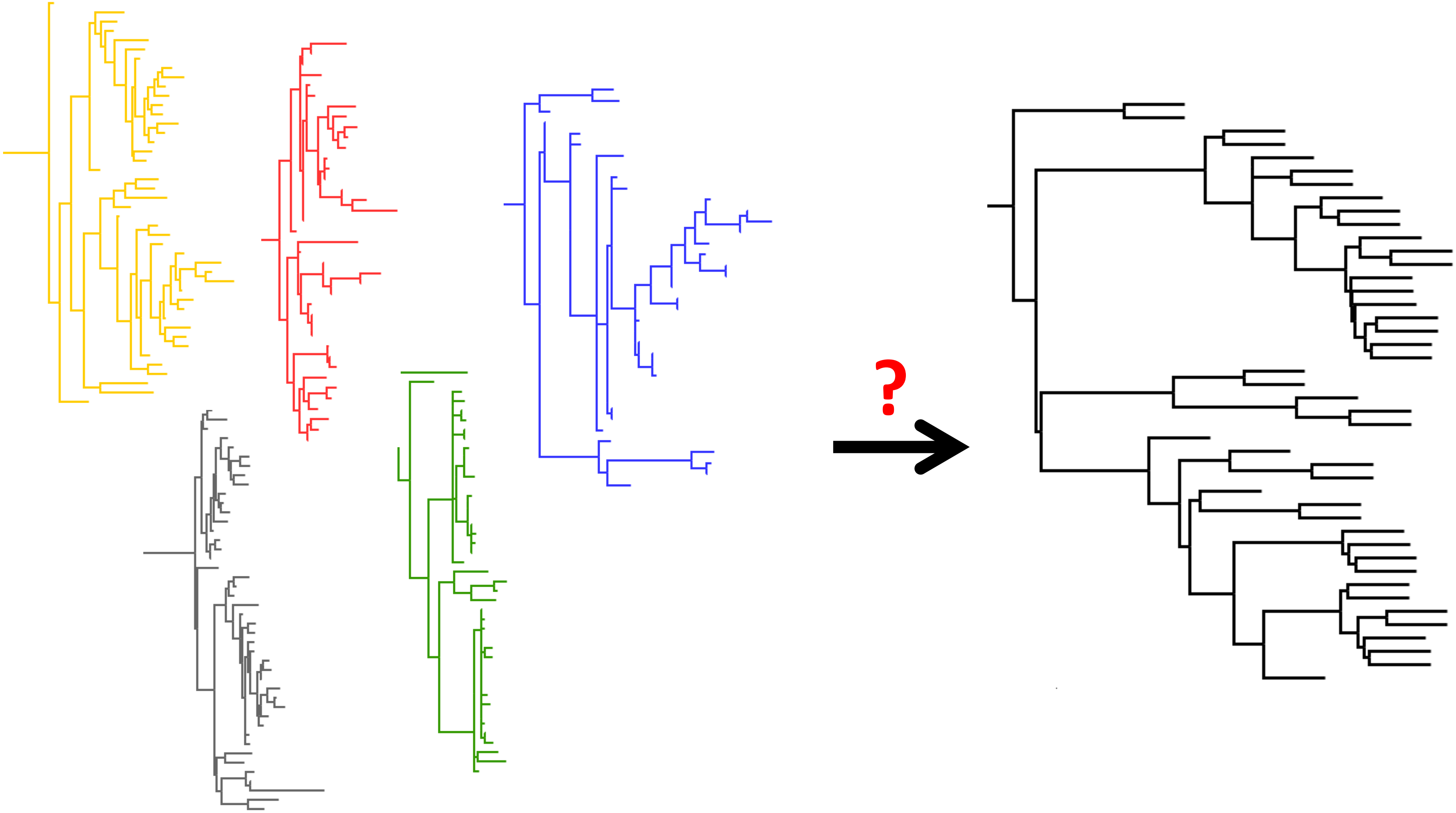
Gene trees vs species tree

Phylogenetic methods

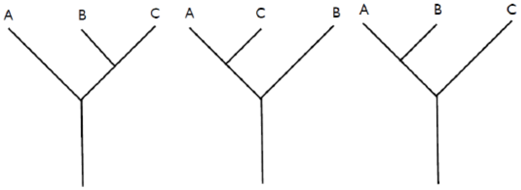
Tomáš Fér

2024

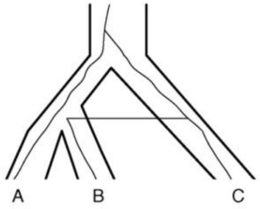
Species tree from gene trees



Incongruencies among loci: gene trees vs species tree

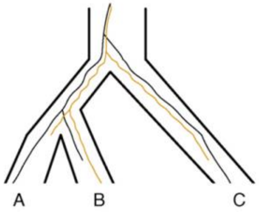


- incomplete lineage sorting (ILS)



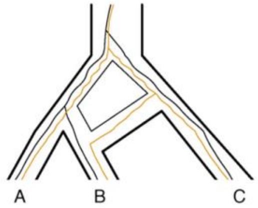
(A(BC))

- horizontal gene transfer (HGT)
  - affects small DNA segments
- gene duplication and loss (GDL)
  - orthology problem



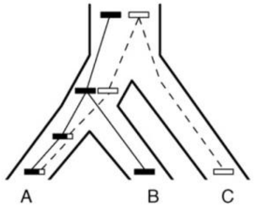
((AC)B)

- hybridization
  - affects whole genomes



((AB)C)
(A(BC))

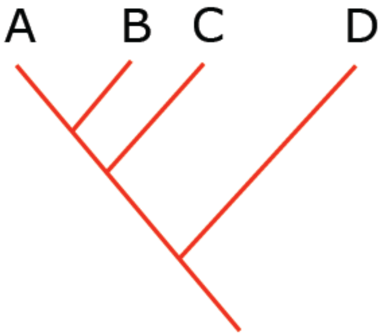
- recombination
  - different histories for neighboring segments in genes



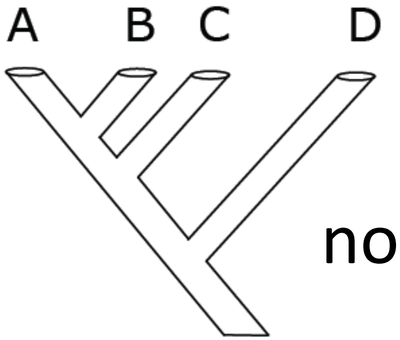
((AB)C)
((AC)B)

Degnan & Rosenberg, 2009

Gene duplications and losses

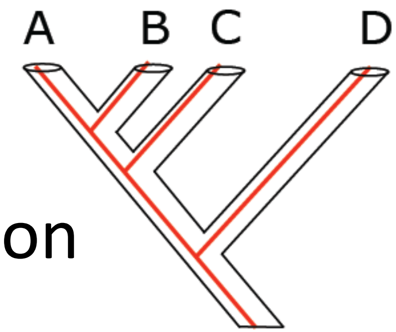


Gene tree

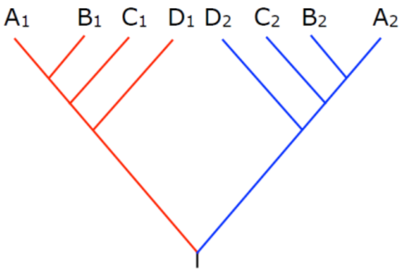


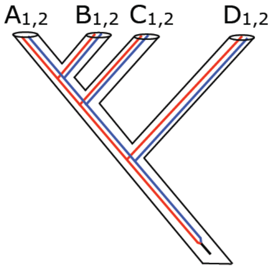
Species tree

no gene duplication

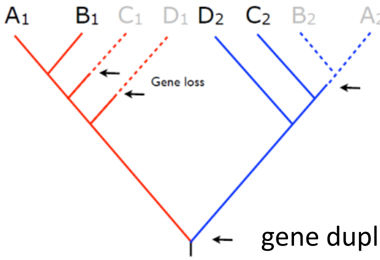


Gene tree = Species tree





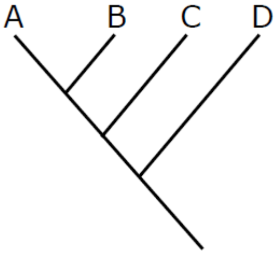
gene duplications and losses (GDL)

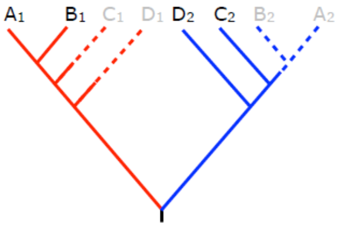


gene loss

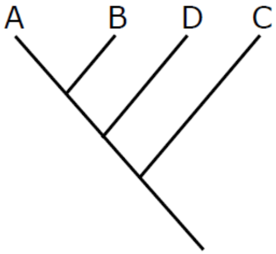
gene duplication

true species tree





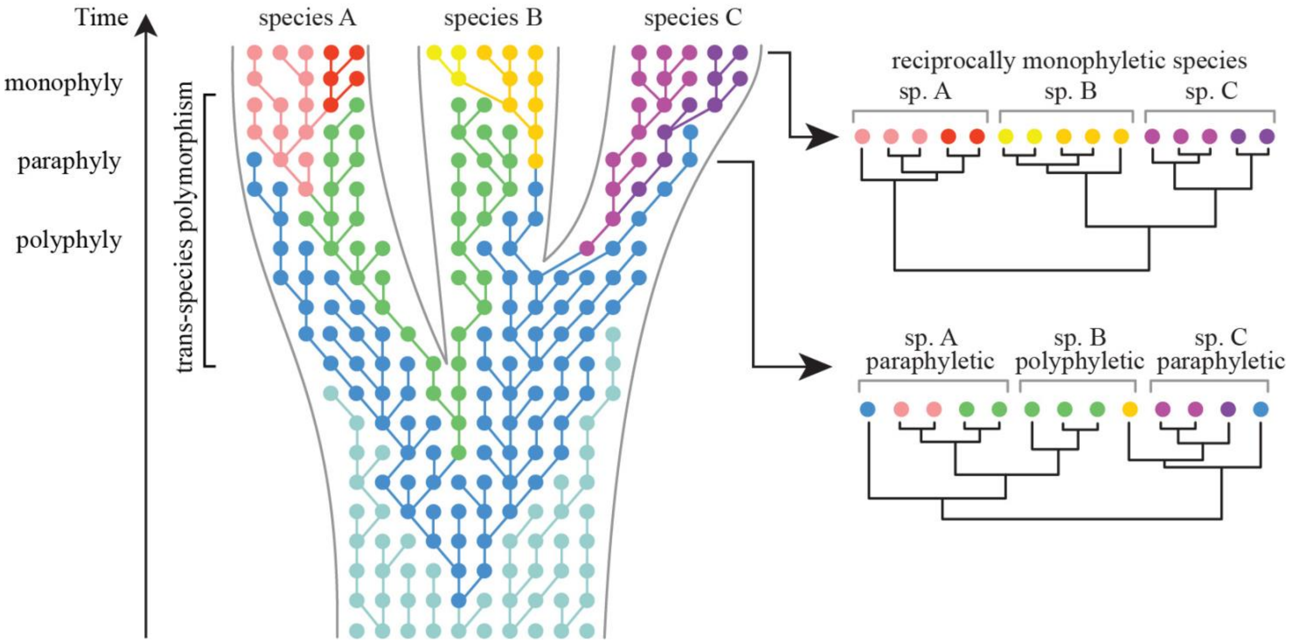
inferred species tree



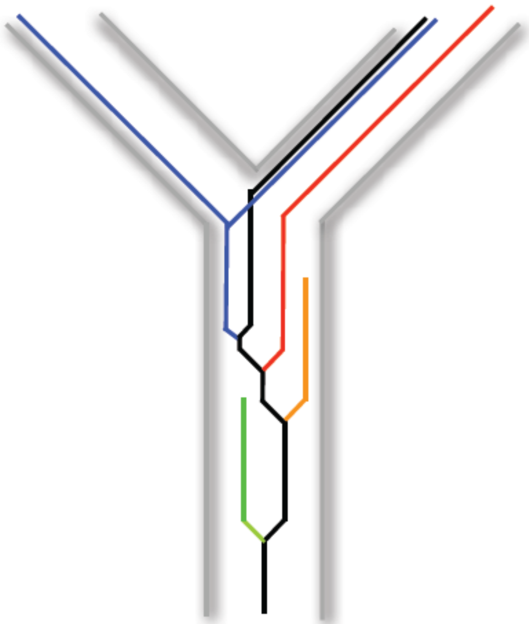
M. Popp, Oslo

Incomplete lineage sorting

Coalescence processes

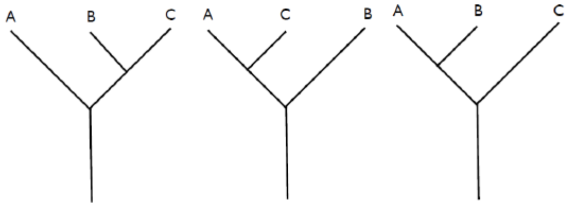


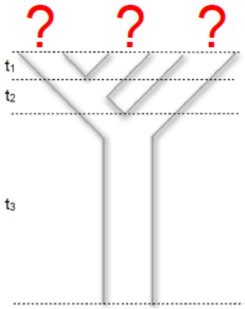
https://frederikleliaert.wordpress.com/green-algae/dna-based-species-delimitation-in-algae/



M. Popp, Oslo

Species tree estimation





- **concatenation**

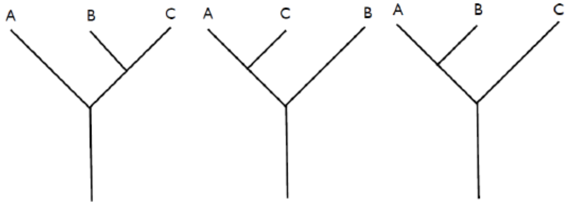
- multispecies coalescence
  - *BEAST (**coestimation** of gene trees and species tree)
  - **summary** methods (combining gene trees)

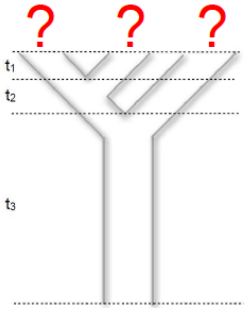
- **supertree** methods
  - MRL (maximum representation using likelihood)

- Bayesian **concordance** analysis (BUCKy)
  - quartet-based Bayesian species tree estimation

- **site-based** methods
  - SNAPP, SVDquartets

Species tree estimation





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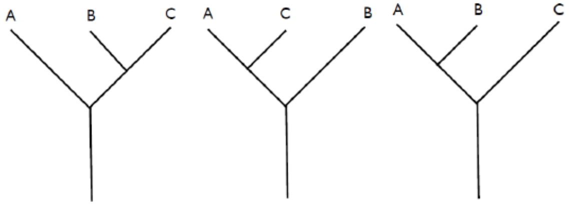
Concatenation

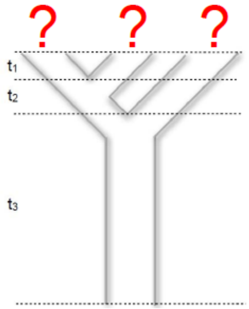
- put all the loci after each other (superalignment, supermatrix)
- very good accuracy under low ILS model conditions
- i.e., good approach unless strong ILS

- **single** partition model
  - the whole alignment analyzed with the same parameters
  - statistically inconsistent

- **multiple** partitions model (ML or Bayesian)
  - each alignment (or even codon position) analyzed with separate parameters
  - best partitioning scheme by, e.g., PartitionFinder or ModeltestNG or IQtree
  - fully partitioned analysis
  - maximum likelihood (CA-ML) – RAxML-ng, ExaML
  - or Bayesian inference – MrBayes, ExaBayes

Species tree estimation





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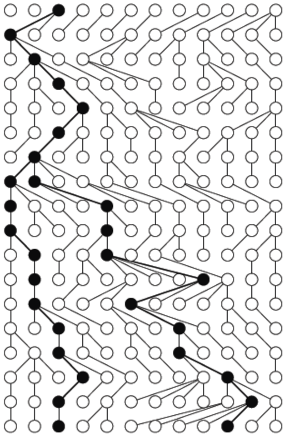
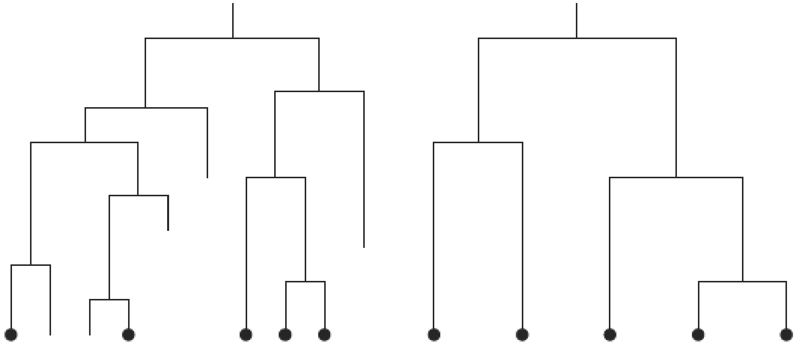
Multispecies coalescent

- coalescent model applied to gene trees in a species tree
  - combines coalescent and birth-death models

coalescence



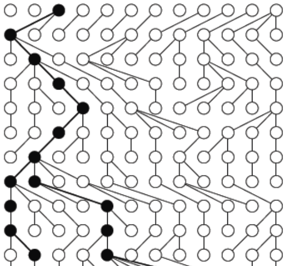
birth-death model



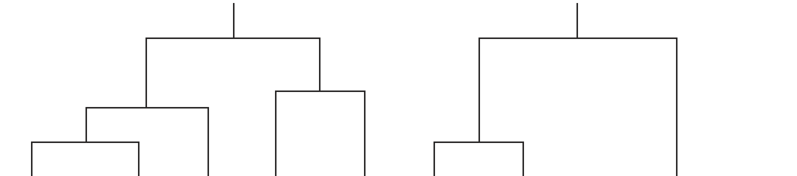
Multispecies coalescent

- used to assemble separate coalescent processes occurring in populations connected by an evolutionary tree
  - coalescent tree distribution (probability of sharing common ancestor t generations back)
  - birth-death model with stochastic rate of birth and death
  - describes probability of gene tree(s) within a species tree

coalescence

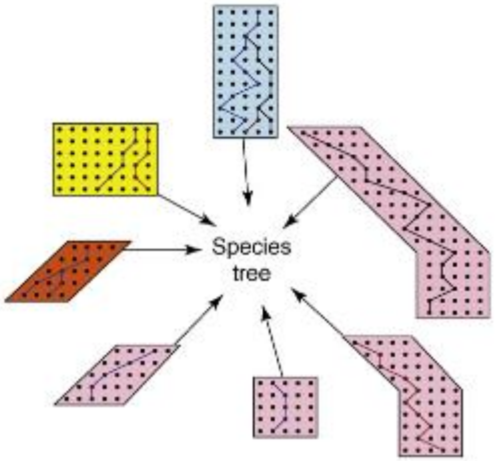


birth-death model



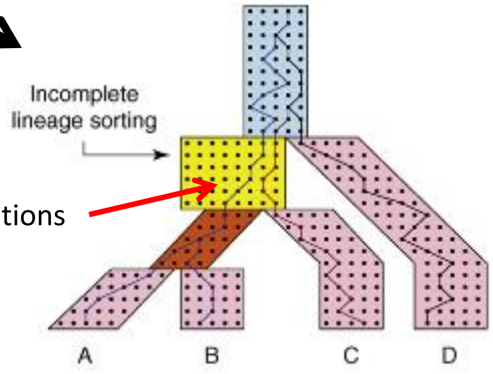
Multispecies coalescent

dot	individual gene copy
row	generation
lines	connection to gene ancestors in previous generations

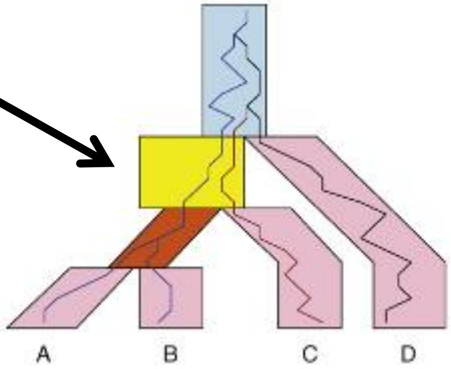


the coalescent in several populations
pink pops – only one lineage (gene copy)

populations arranged by evolutionary relationships



fail to coalesce within populations

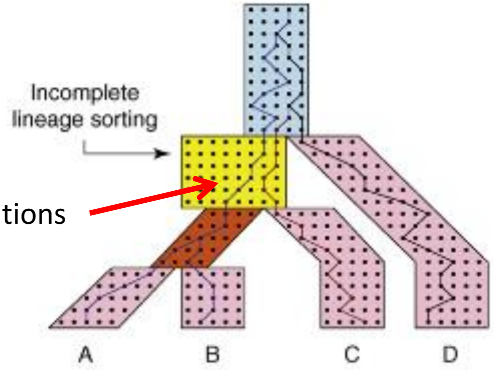


gene tree ((AB)(CD)) in a species tree ((AB)C)D)

Degnan & Rosenberg, 2009

Multispecies coalescent

- (incomplete) lineage sorting
  - particular types of genealogical pattern
  - process explaining gene tree discordance
  - failure of lineages in a population to coalesce



fail to coalesce within populations

*BEAST

STAR-BEAST = **S**pecies **T**ree **A**ncestral **R**econstruction

- Bayesian framework for species tree reconstruction
- assumptions
  - no recombination within locus
  - free recombination between loci
  - no hybridization
  - each sample mapped to appropriate species

prior distribution

likelihood

posterior distribution

$$f(\theta|D) = \frac{\Pr(D|\theta)f(\theta)}{\Pr(D)}$$

marginal likelihood

original Bayesian theorem

gene tree likelihood

probability of the species tree S given the data (D)

prior on species tree

multispecies coalescent likelihood (prior on gene tree given species tree)

$$f(\mathrm{g}, S|D) = \frac{f(S)}{\Pr(D)} \prod_{i=1}^{m} \Pr(D_i|g_i) f(g_i|S).$$

gene tree

marginal likelihood

Drummond & Bouckaert, 2015

*BEAST

STAR-BEAST = **S**pecies **T**ree **A**ncestral **R**econstruction

- co-estimates gene trees and species tree
- most accurate species tree method
- computationally intensive

- not suitable for large datasets, i.e.
  - no more than ~50 loci
  - no more than ~20-30 species

- BBCA – divide-and-conquer technique (Zimmerman et al., 2014)

Summary methods

Estimate each gene tree independently -> summarize them

require rooted gene trees

- MP-EST – **m**aximum **p**seudo-likelihood approach for **e**stimating **s**pecies **t**rees
- STAR – **s**pecies **t**ree estimation using **a**verage **r**anks of coalescences

unrooted gene trees

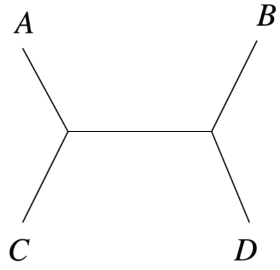
- STEAC – **s**pecies **t**ree **e**stimation using **a**verage **c**oalescence times
- ASTRAL – **A**ccurate **S**pecies **T**ree **R**econstruction **AL**gorithm
- ASTRID – **A**ccurate **S**pecies **TR**ees from **I**nternode **D**istances (reimplementation of NJ_{st} method)

site-based methods (estimate species trees from the distribution on site pattern within unlinked loci)

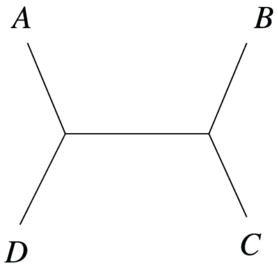
- SNAPP – SNP and AFLP Package for Phylogenetic analysis
- SVDquartets

Tree reconstruction from quartets

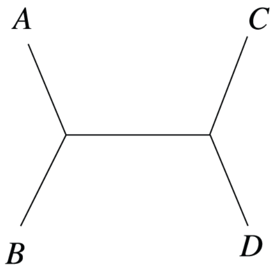
- quartet – unrooted tree over 4 taxa
- three possible quartets
- only one quartet *q* is consistent with final tree **T**



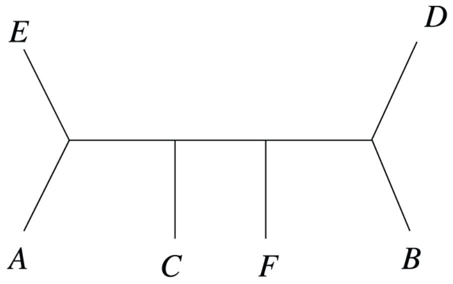
q_1



q_2



q_3



T

Reaz et al. (2015): *Accurate Phylogenetic Tree Reconstruction from Quartets: A Heuristic Approach*. PLoS ONE 9, e104008.

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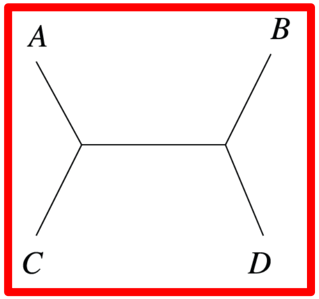
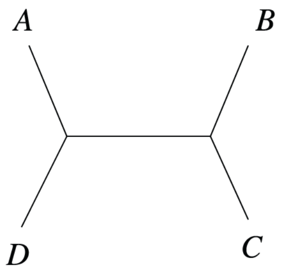
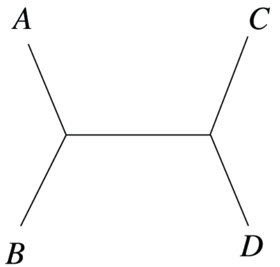


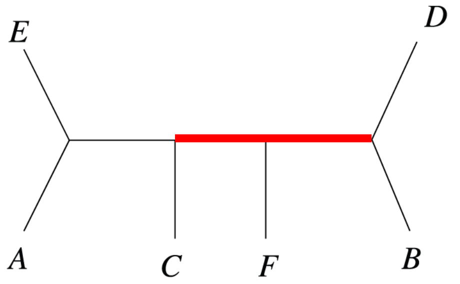
q_1



q_2



q_3



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ASTRAL

Accurate **S**pecies **T**ree **R**econstruction **Al**gorithm
https://github.com/smirarab/ASTRAL

- unrooted gene trees
- species tree that agrees with the largest number of quartet trees induced by the set of gene trees
- weighting all three alternative quartet topologies according to their relative frequencies within gene trees
  - much more frequent topology – trees without this topology are penalized
  - similar frequencies (i.e., close to 0.33) – the quartet has little impact to optimization
- final species tree with
  - local posterior probability that the branch is in the species tree
  - the length of internal branches in coalescent units

Siavash Mirarab

Unrooted quartets under MSC model

- **for a quartet (4 species) –** the most probable unrooted quartet tree (among the gene trees) is the unrooted species tree topology

- **for 5 or more species –** the unrooted species tree topology can be different from the most probable gene tree (called “anomaly zone”)
  - break gene trees into quartets of species
  - find the species tree with the maximum number of induced quartet trees shared with the collection of input gene trees (NP-hard optimization problem)
  - statistically consistent under the multispecies coalescent model with error-free input
  - solved by dynamic programming – ASTRAL

http://tandy.cs.illinois.edu/astral-apro.pdf

ASTRAL input/output

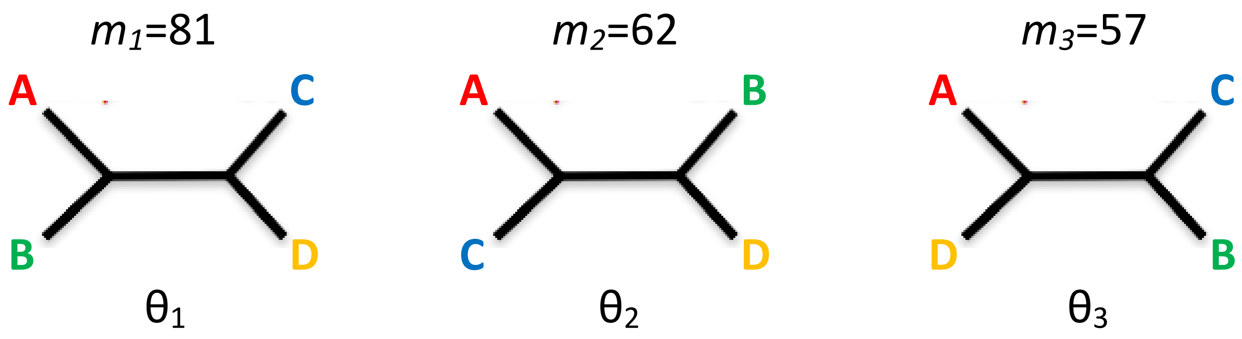
- input – unrooted gene trees
  - missing data allowed
  - polytomies allowed
  - multiple alleles per species allowed

- output – estimated unrooted species tree
  - **branch lengths** in coalescent units (on internal branches)
  - measure **of branch support** (LPP, local posterior probability)

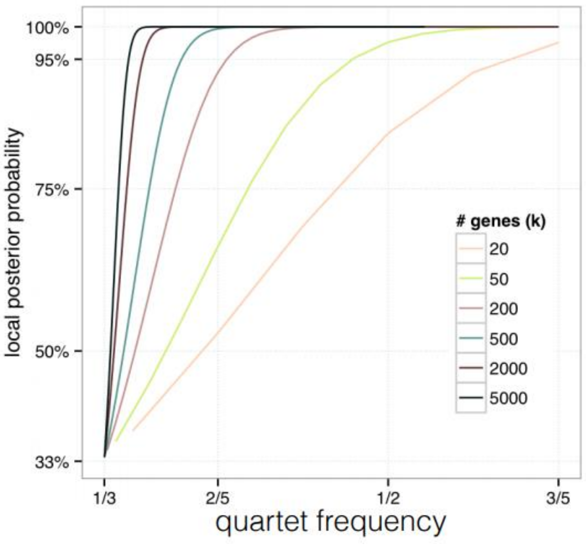
http://tandy.cs.illinois.edu/astral-apro.pdf

Local posterior probability

- quartet frequencies follow a multinomial distribution



- ***P*** (gene tree seen m_1/m times = species tree) = ***P***(θ_1 > 1/3)
  - possible to solve analytically
  - resulting measure is localPP
  - for n>4 – averaging quartet scores
- more accurate and faster than multi-locus bootstrap (MLBS; Seo 2008)

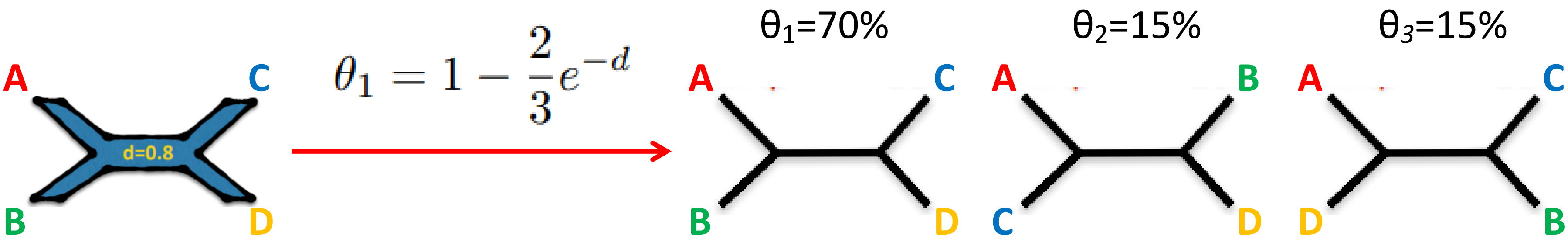


increased number of genes = increased support
decreased discordance = increased support

http://tandy.cs.illinois.edu/astral-apro.pdf

Branch length of ASTRAL trees

- branch length in coalescence units = the level of discordance
- for a single quartet (i.e., *n*=4) – reverse the discordance formula to get multilocus estimate
- for n>4 – average frequencies around the branch



$$\theta_1 = 1 - \frac{2}{3}e^{-d}$$

Sayyari & Mirarab, 2016, MBE

http://tandy.cs.illinois.edu/astral-apro.pdf

ASTRAL problems

- assumption for statistical consistency
  - randomly distributed sample of gene trees
    - recombination-free
    - reticulation-free
    - error-free (i.e., topology correctly estimated)
    - orthologous
- in practice: reduced accuracy with low accuracy gene trees
- branch length
  - only for internal branches (unless multiple individuals per species)
  - in coalescent units, i.e., “true value” is a function of population size and generation time
- local posterior probability (LPP)
  - better than MLBS (empirically) but based on many assumptions

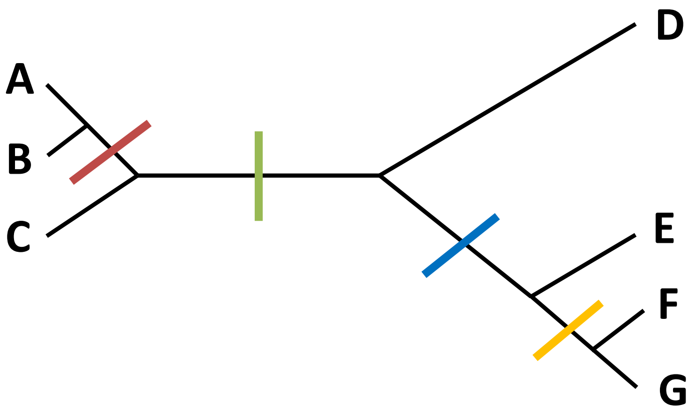
http://tandy.cs.illinois.edu/astral-apro.pdf

MRL

Maximum **R**epresentation with **L**ikelihood; Nguyen et al. 2012

- supertree method – estimates species tree on full taxon sets from sets of smaller trees (i.e., with missing species)
- encodes a set of gene trees by a large randomized matrix
  - using mrp.jar; https://github.com/smirarab/mrpmatrix
- each edge (branch) in each gene tree
  - ‘0’ for the taxa that are on one side of the edge
  - ‘1’ for the taxa on the other side
  - ‘?’ for all the remaining taxa (i.e., the ones that do not appear in the tree)
- MRL matrix is analyzed using heuristics for a symmetric 2-state Maximum Likelihood
  - in RAxML as ‘BINGAMMA’ model

MRL binary matrix



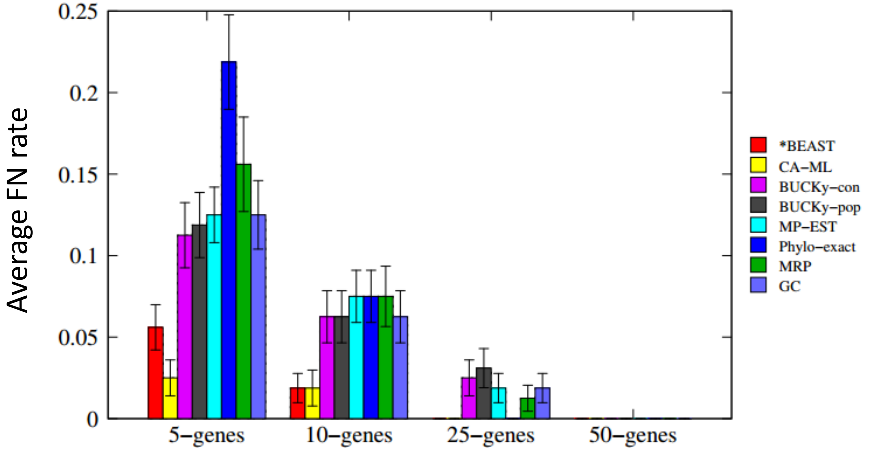
	*	*	*	*	…
A	1	1	1	1	
B	1	1	1	1	
C	0	1	1	1	
D	0	0	1	1	
E	0	0	0	1	
F	0	0	0	0	
G	0	0	0	0	
H	?	?	?	?	

randomization →

	*	*	*	*	…
A	0	1	1	0	
B	0	1	1	0	
C	1	1	1	0	
D	1	0	1	0	
E	1	0	0	0	
F	1	0	0	1	
G	1	0	0	1	
H	?	?	?	?	

Methods comparison

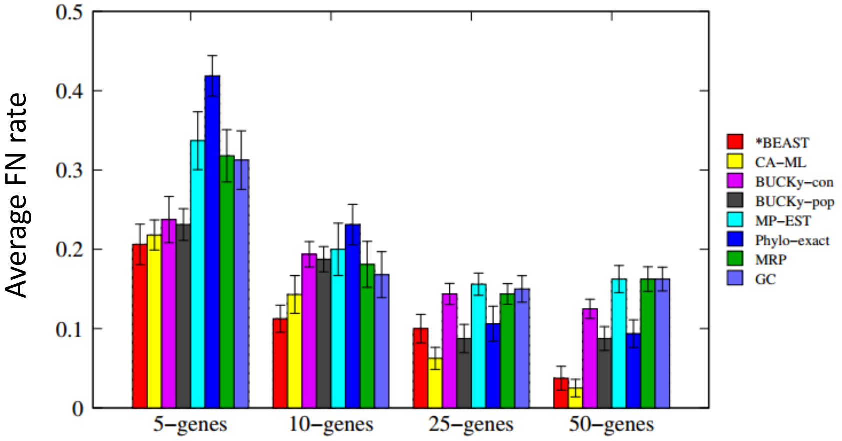
Results on 11-taxon datasets with weak ILS



*BEAST more accurate than summary methods (MP-EST, BUCKy, etc)
CA-ML: concatenated analysis) most accurate

Datasets from Chung and Ané, 2011
Bayzid & Warnow, Bioinformatics 2013

Results on 11-taxon datasets with strongILS



*BEAST more accurate than summary methods (MP-EST, BUCKy, etc)
CA-ML: (concatenated analysis) also very accurate

Datasets from Chung and Ané, 2011
Bayzid & Warnow, Bioinformatics 2013

T. Warnow, The University of Texas
https://www.cs.utexas.edu/users/tandy/394C-nov20-2013.pdf

Quartet Sampling (QS)

Replacement for bootstrap in phylogenomic studies…

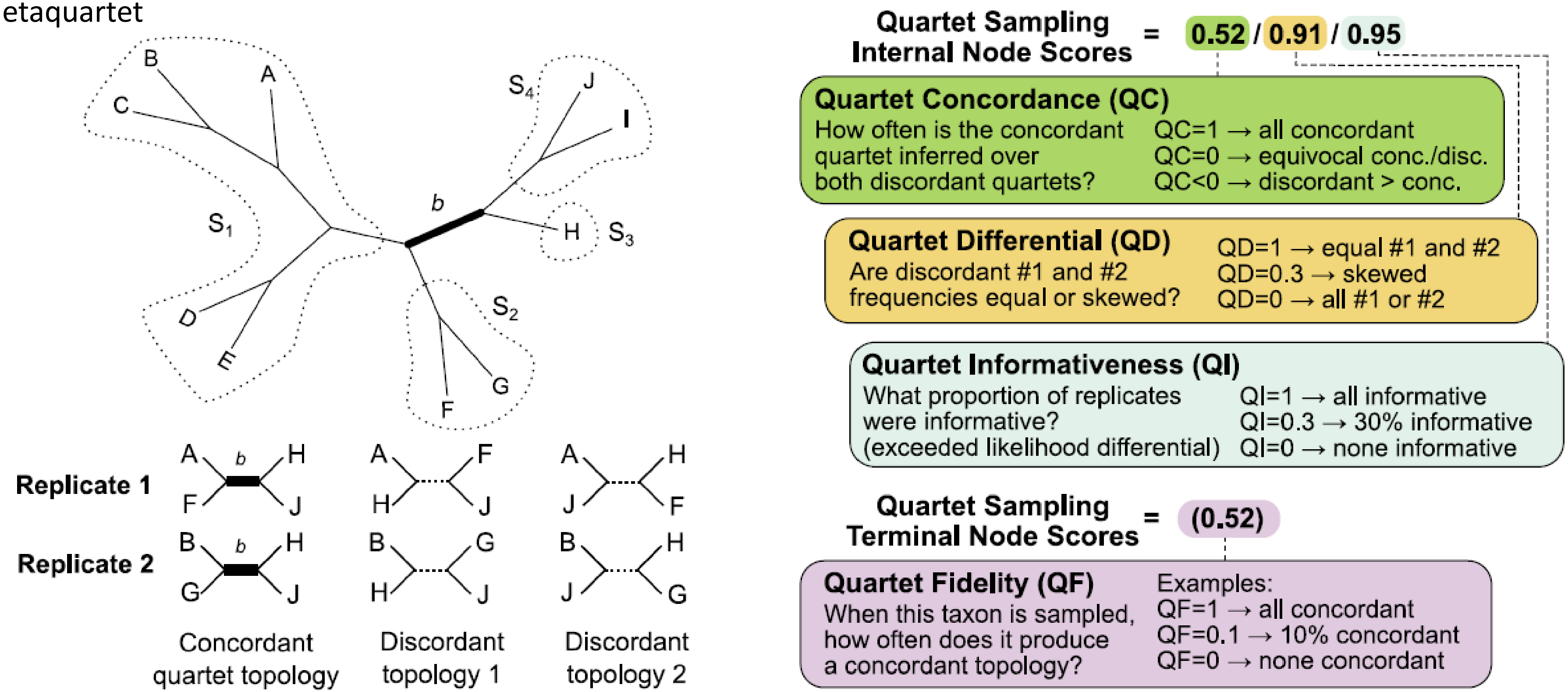
- quartet-based evaluation system
- synthetizes several phylogenetic and genomic analytical approaches
- discordance testing
- distinguishes strong conflict from weak support
- three different scores per branch
  - Quartet Concordance (QC)
  - Quartet Differential (QD)
  - Quartet Informativeness (QI)
- terminal node score
  - Quartet Fidelity (QF)

Pease et al. (2018): Quartet Sampling distinguishes lack of support from conflicting support in the green plant tree of life. *American Journal of Botany* 105(3): 385–403.

Quartet Sampling

- takes an existing phylogenetic topology and a molecular dataset
- evaluates internal branches – likelihood for all three possible phylogenies for the randomly selected quartets spanning particular branch

metaquartet



Quartet Sampling Internal Node Scores = 0.52 / 0.91 / 0.95

Quartet Concordance (QC)
How often is the concordant quartet inferred over both discordant quartets?
QC=1 → all concordant
QC=0 → equivocal conc./disc.
QC<0 → discordant > conc.

Quartet Differential (QD)
Are discordant #1 and #2 frequencies equal or skewed?
QD=1 → equal #1 and #2
QD=0.3 → skewed
QD=0 → all #1 or #2

Quartet Informativeness (QI)
What proportion of replicates were informative? (exceeded likelihood differential)
QI=1 → all informative
QI=0.3 → 30% informative
QI=0 → none informative

Quartet Sampling Terminal Node Scores = (0.52)

Quartet Fidelity (QF)
When this taxon is sampled, how often does it produce a concordant topology?
Examples:
QF=1 → all concordant
QF=0.1 → 10% concordant
QF=0 → none concordant

Pease et al. (2018): Quartet Sampling distinguishes lack of support from conflicting support in the green plant tree of life. *American Journal of Botany* 105(3): 385–403.

Quartet Sampling

Replacement for bootstrap in phylogenomic studies…

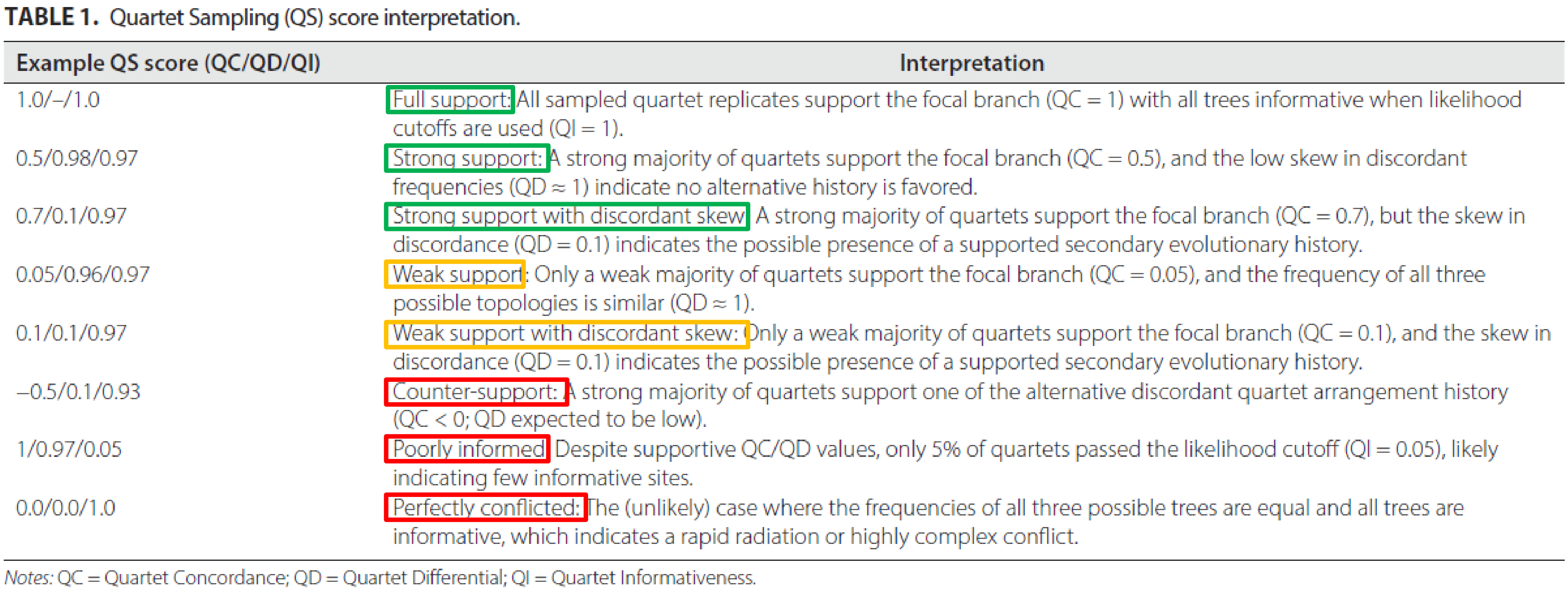


TABLE 1. Quartet Sampling (QS) score interpretation.

Example QS score (QC/QD/QI)	Interpretation
1.0/–/1.0	Full support: All sampled quartet replicates support the focal branch (QC = 1) with all trees informative when likelihood cutoffs are used (QI = 1).
0.5/0.98/0.97	Strong support: A strong majority of quartets support the focal branch (QC = 0.5), and the low skew in discordant frequencies (QD ≈ 1) indicate no alternative history is favored.
0.7/0.1/0.97	Strong support with discordant skew: A strong majority of quartets support the focal branch (QC = 0.7), but the skew in discordance (QD = 0.1) indicates the possible presence of a supported secondary evolutionary history.
0.05/0.96/0.97	Weak support: Only a weak majority of quartets support the focal branch (QC = 0.05), and the frequency of all three possible topologies is similar (QD ≈ 1).
0.1/0.1/0.97	Weak support with discordant skew: Only a weak majority of quartets support the focal branch (QC = 0.1), and the skew in discordance (QD = 0.1) indicates the possible presence of a supported secondary evolutionary history.
–0.5/0.1/0.93	Counter-support: A strong majority of quartets support one of the alternative discordant quartet arrangement history (QC < 0; QD expected to be low).
1/0.97/0.05	Poorly informed: Despite supportive QC/QD values, only 5% of quartets passed the likelihood cutoff (QI = 0.05), likely indicating few informative sites.
0.0/0.0/1.0	Perfectly conflicted: The (unlikely) case where the frequencies of all three possible trees are equal and all trees are informative, which indicates a rapid radiation or highly complex conflict.

Notes: QC = Quartet Concordance; QD = Quartet Differential; QI = Quartet Informativeness.

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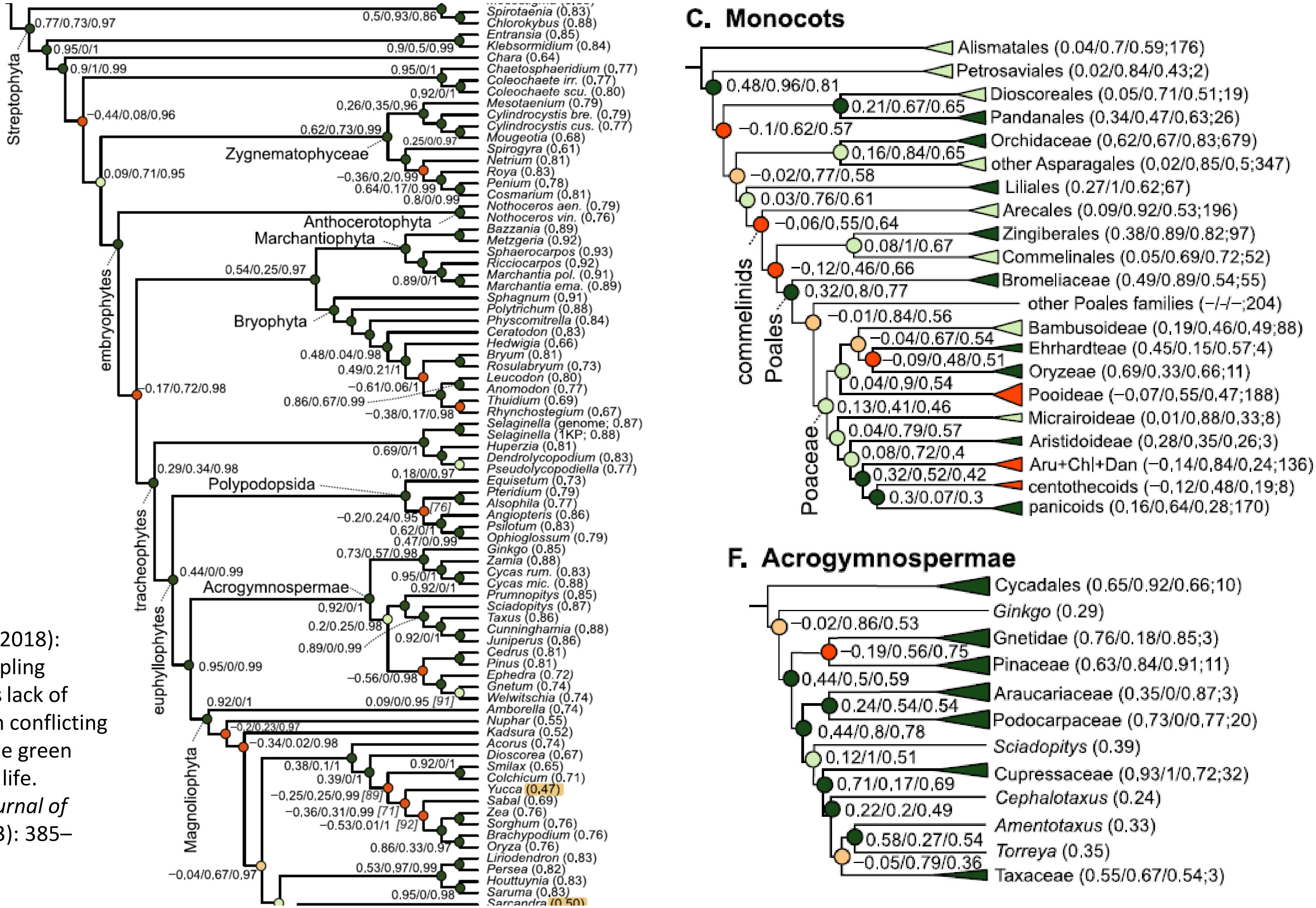
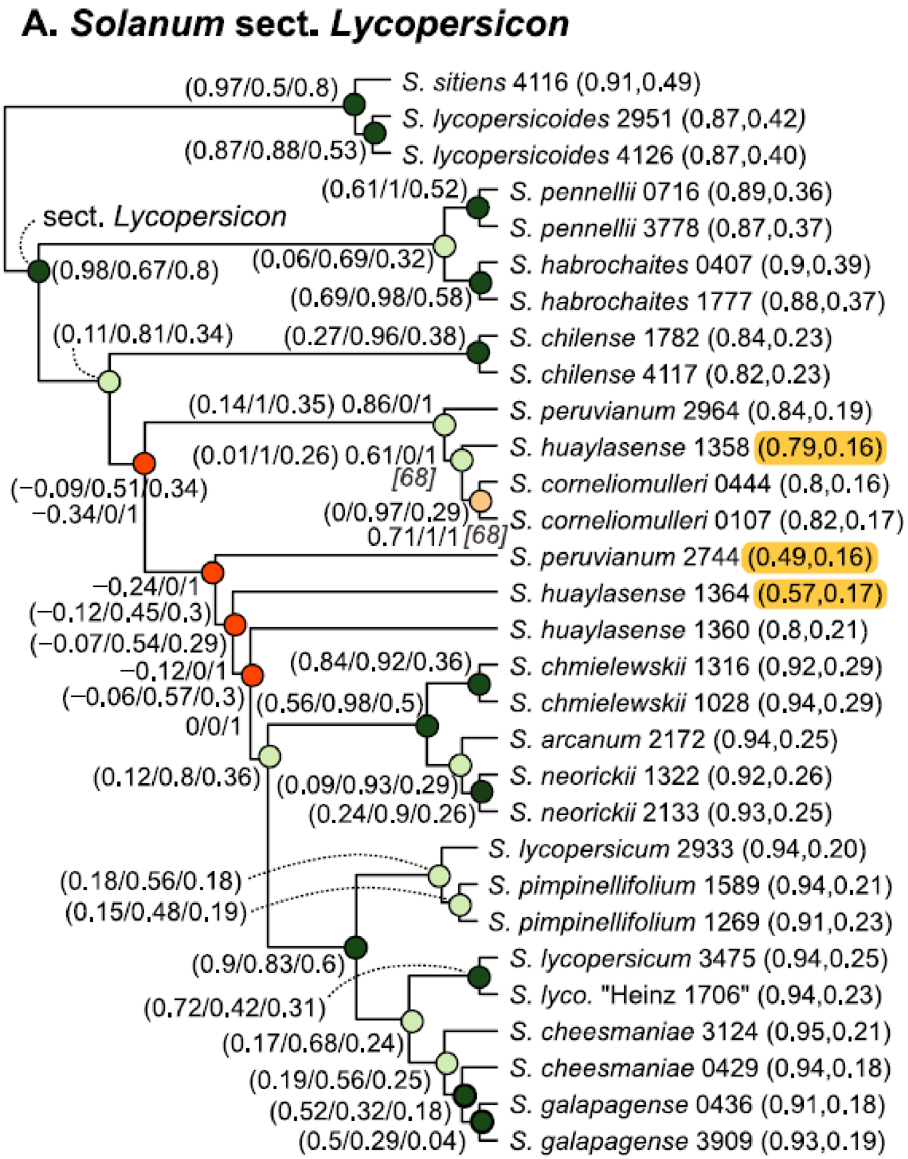
Quartet Sampling – land plants



Pease et al. (2018): Quartet Sampling distinguishes lack of support from conflicting support in the green plant tree of life. *American Journal of Botany* 105(3): 385–403.

Quartet Sampling – generic level


A. Solanum sect. Lycopersicon
(0.97/0.5/0.8)
S. sitiens 4116 (0.91,0.49)
S. lycopersicoides 2951 (0.87,0.42)
(0.87/0.88/0.53)
S. lycopersicoides 4126 (0.87,0.40)
(0.61/1/0.52)
S. pennellii 0716 (0.89,0.36)
sect. Lycopersicon
S. pennellii 3778 (0.87,0.37)
(0.06/0.69/0.32)
(0.98/0.67/0.8)
S. habrochaites 0407 (0.9,0.39)
(0.69/0.98/0.58)
S. habrochaites 1777 (0.88,0.37)
(0.11/0.81/0.34)
(0.27/0.96/0.38)
S. chilense 1782 (0.84,0.23)
S. chilense 4117 (0.82,0.23)
(0.14/1/0.35) 0.86/0/1
S. peruvianum 2964 (0.84,0.19)
(0.01/1/0.26) 0.61/0/1
S. huaylasense 1358 (0.79,0.16)
[68]
(−0.09/0.51/0.34)
−0.34/0/1
S. corneliomulleri 0444 (0.8,0.16)
(0/0.97/0.29)
S. corneliomulleri 0107 (0.82,0.17)
0.71/1/1 [68]
S. peruvianum 2744 (0.49,0.16)
−0.24/0/1
(−0.12/0.45/0.3)
S. huaylasense 1364 (0.57,0.17)
(−0.07/0.54/0.29)
S. huaylasense 1360 (0.8,0.21)
−0.12/0/1
(0.84/0.92/0.36)
S. chmielewskii 1316 (0.92,0.29)
(−0.06/0.57/0.3)
(0.56/0.98/0.5)
S. chmielewskii 1028 (0.94,0.29)
0/0/1
S. arcanum 2172 (0.94,0.25)
(0.12/0.8/0.36)
(0.09/0.93/0.29)
S. neorickii 1322 (0.92,0.26)
(0.24/0.9/0.26)
S. neorickii 2133 (0.93,0.25)
S. lycopersicum 2933 (0.94,0.20)
(0.18/0.56/0.18)
S. pimpinellifolium 1589 (0.94,0.21)
(0.15/0.48/0.19)
S. pimpinellifolium 1269 (0.91,0.23)
S. lycopersicum 3475 (0.94,0.25)
(0.9/0.83/0.6)
S. lyco. "Heinz 1706" (0.94,0.23)
(0.72/0.42/0.31)
S. cheesmaniae 3124 (0.95,0.21)
(0.17/0.68/0.24)
S. cheesmaniae 0429 (0.94,0.18)
(0.19/0.56/0.25)
S. galapagense 0436 (0.91,0.18)
(0.52/0.32/0.18)
(0.5/0.29/0.04)
S. galapagense 3909 (0.93,0.19)

Pease et al. (2016)

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