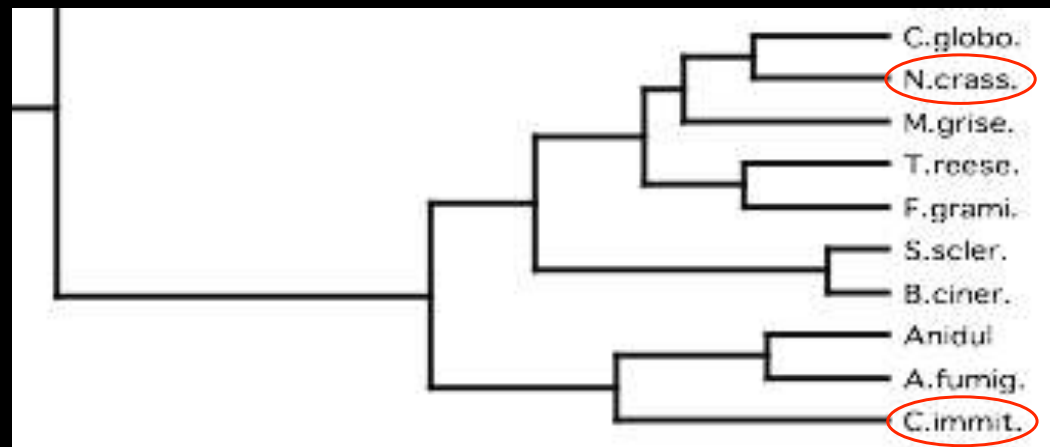
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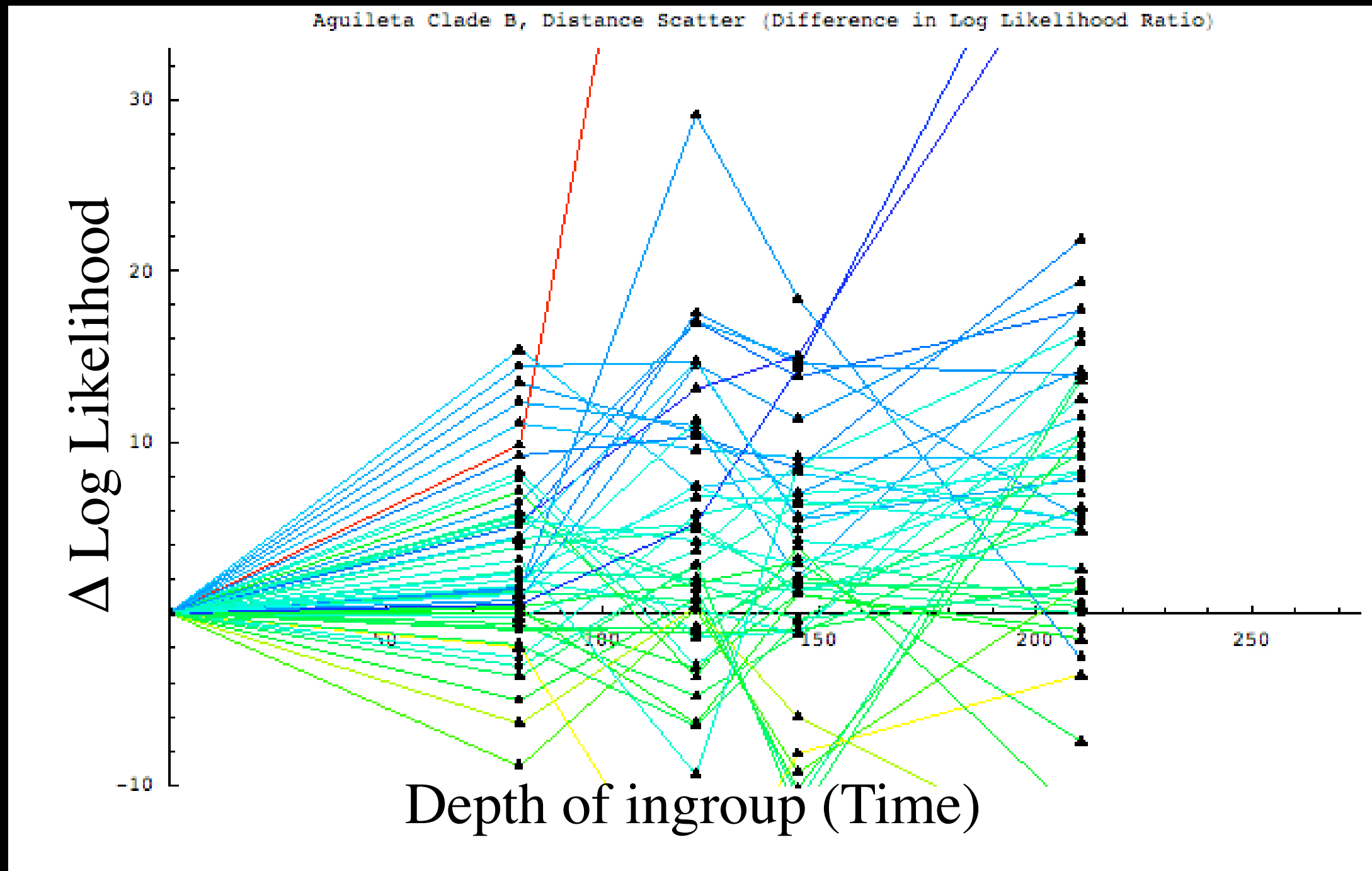


The Pezizomycetes chronogram features



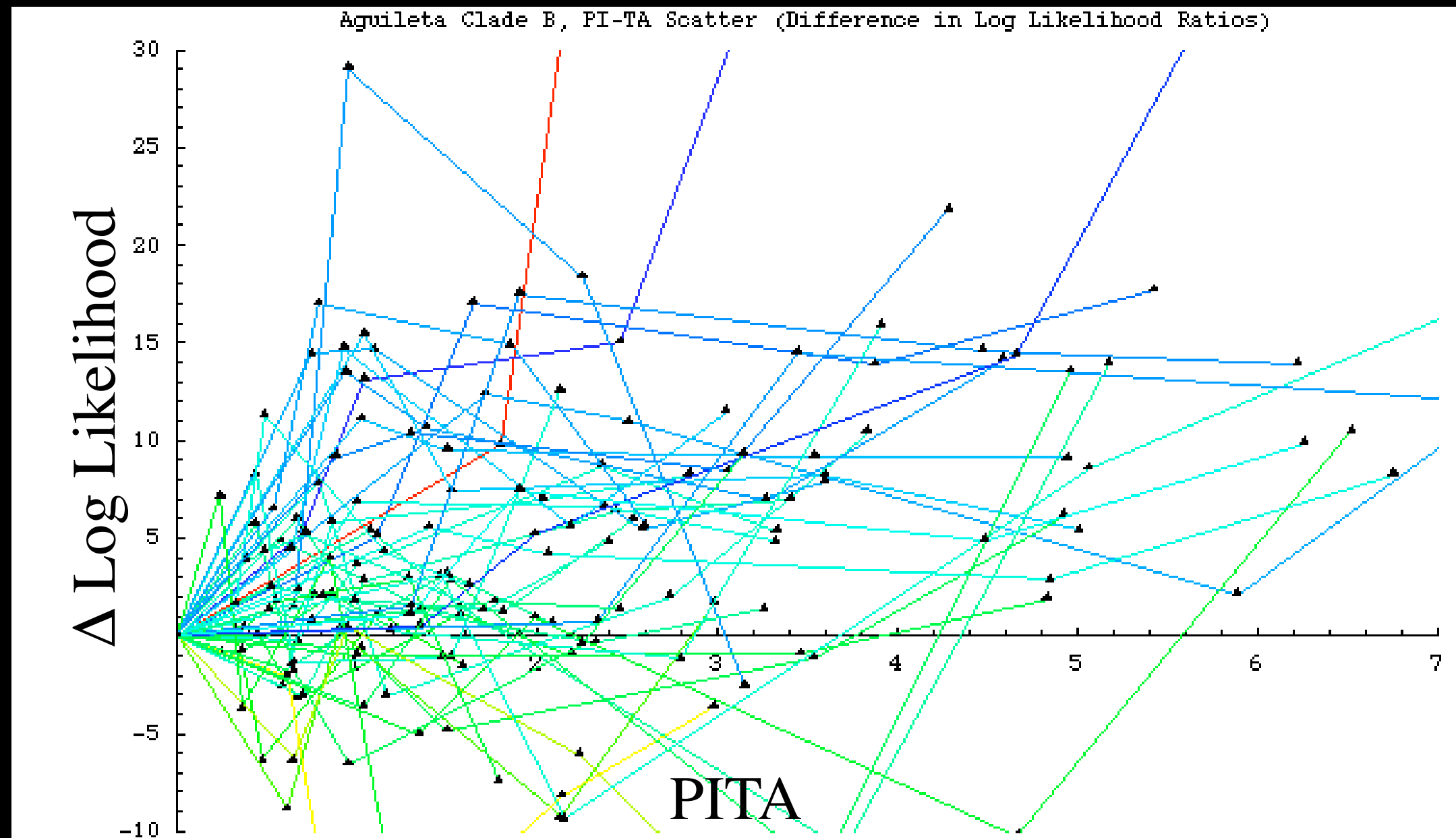
- no lineages closely related to *N. crassa* or *C. immitis*
- a smaller range of depths of ingroup taxa than in the Saccharomycetes

Sampling the deepest ingroups yields the greatest resolution



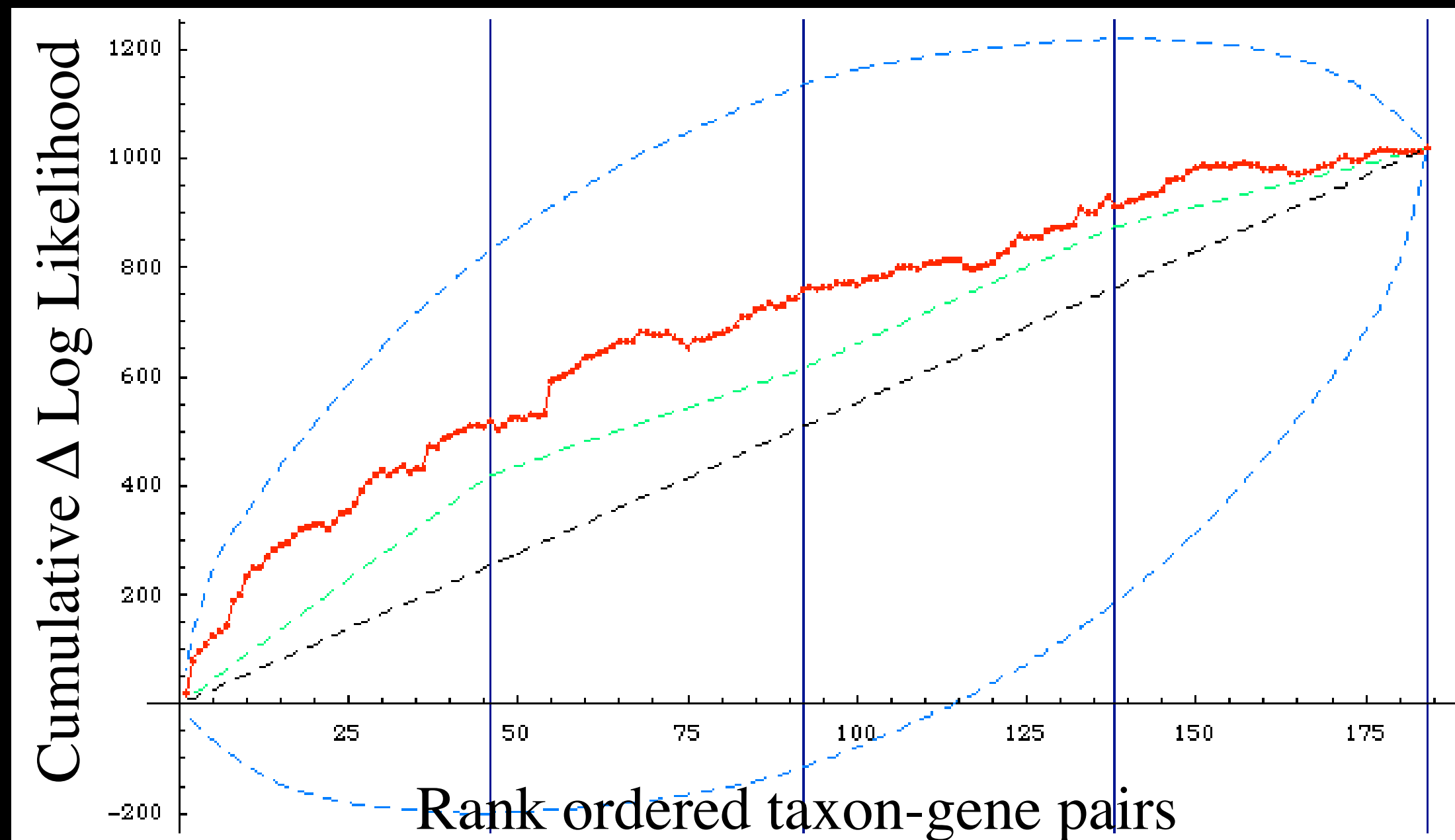
Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

PITA is correlated with support



Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

Pezizomycete clade: PITA performs best



Townsend & Lopez-Giraldez, *Systematic Biology* 59: 446-457

Conclusions

- Large data sets contribute both signal and noise.
- Phylogenetic informativeness profiles can help you prioritize loci - but remember the effect of noise.
- With fast-evolving characters, increase taxa.
- With slow-evolving characters, increase characters.
- The most informative taxa to sample to resolve a node are the deepest ingroups to the node.



Townsend Lab

Web 2.0:
Scientific Social Collaboration

Transcriptomics

Computational and
statistical analysis of
large datasets

Phylogenomics

Fungal Biology and Phylogeny