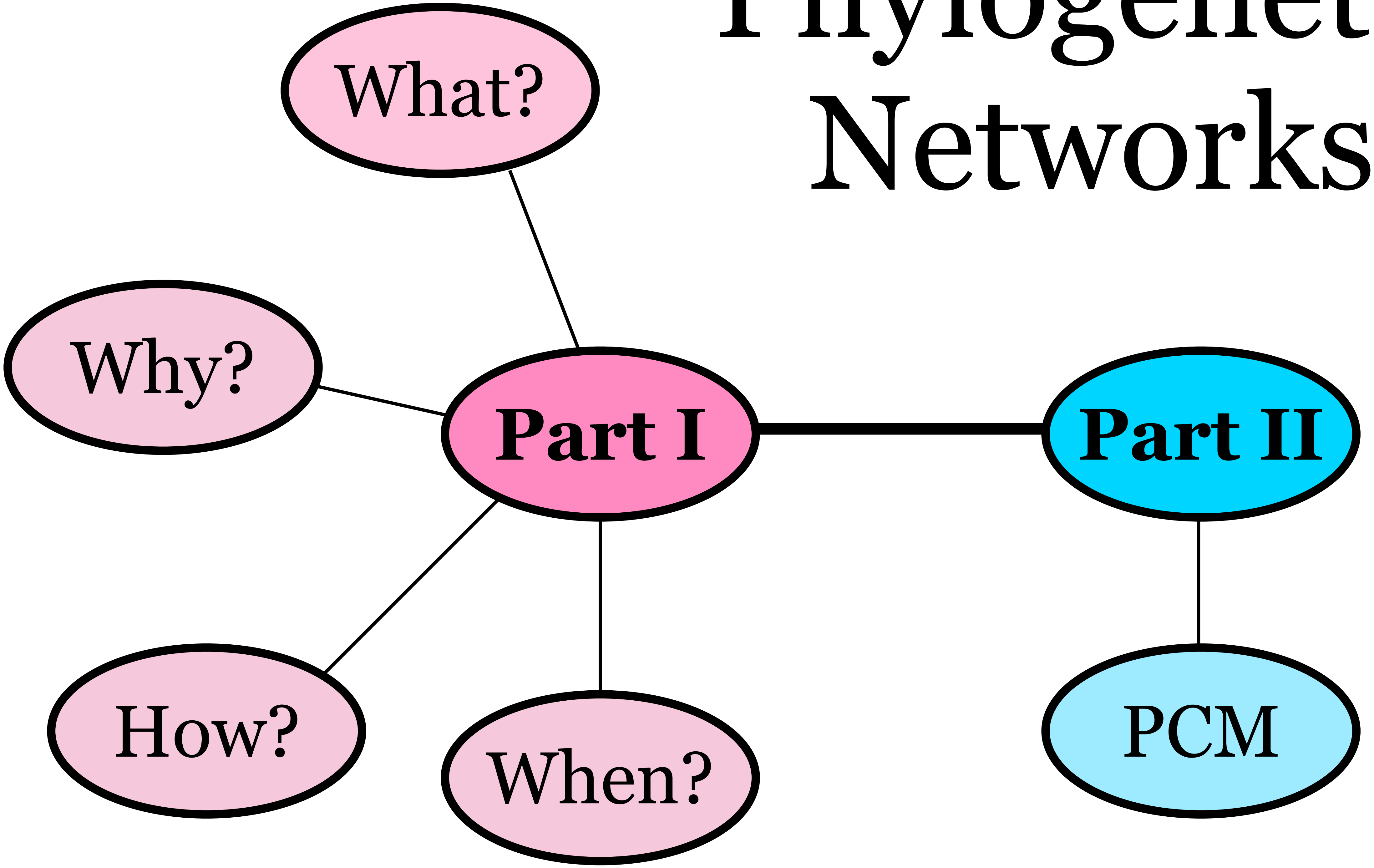
Statistical models on phylogenetic networks

Claudia Solís-Lemus, PhD
University of Wisconsin-Madison
Wisconsin Institute for Discovery
Department of Plant Pathology

June 3, 2022

https://solislemuslab.github.io/ @solislemuslab crsl4 @thestatistician

Phylogenetic Networks



What?

Why?

Part I

Part II

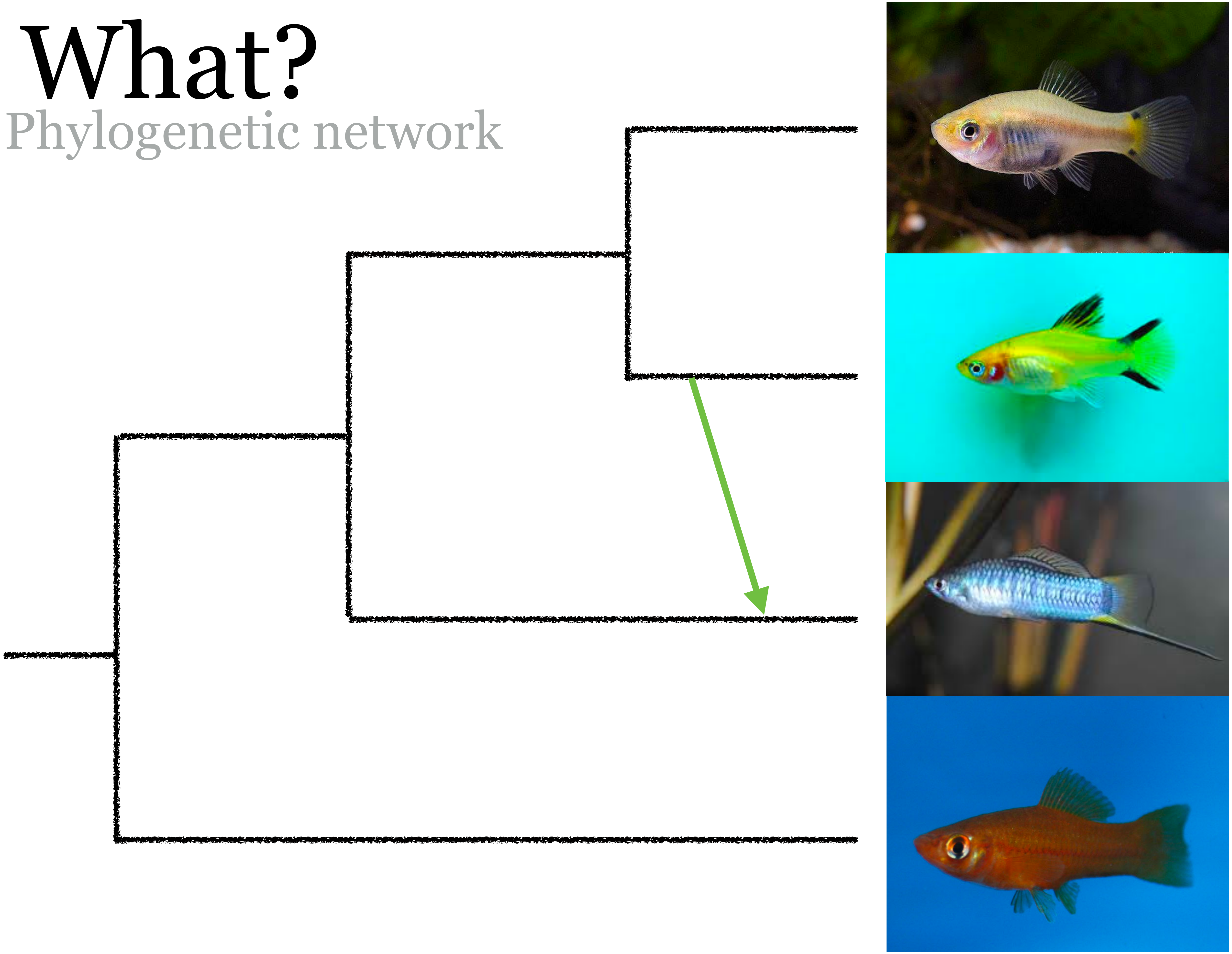
How?

When?

PCM

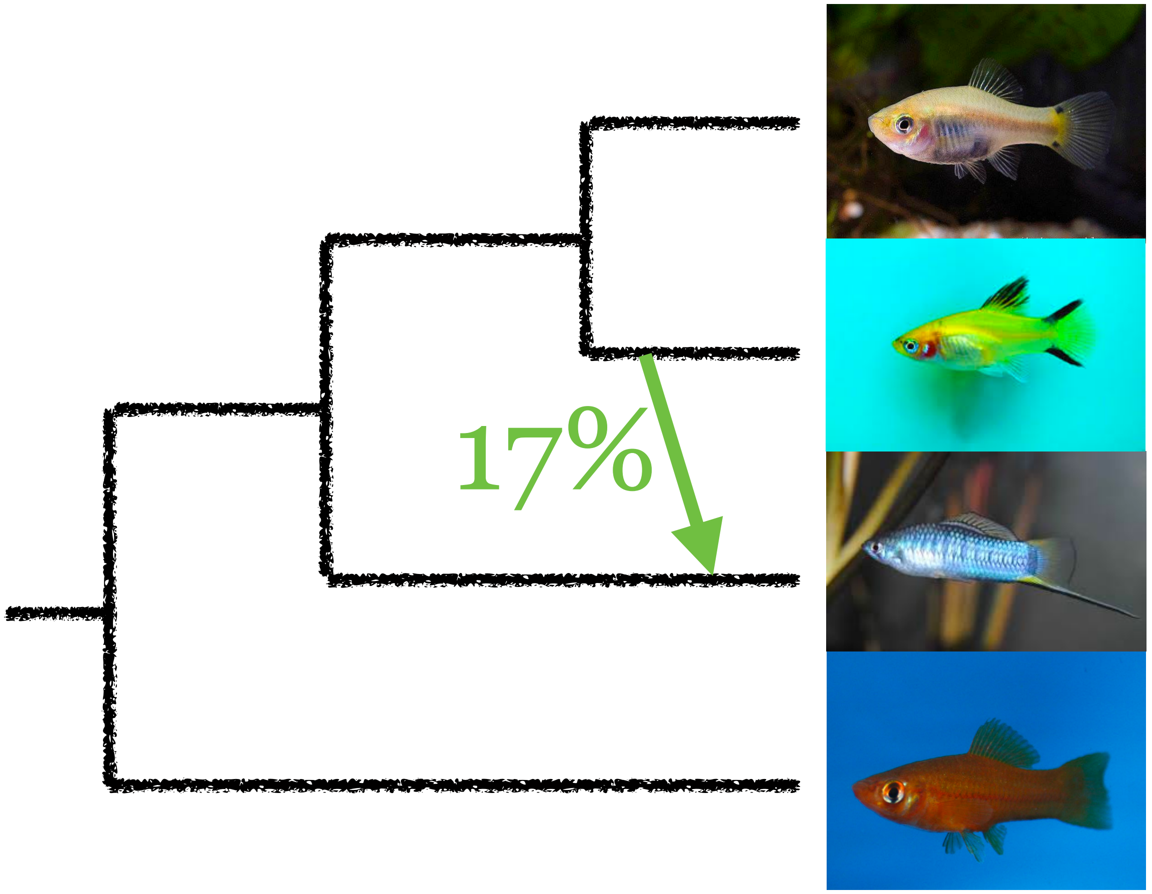
What?

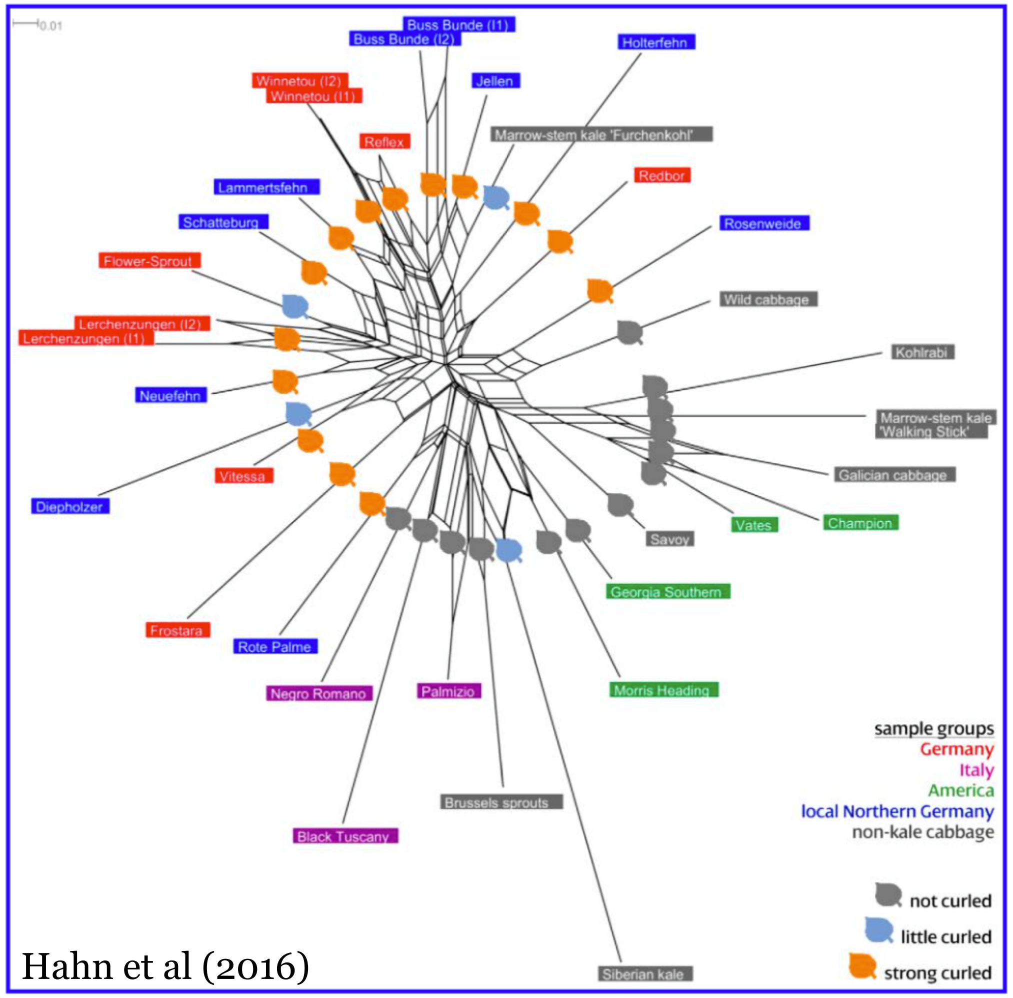
Phylogenetic network



What?

Phylogenetic network





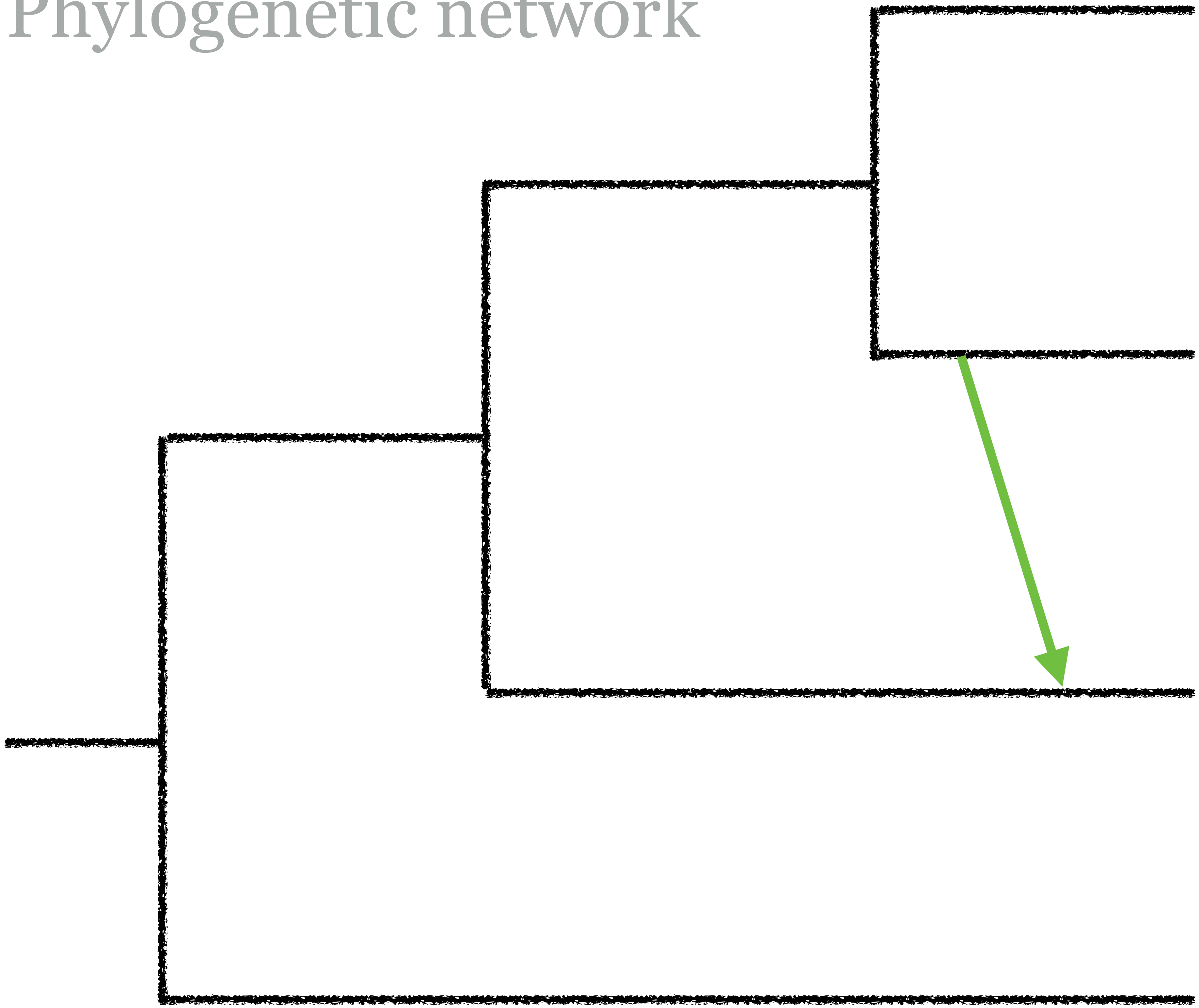
Hahn et al (2016)

Explicit

Implicit

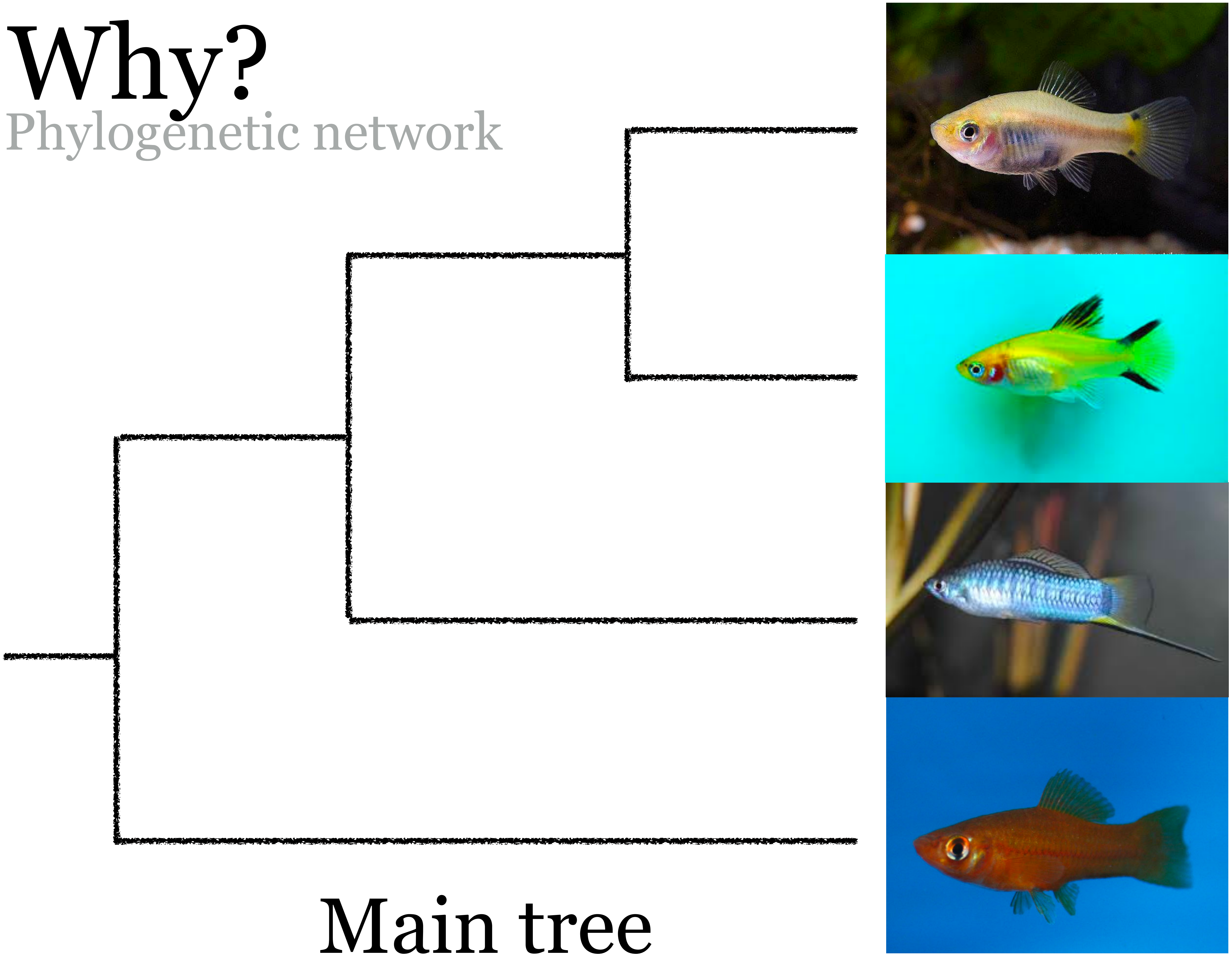
Why?

Phylogenetic network



Why?

Phylogenetic network

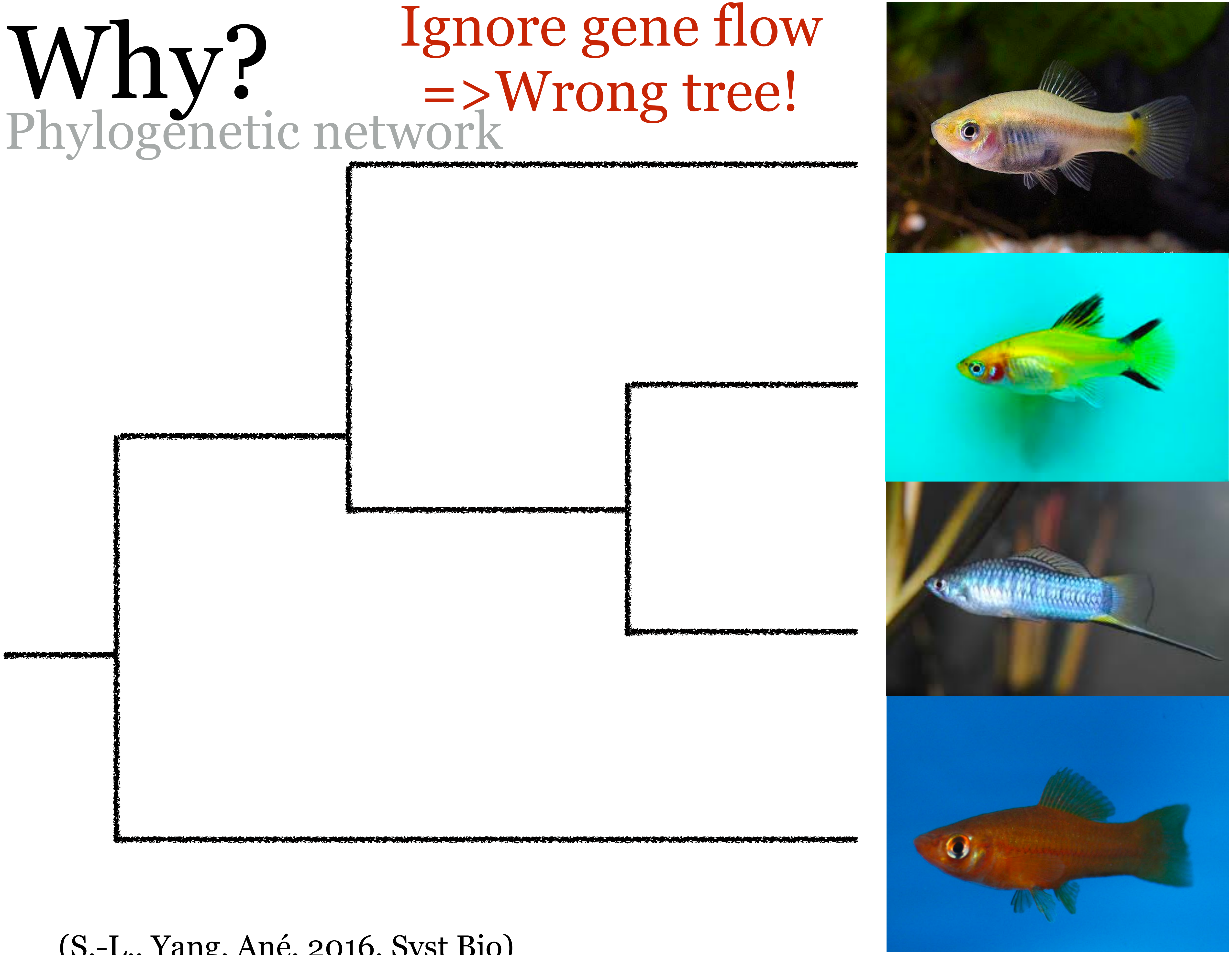


Main tree

Why?

Phylogenetic network

Ignore gene flow
=>Wrong tree!

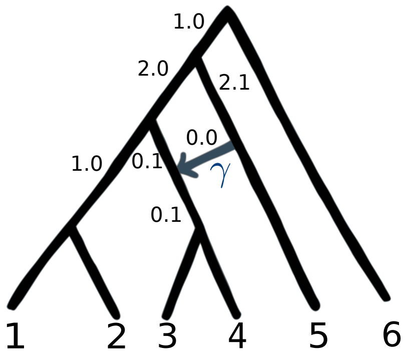


(S.-L., Yang, Ané, 2016, Syst Bio)

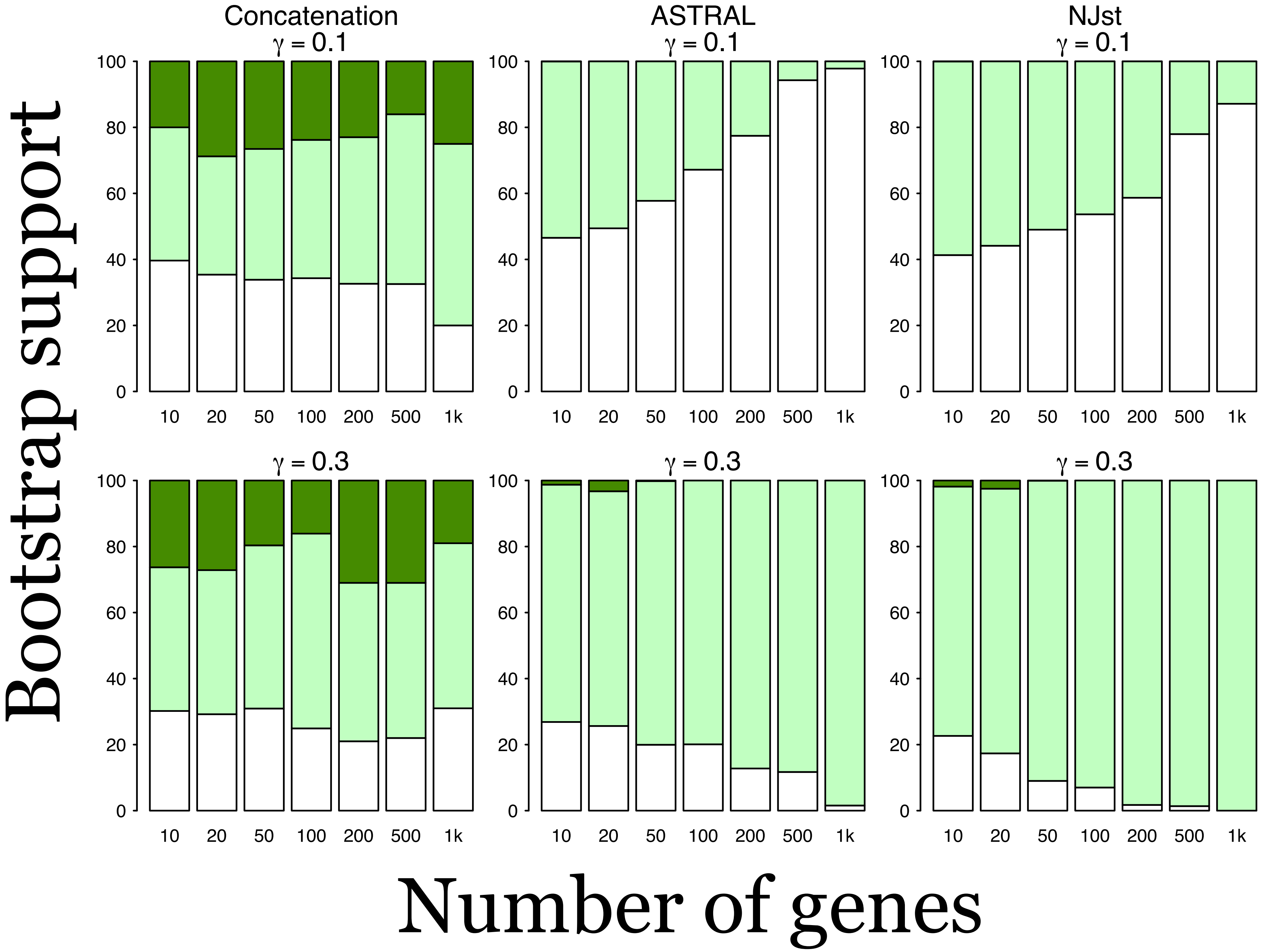
Why?

Phylogenetic network

Coalescent tree methods
not robust to gene flow



White:
true tree



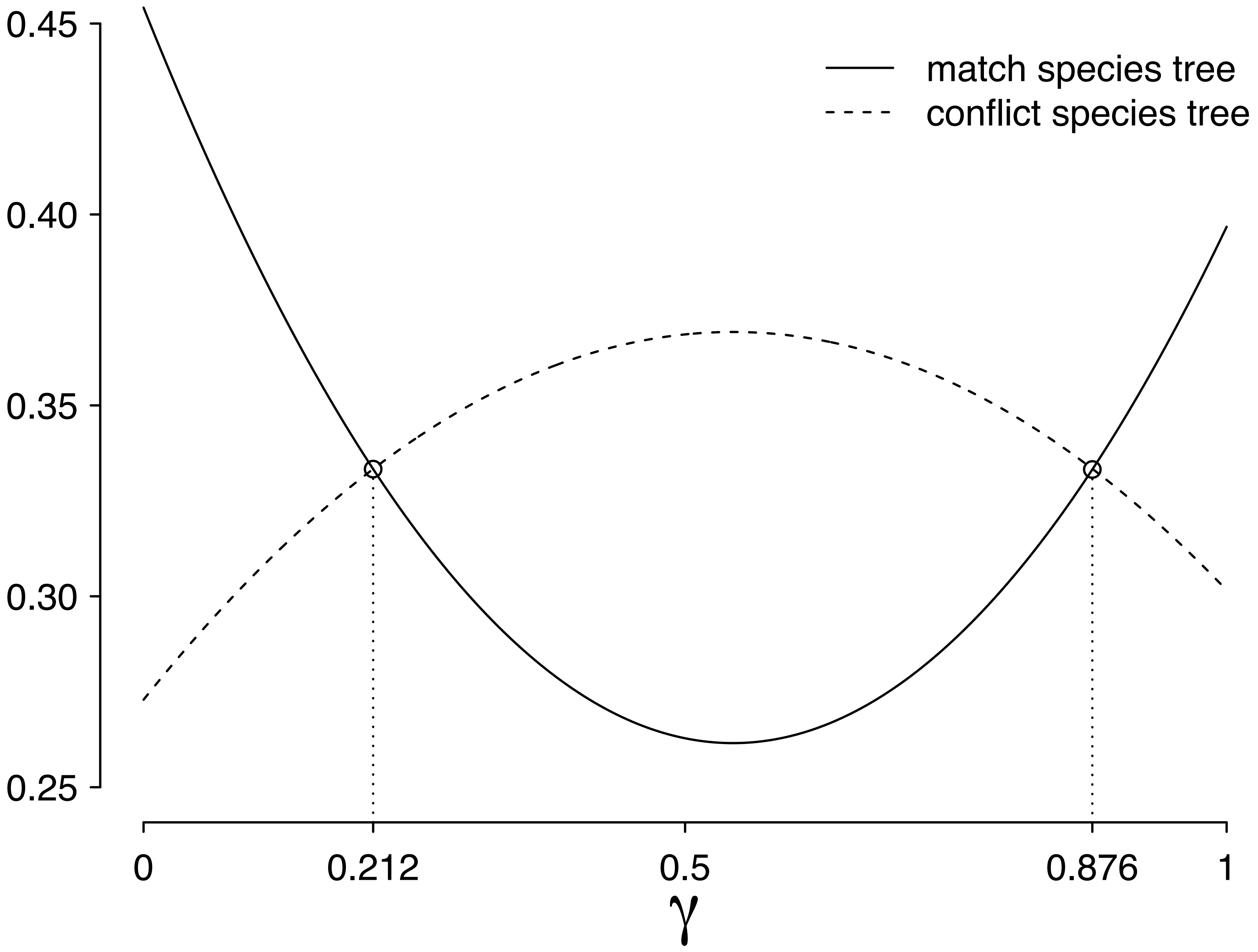
(S.-L., Yang, Ané, 2016, Syst Bio)

ASTRAL (Mirarab et al, 2014)
NJst (Liu&Yu,2011)

Why?

Phylogenetic network

Anomaly zone with gene flow

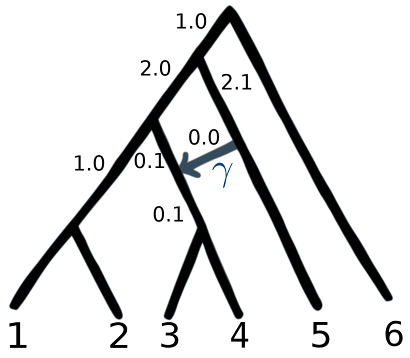


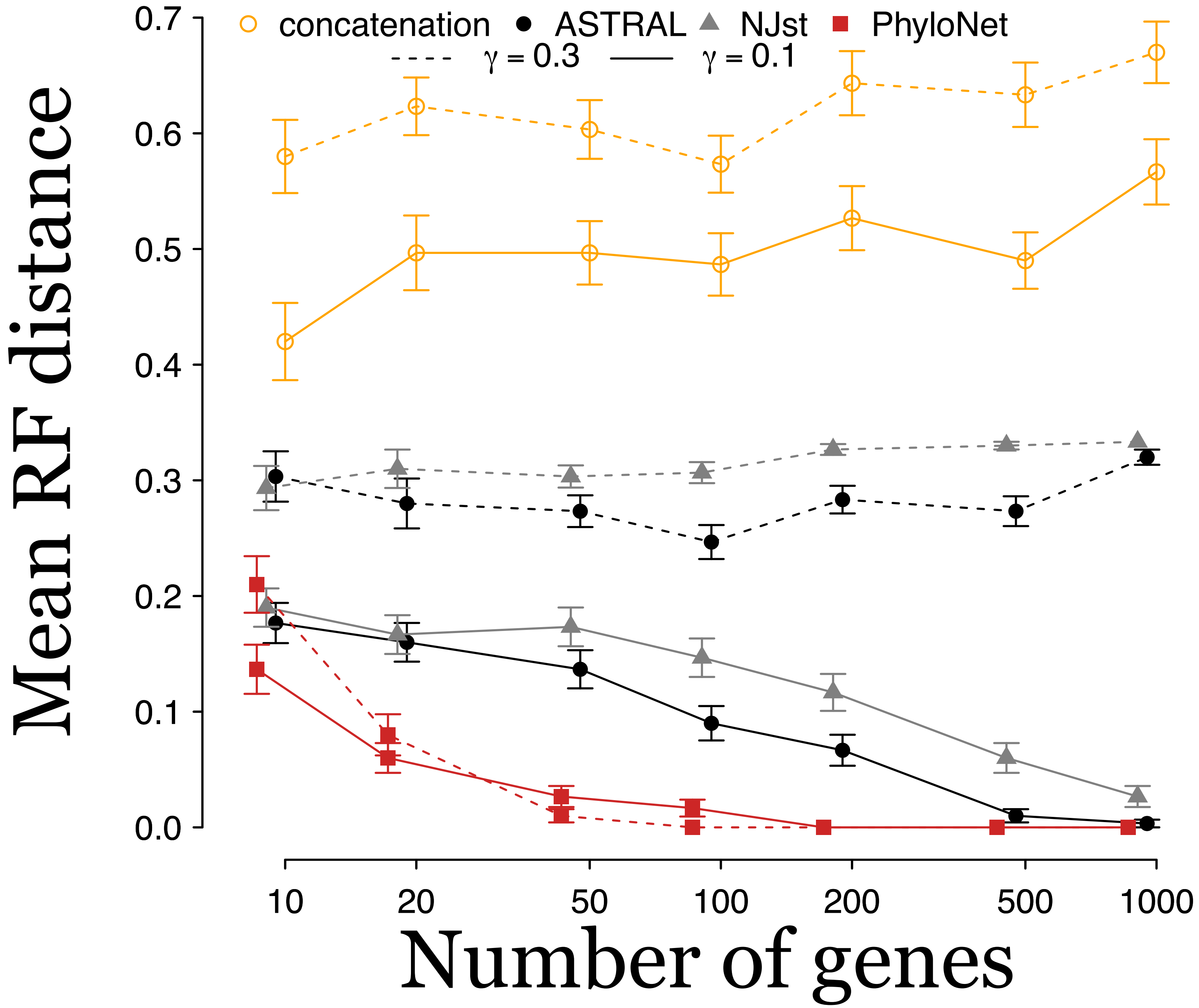
(S.-L., Yang, Ané, 2016, Syst Bio)

Why?

Phylogenetic network

Coalescent tree methods not robust to gene flow





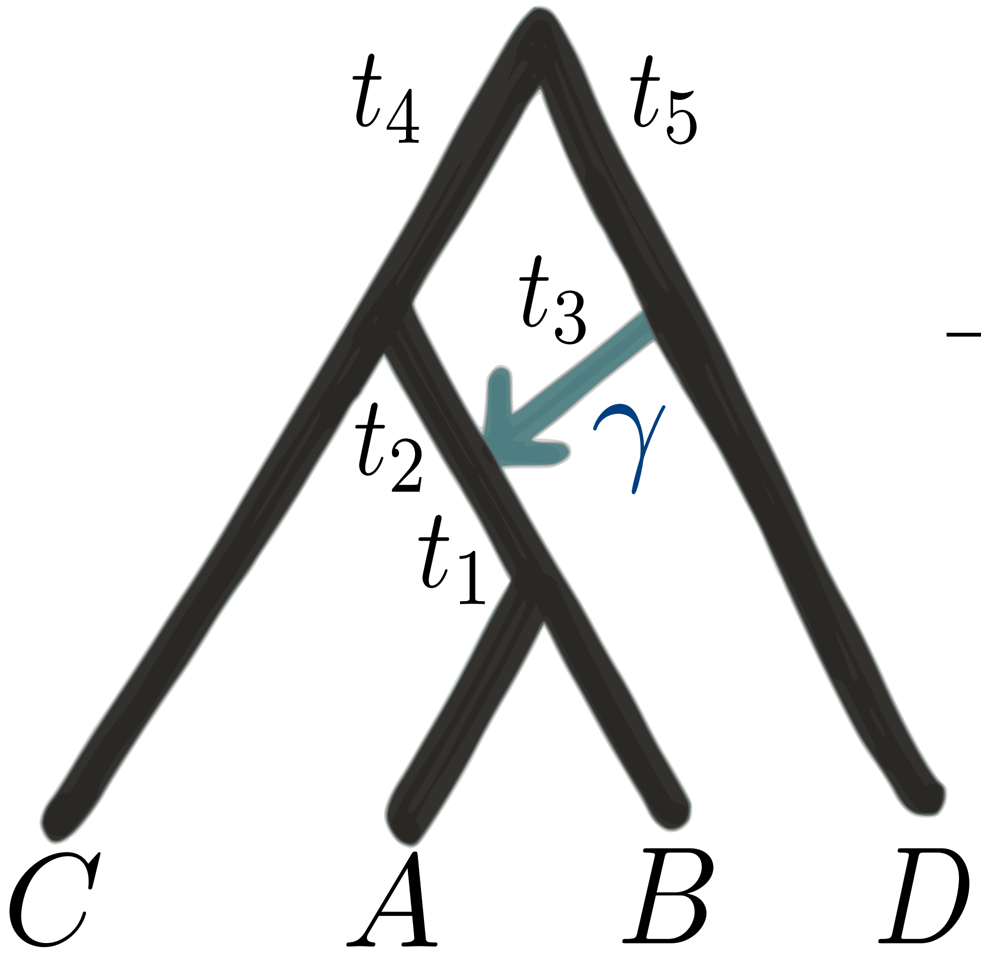
(S.-L., Yang, Ané, 2016, Syst Bio)

ASTRAL (Mirarab et al, 2014)
NJst (Liu&Yu,2011)
PhyloNet (Yu et al 2012, 2014)

Why?

Phylogenetic network

Anomalous unrooted gene trees with gene flow



Frequency among gene trees

Quartet	$\gamma = 0.0$	$\gamma = 0.1$	$\gamma = 0.3$
$AB\|CD$	**0.347**	**0.298**	**0.260**
$CA\|BD$	0.327	0.351	0.370
$CB\|AD$	0.327	0.351	0.370

$$t_1 = t_2 = 0.01, t_3 = t_4 = t_5 = 1$$

- **ILS**: no AUGT on 4 taxa (Degnan, 2013)
- **ILS**+**HGT**: AUGT on 4 taxa (S.-L., Yang, Ané, 2016, Syst Bio)

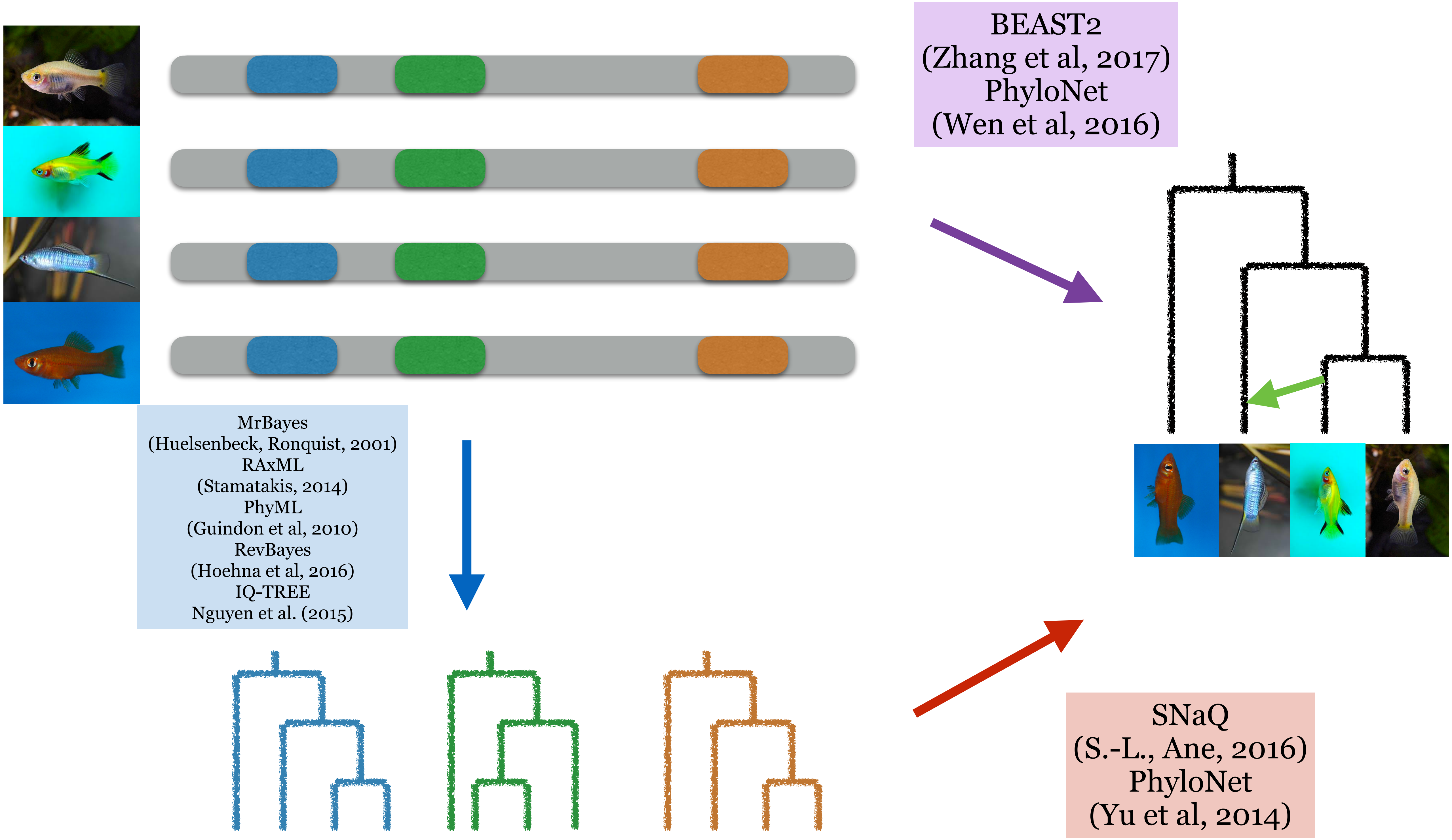
See also Long & Kubatko (2018) for AUGT under continuous gene flow between sister species

So far…

- Networks are good
- Explicit networks are better
- If you ignore gene flow, you can estimate the wrong tree

How?

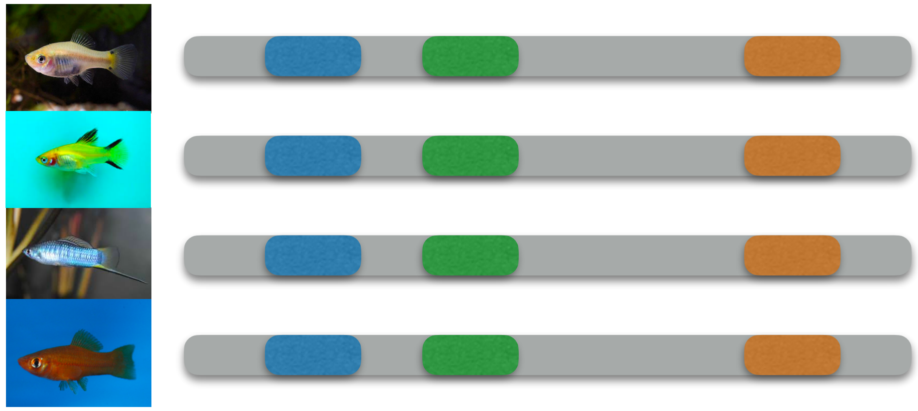
Phylogenetic network



MrBayes
(Huelsenbeck, Ronquist, 2001)
RAxML
(Stamatakis, 2014)
PhyML
(Guindon et al, 2010)
RevBayes
(Hoehna et al, 2016)
IQ-TREE
Nguyen et al. (2015)

BEAST2
(Zhang et al, 2017)
PhyloNet
(Wen et al, 2016)

SNaQ
(S.-L., Ane, 2016)
PhyloNet
(Yu et al, 2014)



network

$$P(N, G, \theta | D) \propto \pi(N)\pi(\theta)\prod_{i=1}^{L} P(D_i|G_i)P(G_i|N)$$

gene trees

L loci

Prior Network

Substitution Model

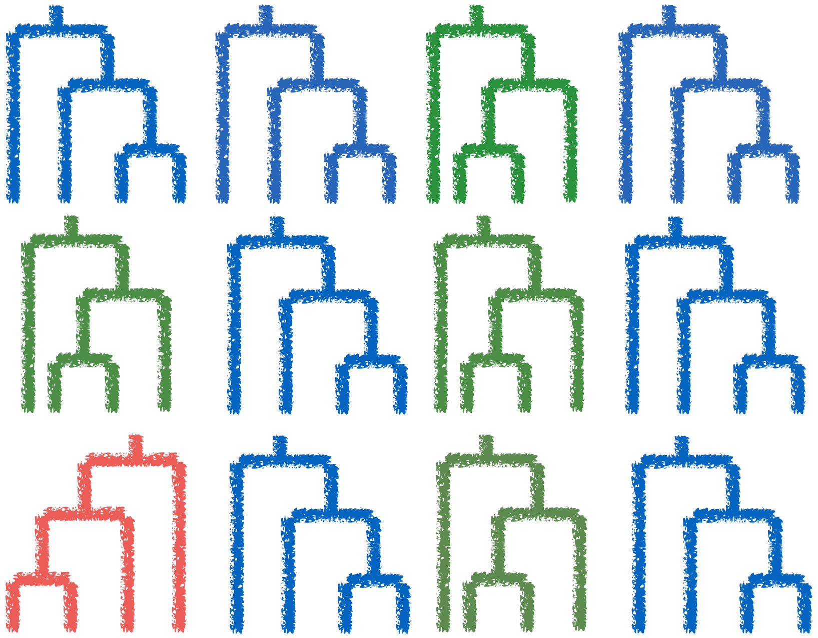
Multispecies Coalescent

Birth-hybridization process

BEAST2
(Zhang et al, 2017)

reticulations, cycle diameter

PhyloNet Bayesian
(Wen et al, 2016)

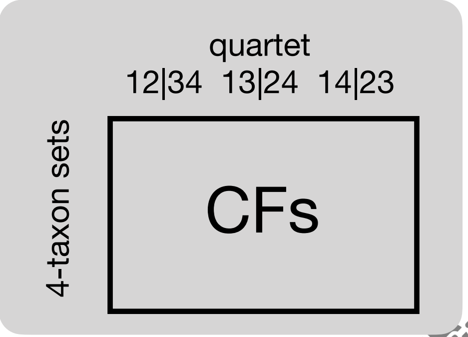


$$P(N, \theta | G) \propto \pi(N)\pi(\theta)\prod_{i=1}^{L} P(G_i|N,\theta)$$

PhyloNet Bayesian
(Wen et al, 2016)

$$L(N, \theta) = \prod_{i=1}^{L} P(G_i|N,\theta)$$

PhyloNet Likelihood
(Yu et al, 2014)



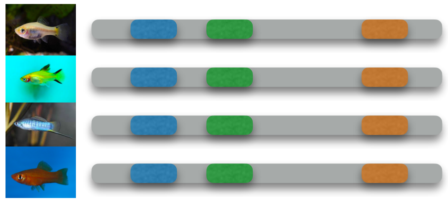
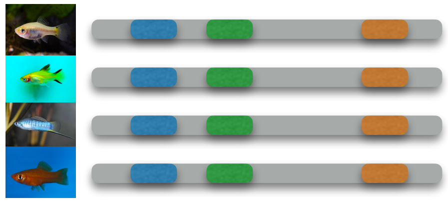
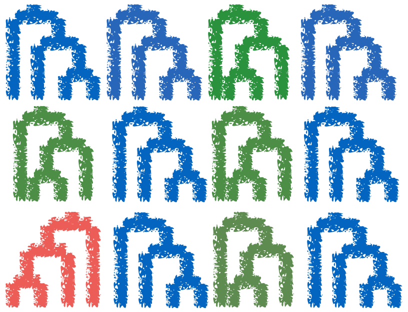
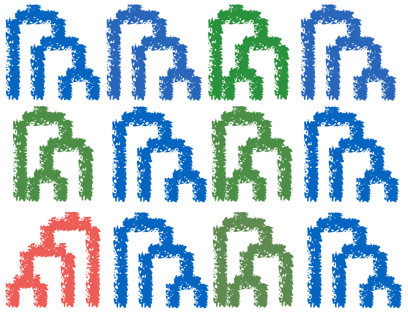
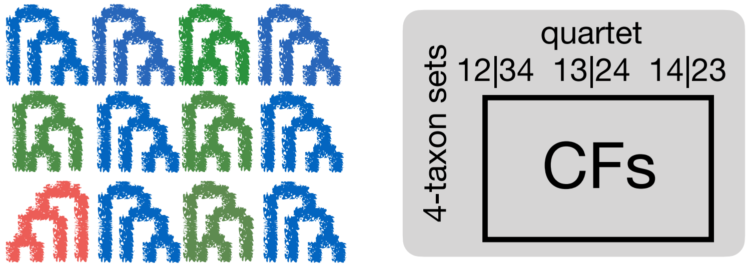
quartet
12|34 13|24 14|23

4-taxon sets

CFs

$$\tilde{L}(N, \theta) \propto \prod_{q} L(q|N,\theta)$$

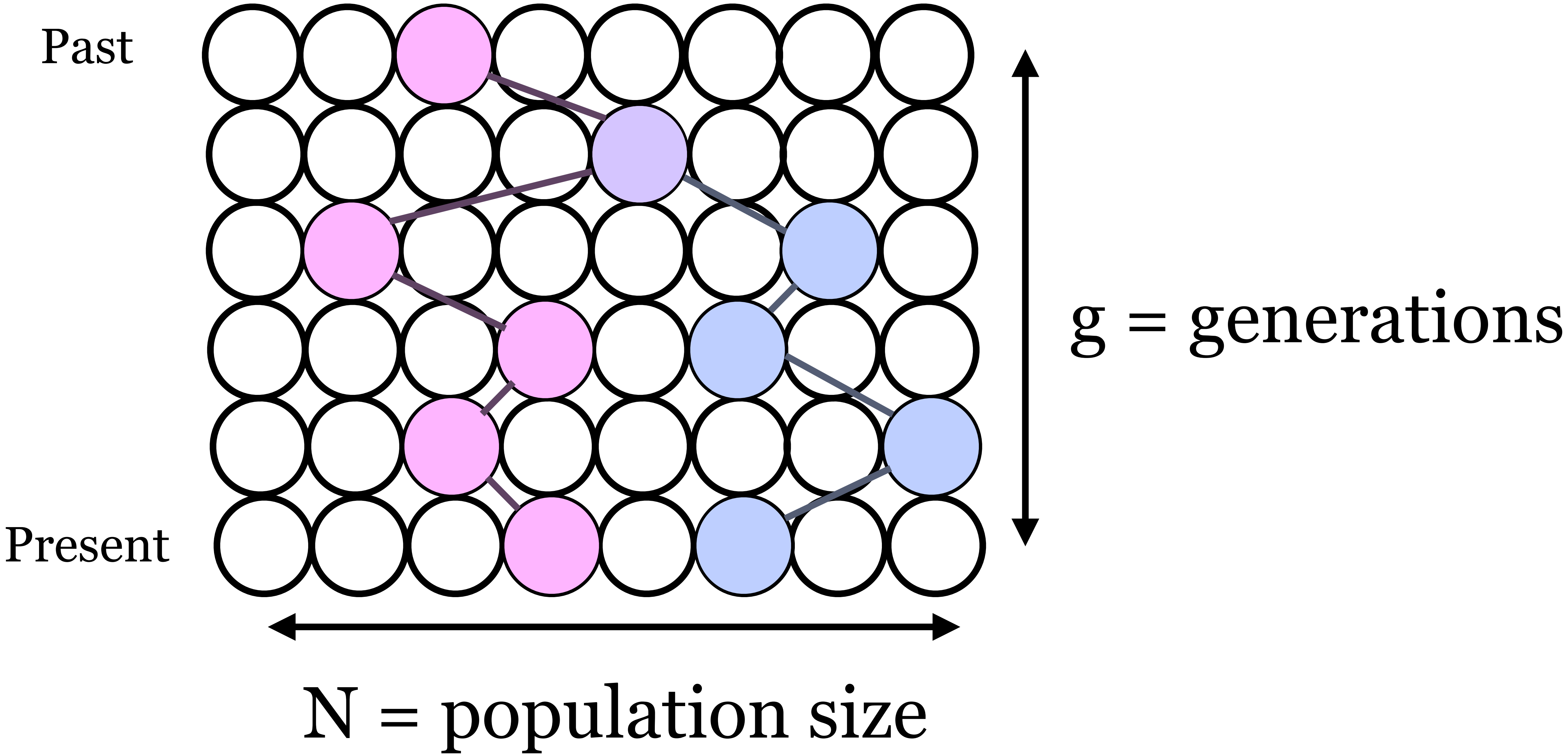
SNaQ
(S.-L., Ane, 2016)

	BEAST2 (Zhang et al, 2017)	Birth-hybridization process	**MCMC:** Network moves, mixing	Most accurate, not scalable
	PhyloNet Bayesian (Wen et al, 2016)	# reticulations, cycle diameter		
 Rooted	PhyloNet Bayesian (Wen et al, 2016)			More scalable, Robust
 Rooted	PhyloNet Likelihood (Yu et al, 2014)		**Heuristic search:** Network moves	
 Unrooted	SNaQ (S.-L., Ane, 2016)	Level-1 networks		

STEM-hy	gene trees rooted, BL	likelihood	hybridization b/w sister lineages
PhyloNet `InferNetwork_ML`	gene trees rooted	likelihood	
PhyloNet `InferNetwork_MPL`	gene trees rooted	triplet likelihood	
PhyloNetworks `SNaQ`	gene trees or quartet CFs	quartet likelihood	level-1 network
PhyloNet `MCMC_GT`	gene trees rooted	Bayesian	compound prior
PhyloNet `MCMC_SEQ`	alignments	Bayesian	compound prior no rate variation
BEAST2 `SpeciesNetwork`	alignments	Bayesian	birth-hyb prior
PhyloNet `MLE_BiMarkers`	biallelic sites	likelihood	compound prior
PhyloNet `MCMC_BiMarkers`	biallelic sites	Bayesian	compound prior
HyDe	sites	invariants	4 taxa, 1 hyb.

Slide by Cecile Ane

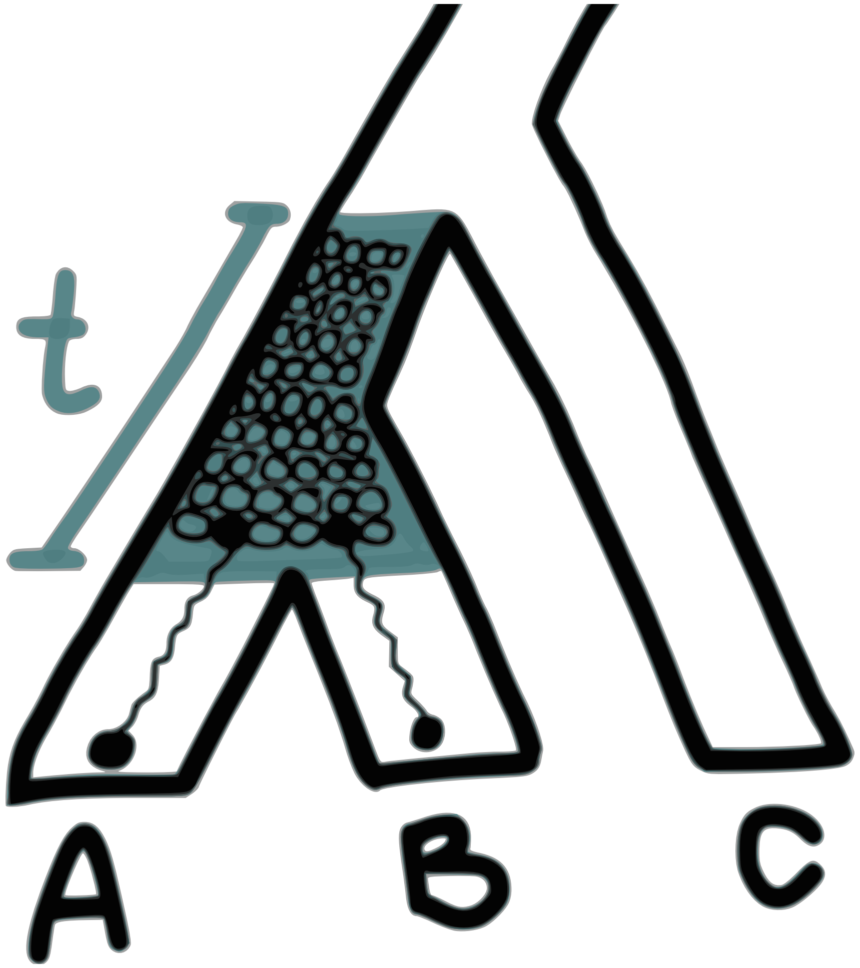
Coalescent model within 1 population



Probability of no coalescence in g generations: $\left(1 - \frac{1}{N}\right)^g$

$$t = g/N \Rightarrow \left(1 - \frac{t}{Nt}\right)^{Nt} \xrightarrow[N \to \infty]{} e^{-t}$$

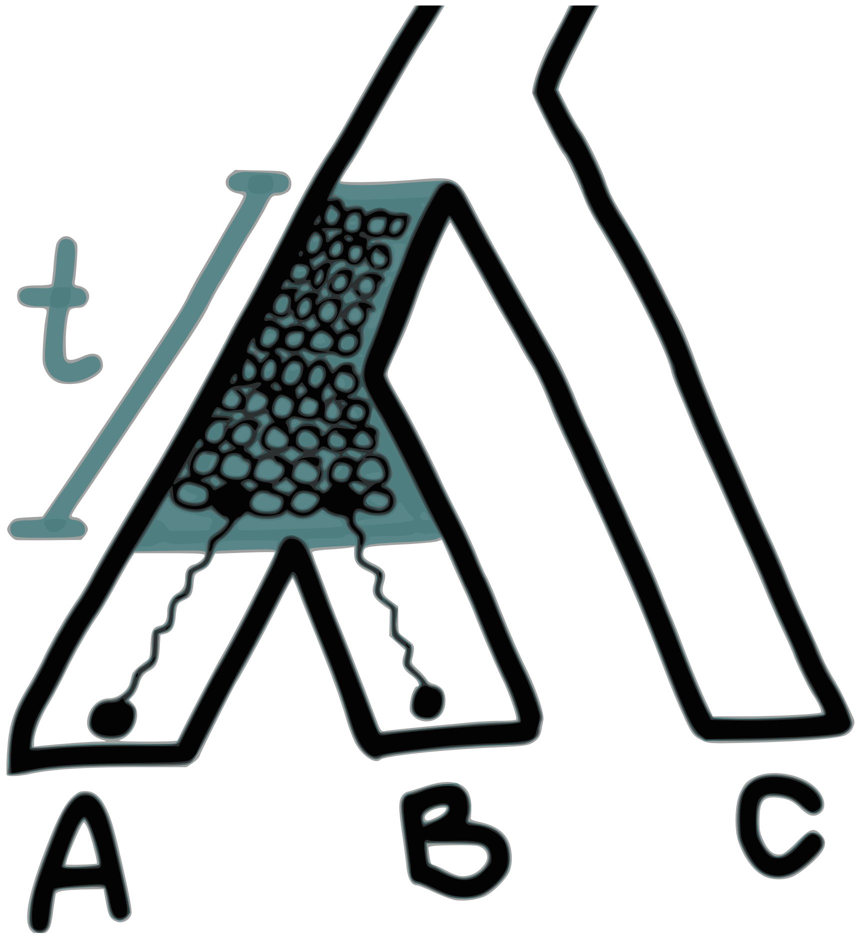
Multispecies coalescent on a tree



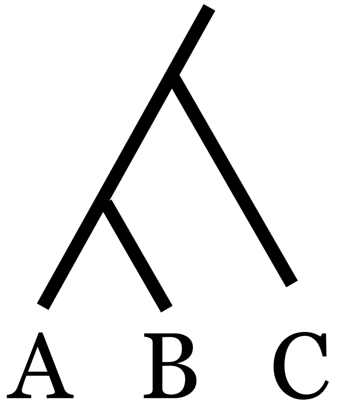
$$P(T > t) = e^{-t}$$

$$T = \frac{g}{N} \text{ coalescent units } \sim Exp(1)$$

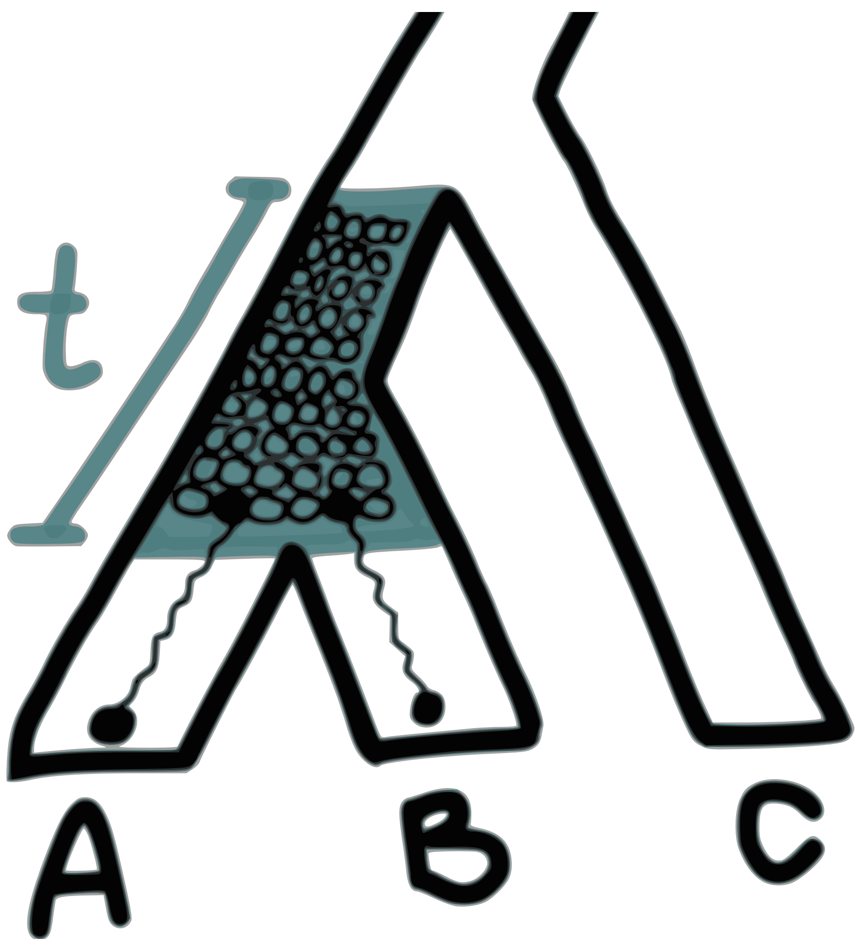
Multispecies coalescent on a tree



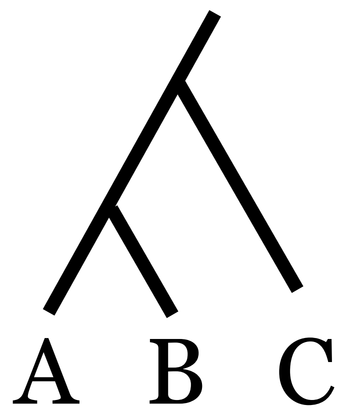
$$P(T > t) = e^{-t}$$

$\mathbb{P}\Big($  $\Big) =$

Multispecies coalescent on a tree

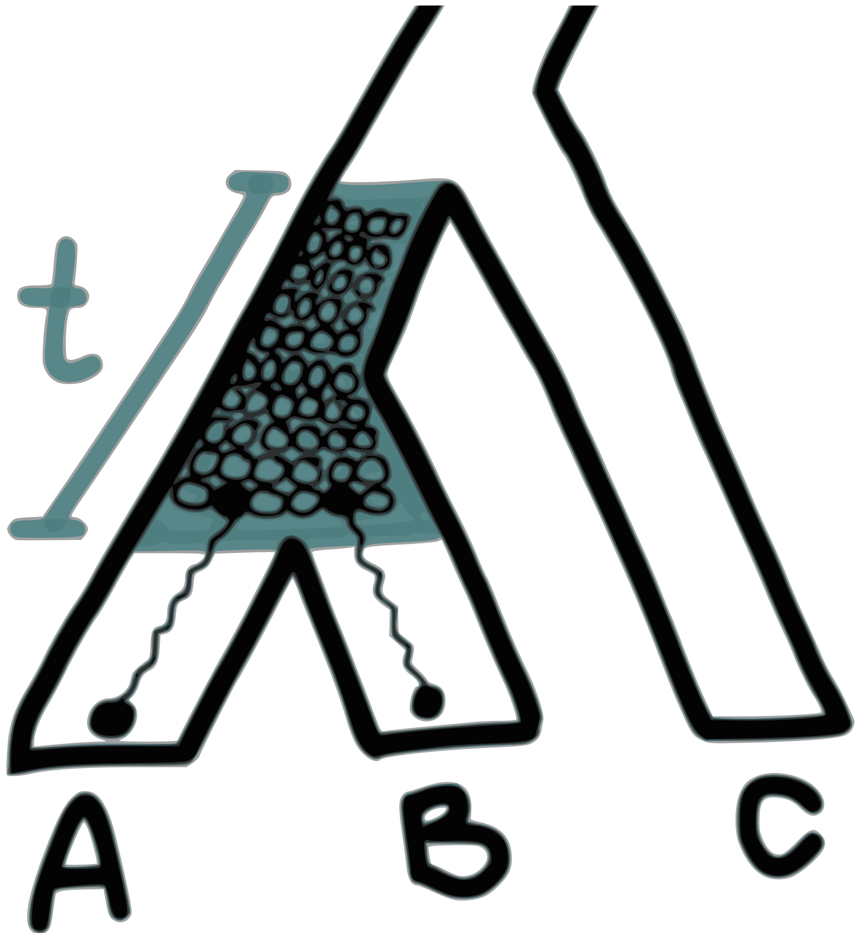


$P(T > t) = e^{-t}$

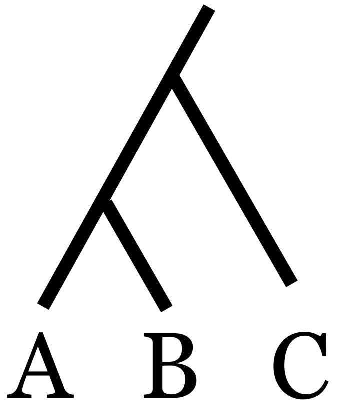
$\mathbb{P}\Big($  $\Big) =$

$$1 - e^{-t}$$

Multispecies coalescent on a tree

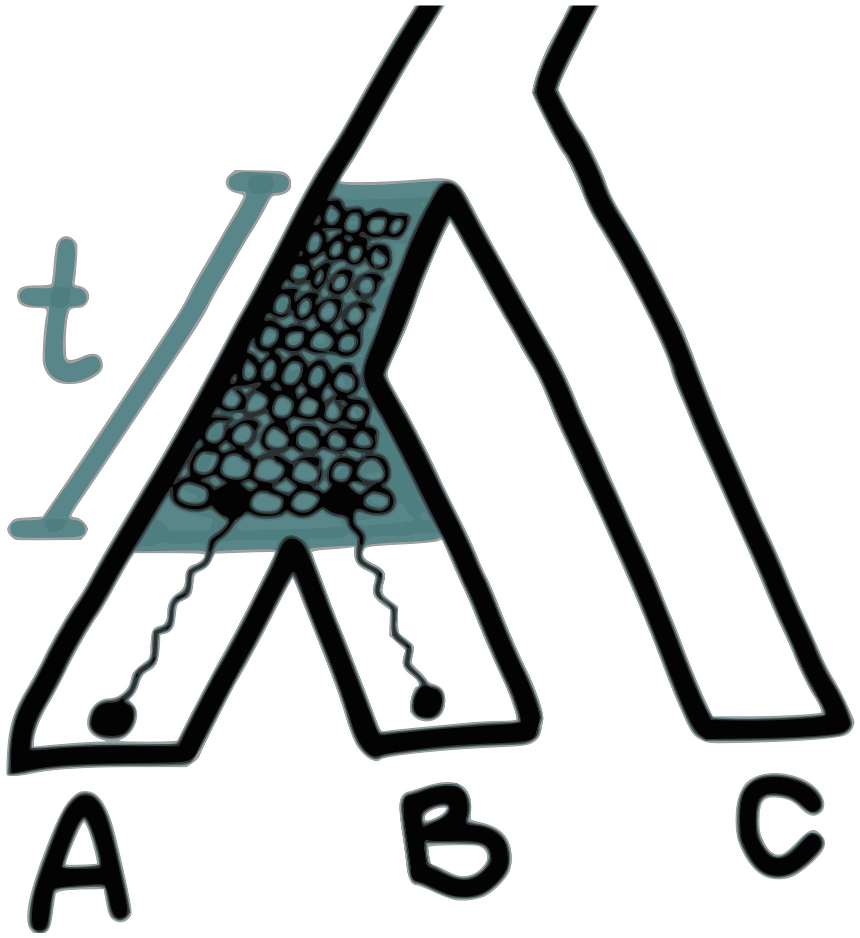


$$P(T > t) = e^{-t}$$

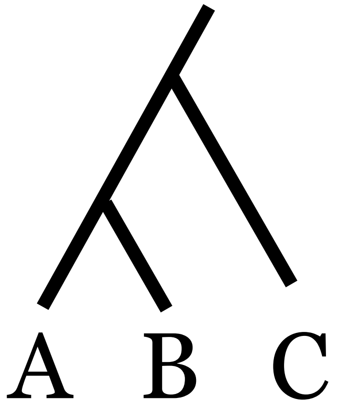


$$\mathbb{P}\Big(\qquad \Big) = 1 - e^{-t} +$$

Multispecies coalescent on a tree

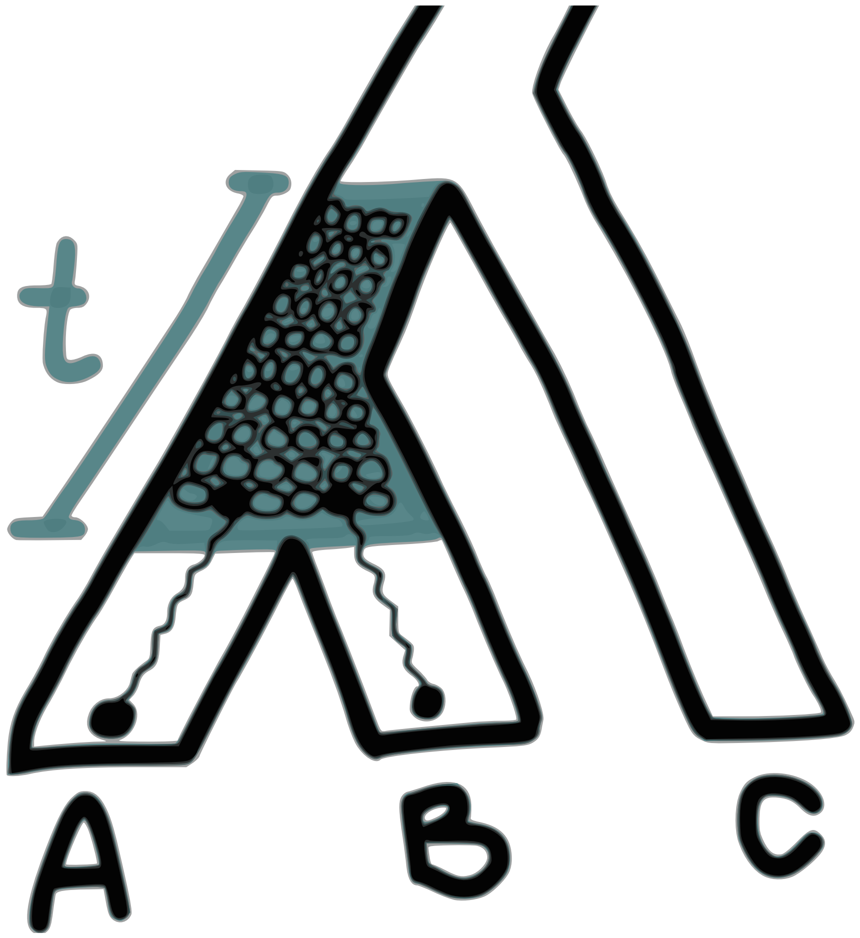


$$P(T > t) = e^{-t}$$

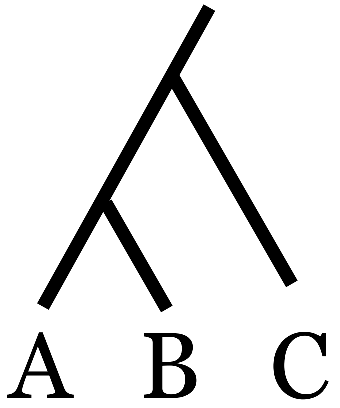


$$\mathbb{P}\Big(\quad \Big) = 1 - e^{-t} + e^{-t} \times 1/3$$

Multispecies coalescent on a tree



$$P(T > t) = e^{-t}$$



$$\mathbb{P}\Big(\quad \Big) =$$

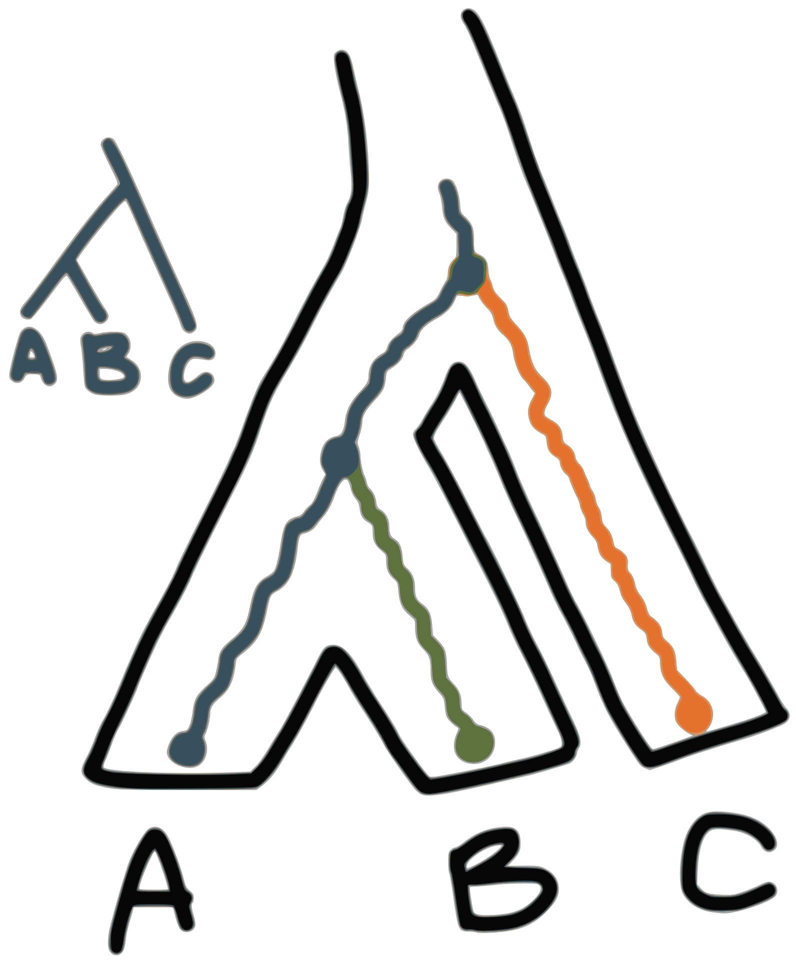
$$1 - e^{-t}$$

$$+$$

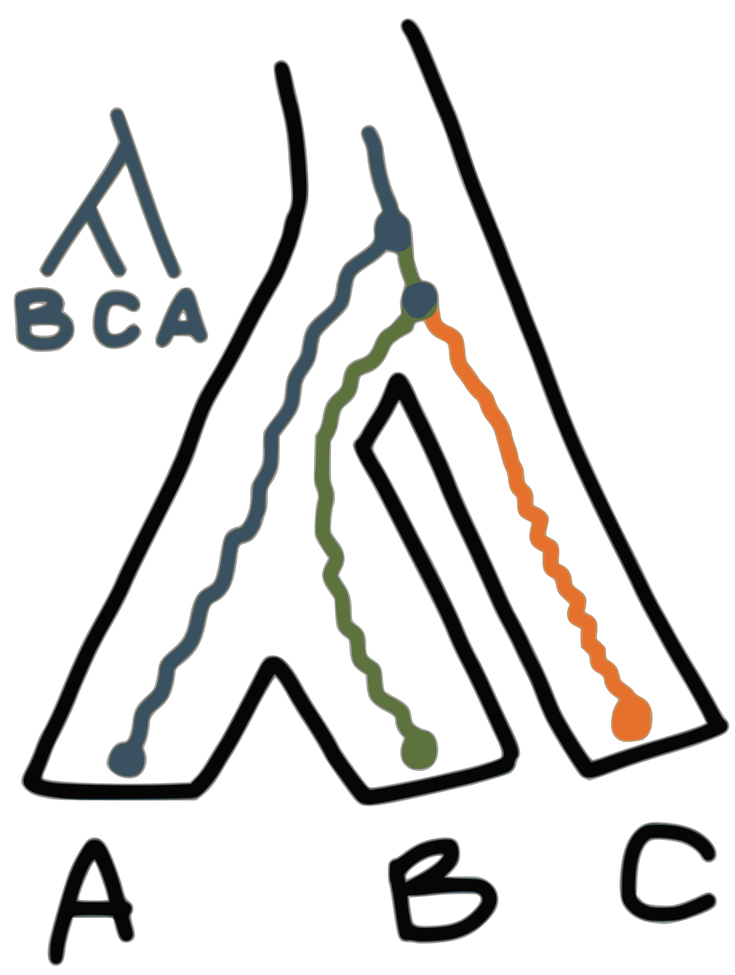
$$e^{-t} \times 1/3$$

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

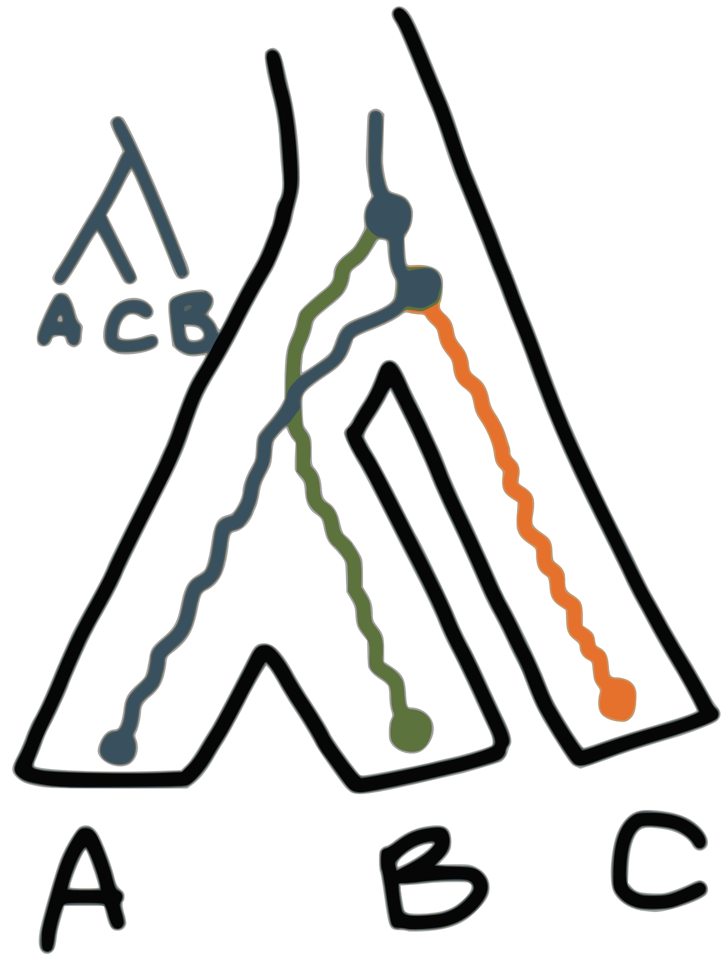
Multispecies coalescent on a tree



$$1 - \frac{2}{3}e^{-t}$$

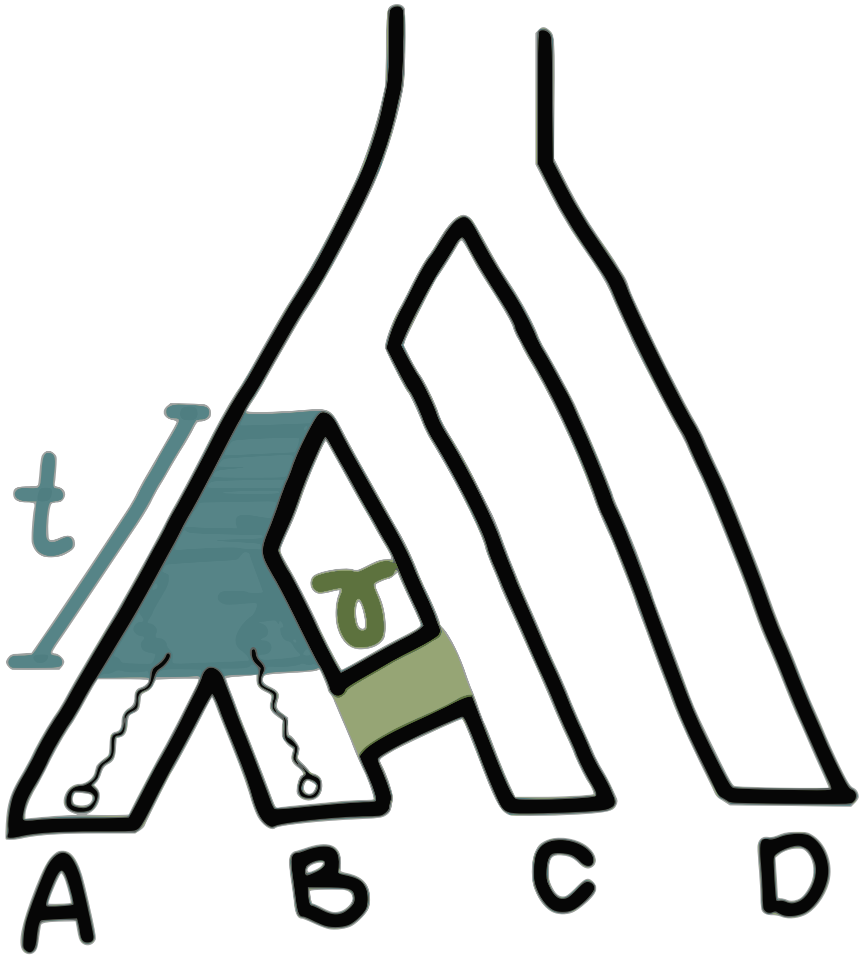


$$\frac{1}{3}e^{-t}$$



$$\frac{1}{3}e^{-t}$$

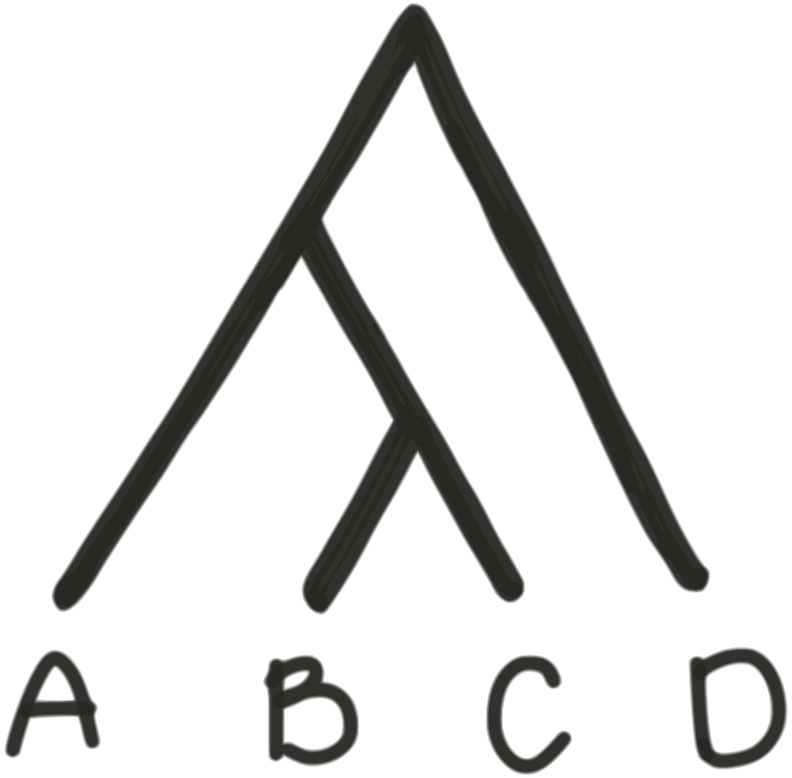
Multispecies coalescent on a network



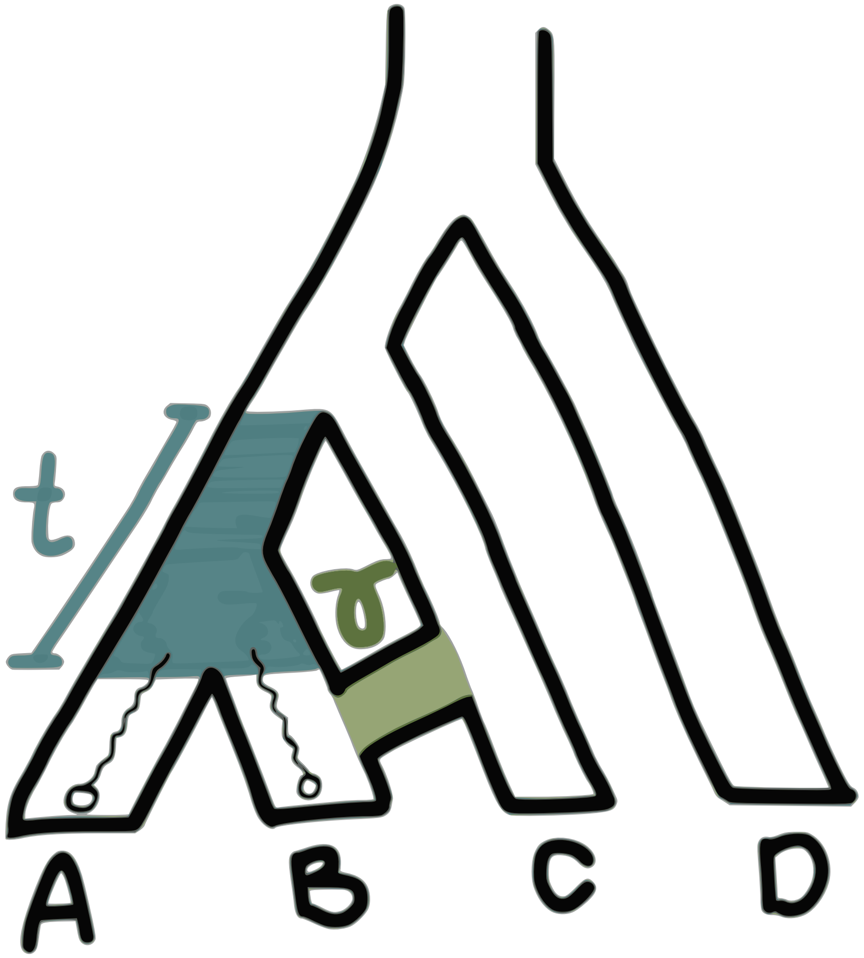
(Meng, Kubatko, 2009)
(Yu, Degnan, Nakhleh, 2012)

Multispecies coalescent on a network

$P($



$|$



$)$

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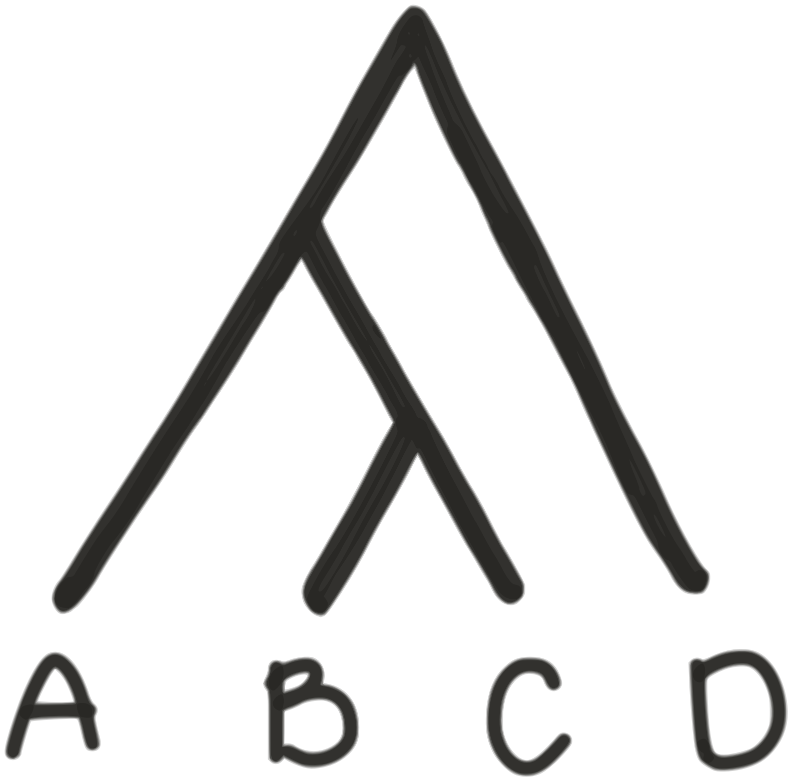
Multispecies coalescent on a network

$P($



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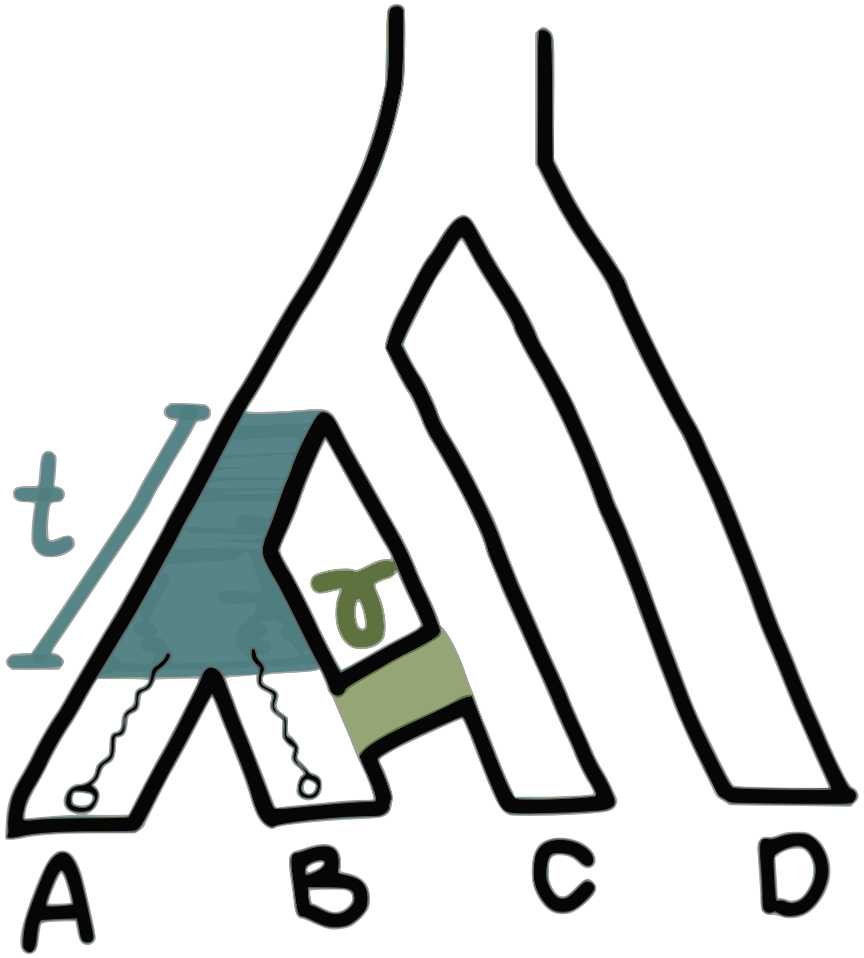


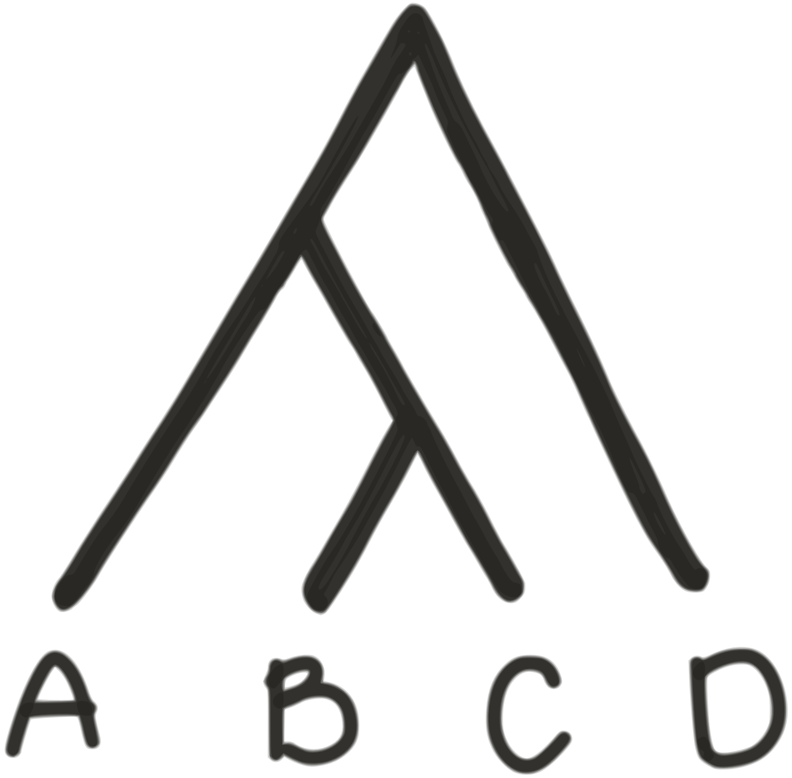
$)$

$$(1-\gamma)\frac{1}{3}e^{-t}+\gamma(1-\frac{2}{3}e^{-t_2})$$

(Meng, Kubatko, 2009)
(Yu, Degnan, Nakhleh, 2012)

Multispecies coalescent on a network

$P($



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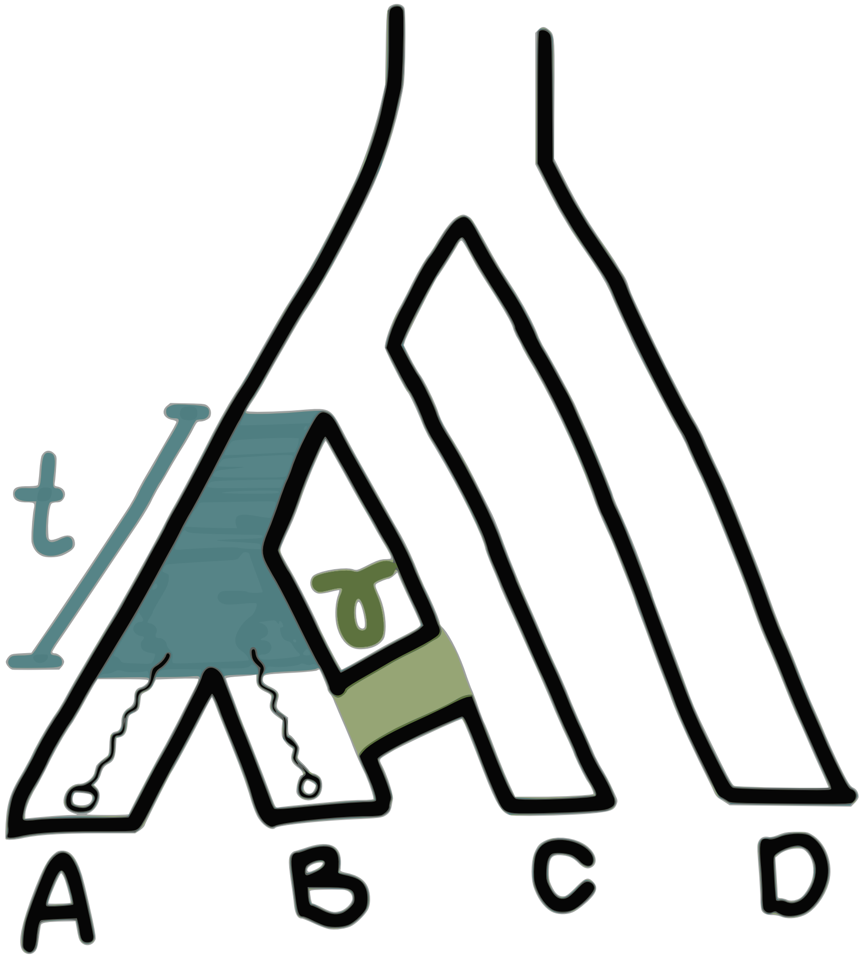
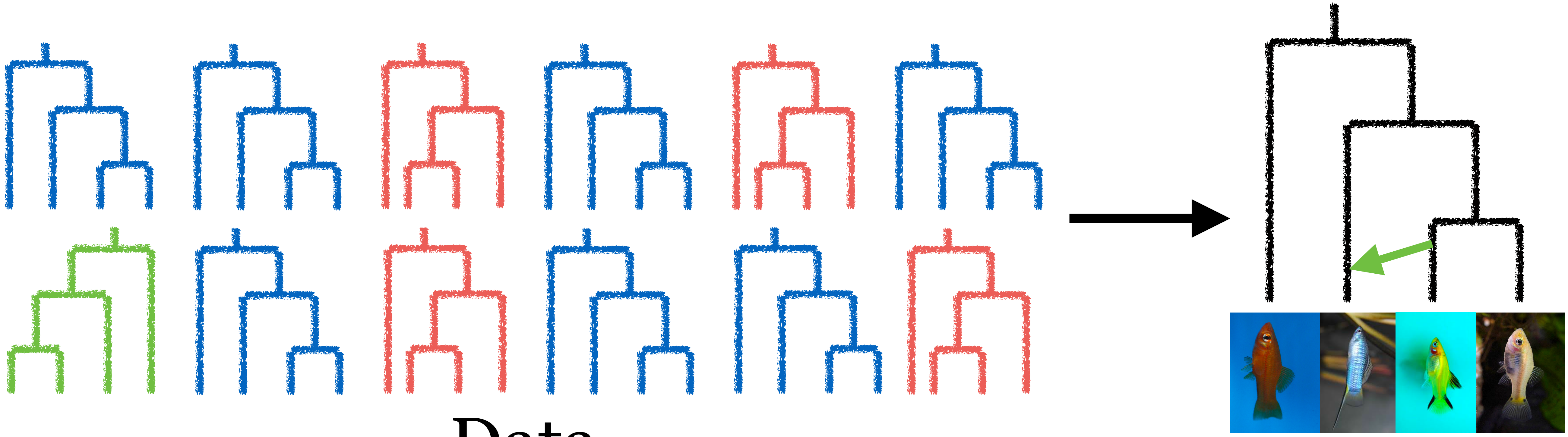


$)$

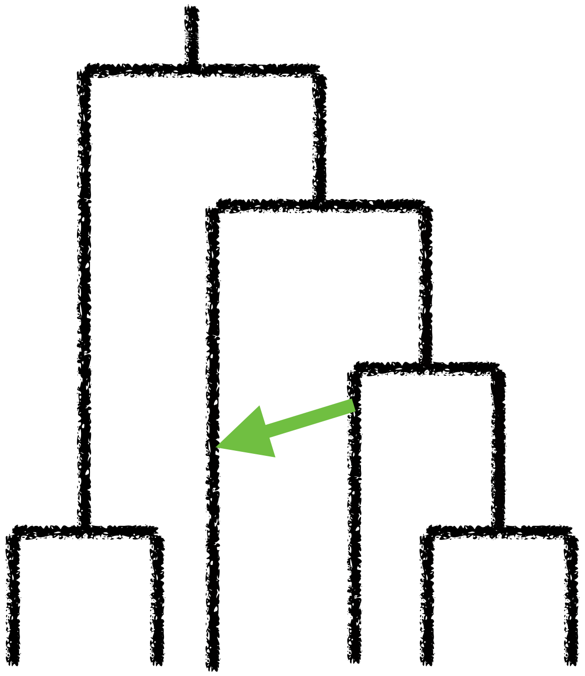
$$CF_{BC|AD}(t, t_2, \gamma) = (1-\gamma)\frac{1}{3}e^{-t} + \gamma(1 - \frac{2}{3}e^{-t_2})$$

(Meng, Kubatko, 2009)
(Yu, Degnan, Nakhleh, 2012)

Maximum **pseudo**likelihood



Data



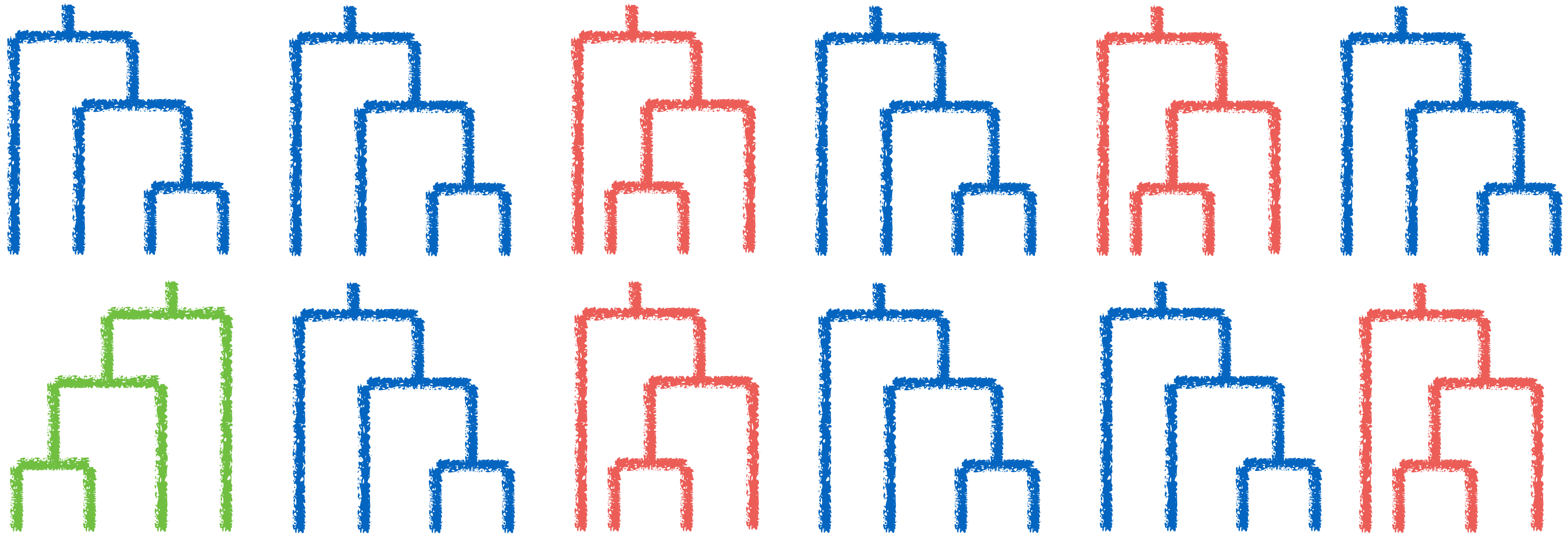
Quartet-based inference

$$\tilde{L}(network) = \prod L(quartet)$$

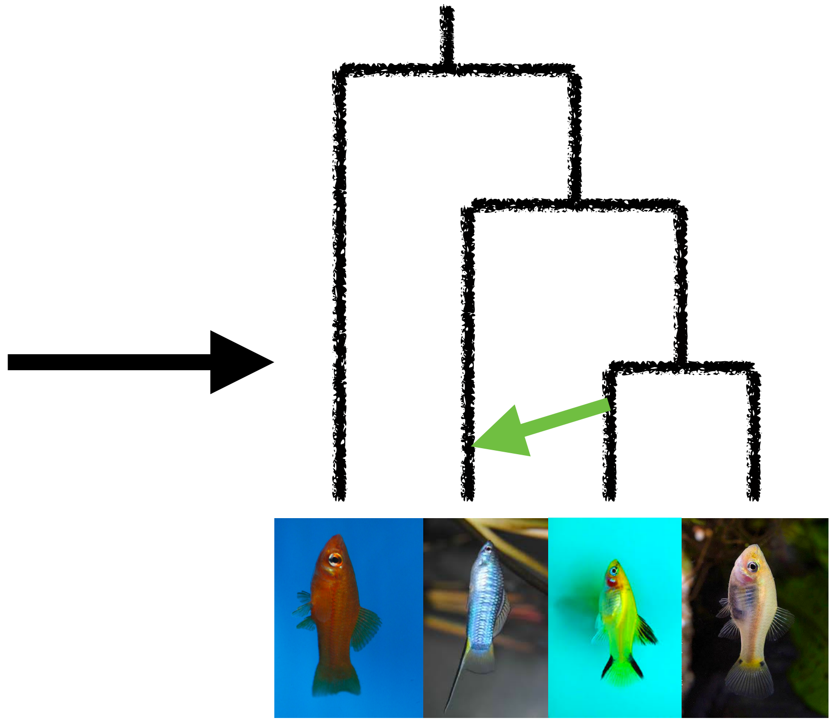
(S-L, Ané, 2016, PLoS Genetics)

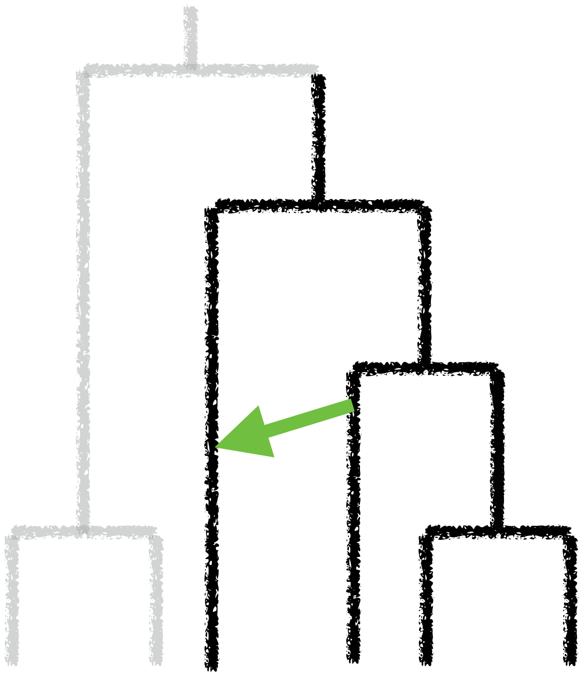
`www.github.com/CRSL4/PhyloNetworks`

Maximum **pseudo**likelihood



Data





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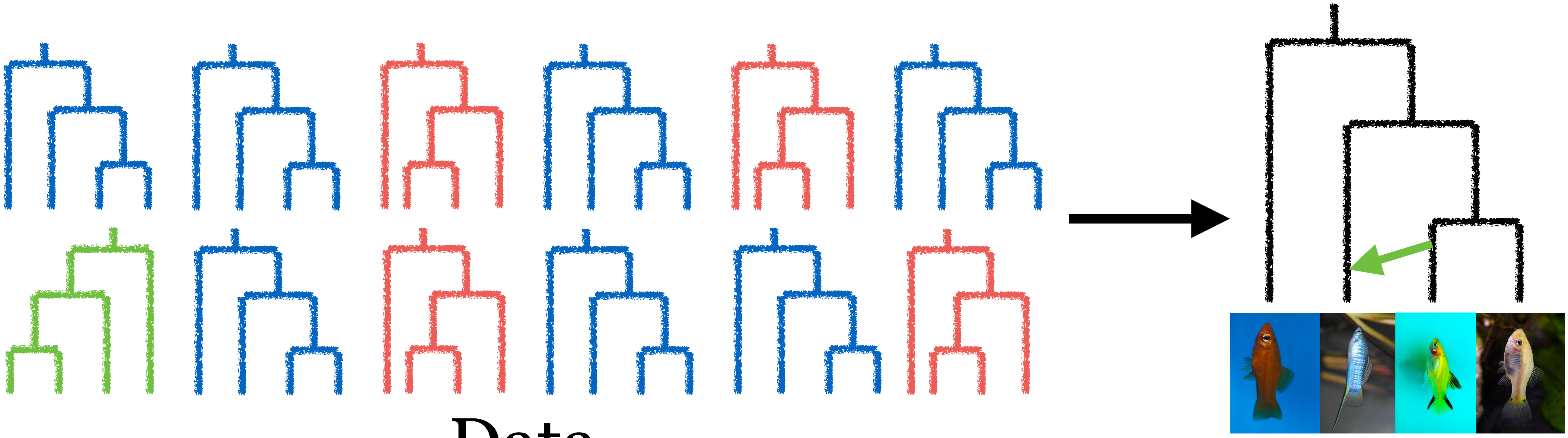

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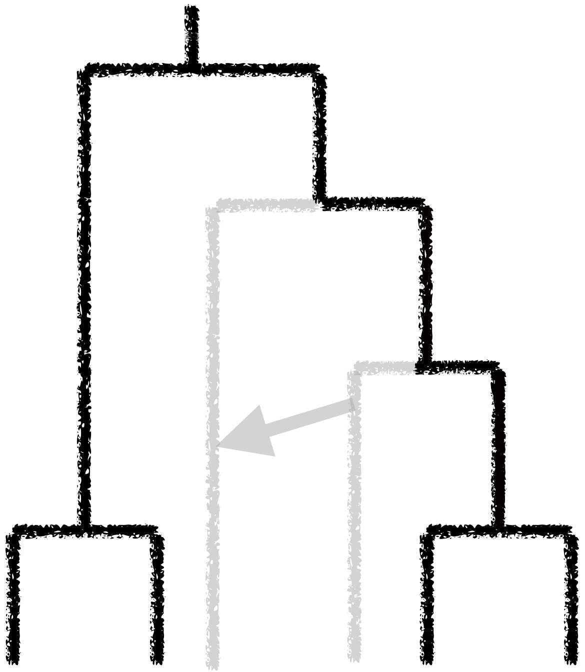

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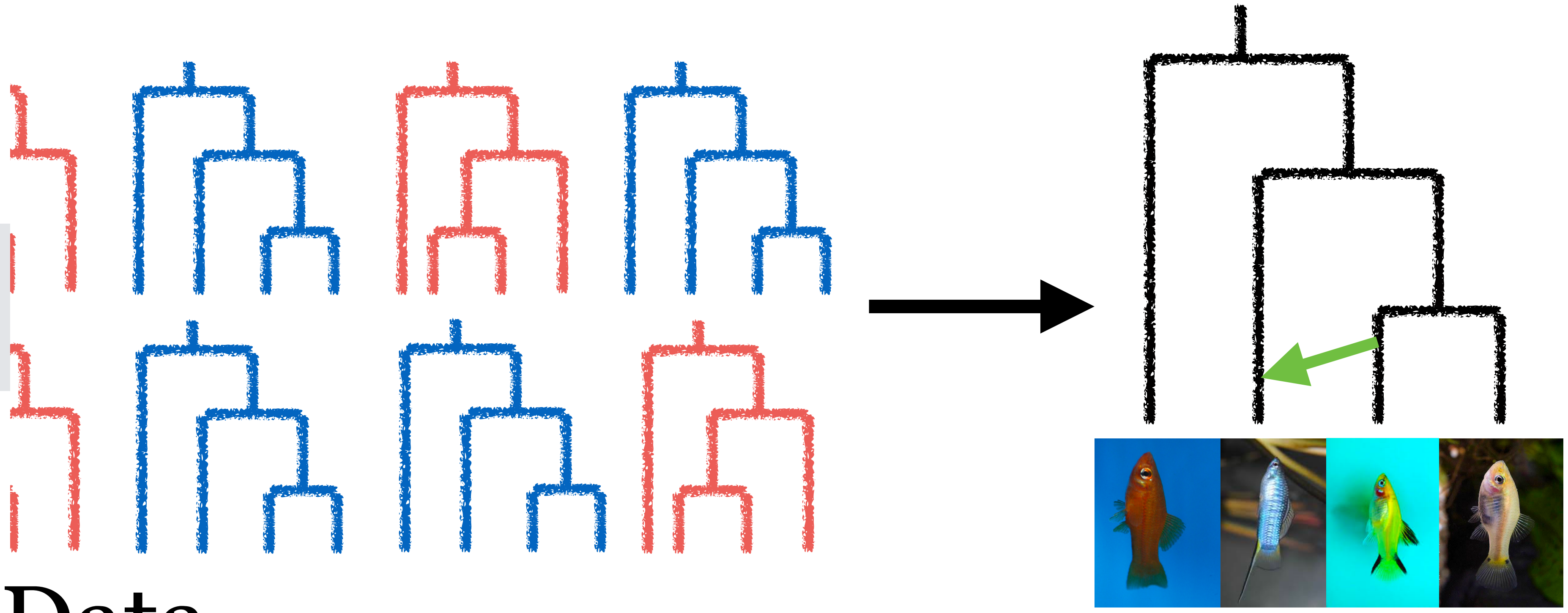
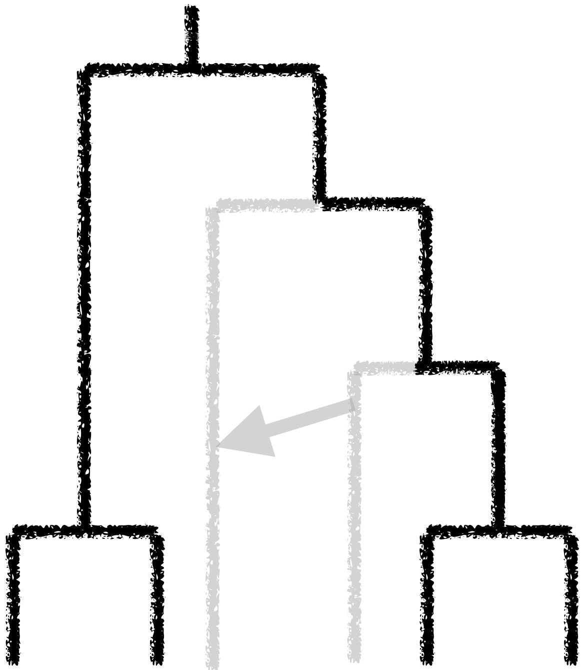
Maximum **pseudo**likelihood

Unrooted gene trees	No rooting error
No branch lengths	No molecular clock assumption
Concordance factors	Account for tree estimation error



Data



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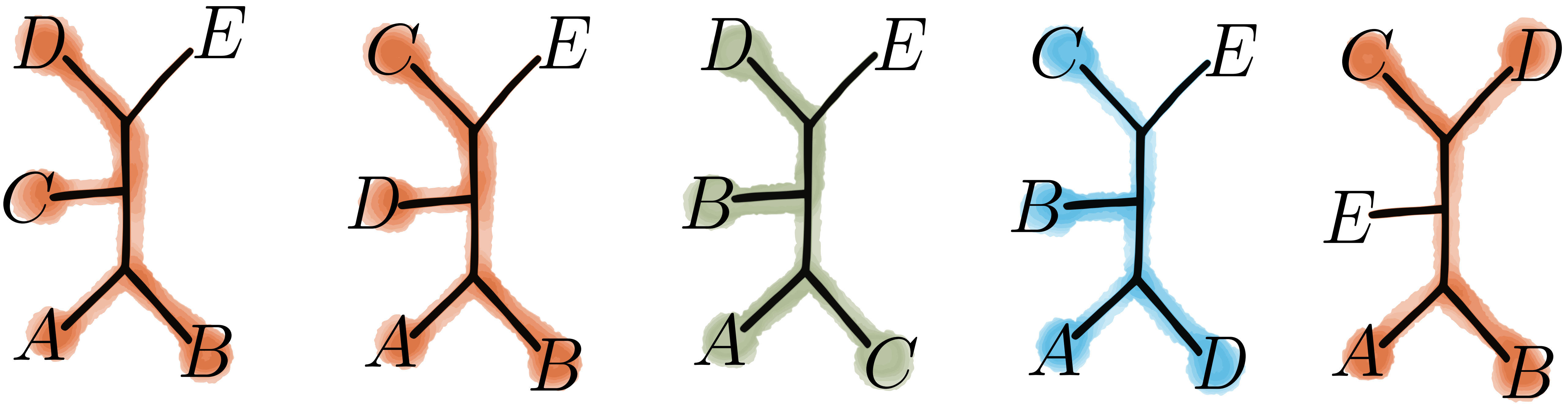
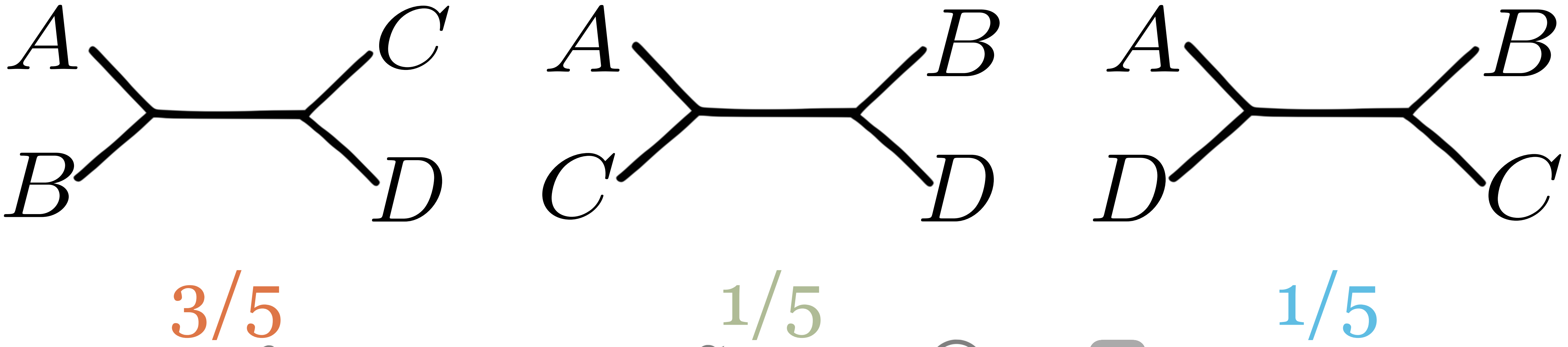
`www.github.com/CRSL4/PhyloNetworks`

Quartet-based inference



Concordance factors (CF):
% of genes having the quartet in their tree



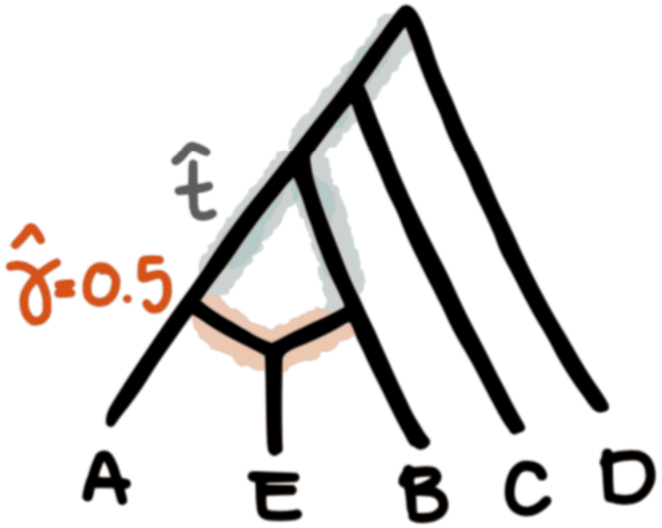
Quartet-based inference

Observed **quartet** CFs:

4 taxon set	CF_1	CF_2	CF_3
A B C D	.80	.10	.10
A B C E	.40	.40	.20
A B D E	.40	.40	.20
A C D E	.84	.08	.08
B C D E	.82	.10	.08

→

inferred network:

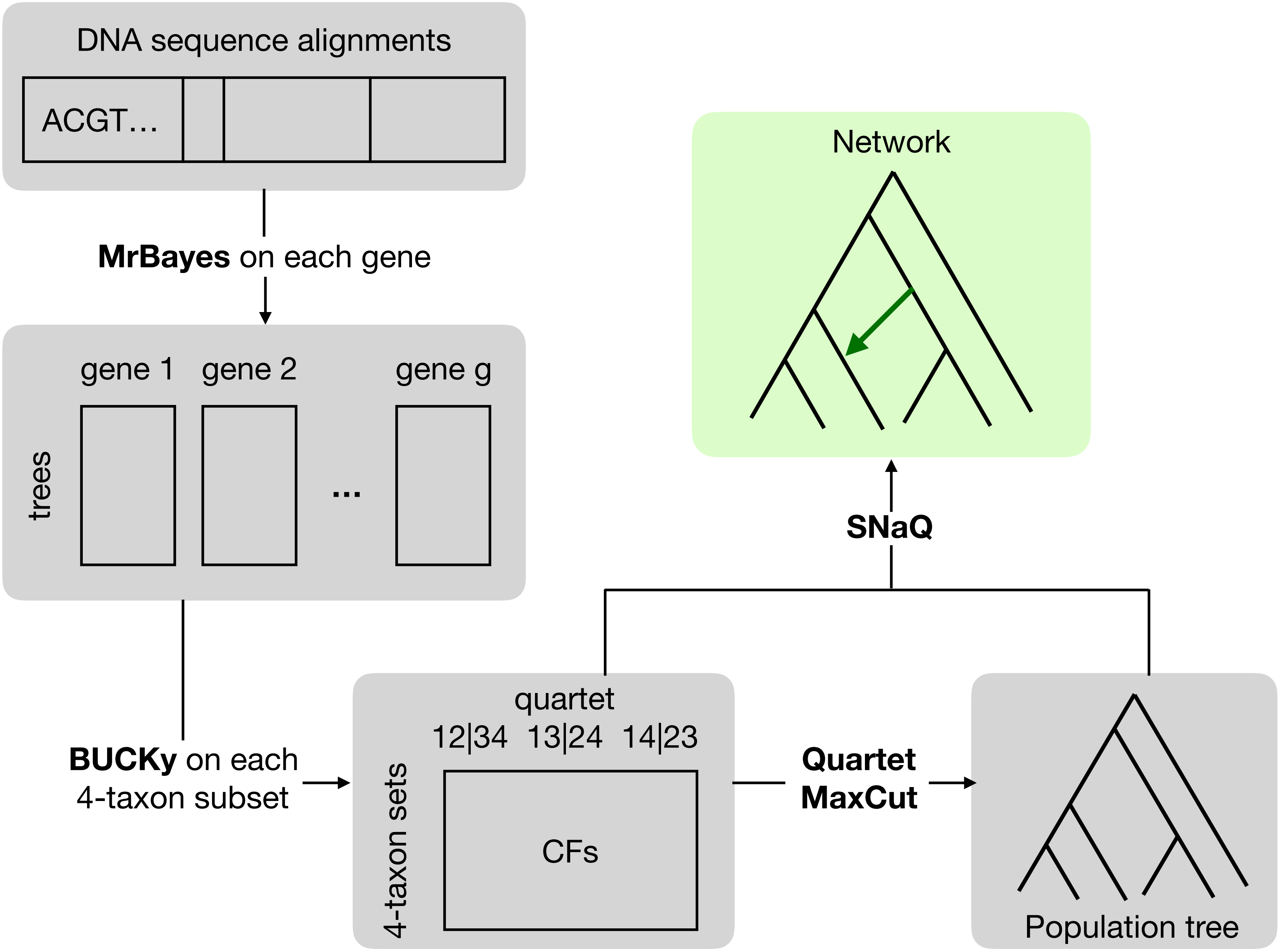


Maximum Pseudo-Likelihood:

$$\log \tilde{L} = \sum_{q\in Q(N)} \mathrm{CF}_{in,1}\log(\mathrm{CF}_{net,1})+\mathrm{CF}_{in,2}\log(\mathrm{CF}_{net,2})+\mathrm{CF}_{in,3}\log(\mathrm{CF}_{net,3})$$

How?

Phylogenetic network



DNA sequence alignments

ACGT…

MrBayes on each gene

trees

gene 1 gene 2 … gene g

BUCKy on each 4-taxon subset

quartet

12|34 13|24 14|23

4-taxon sets

CFs

Quartet MaxCut

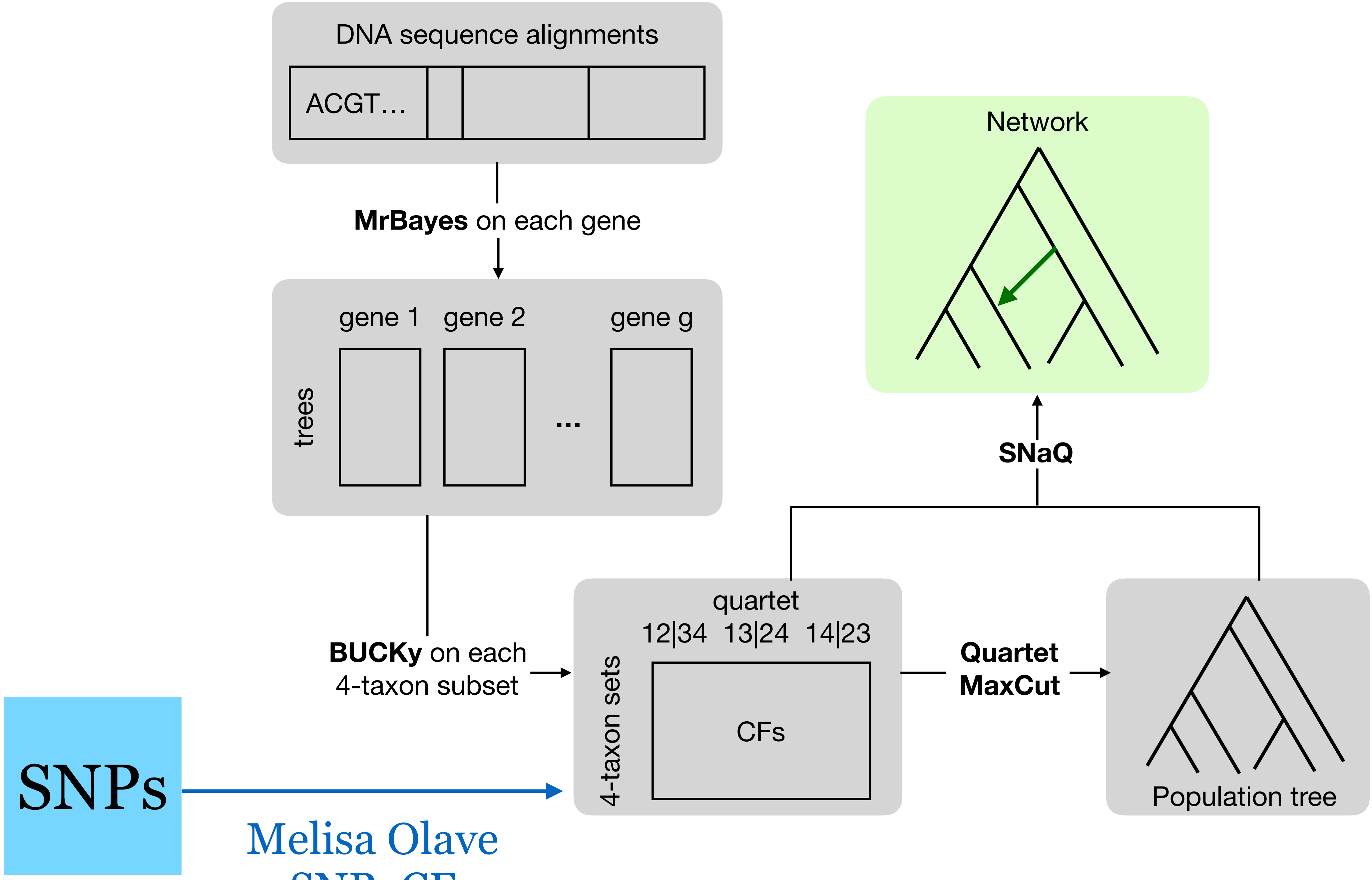
Population tree

SNaQ

Network

How?

Phylogenetic network

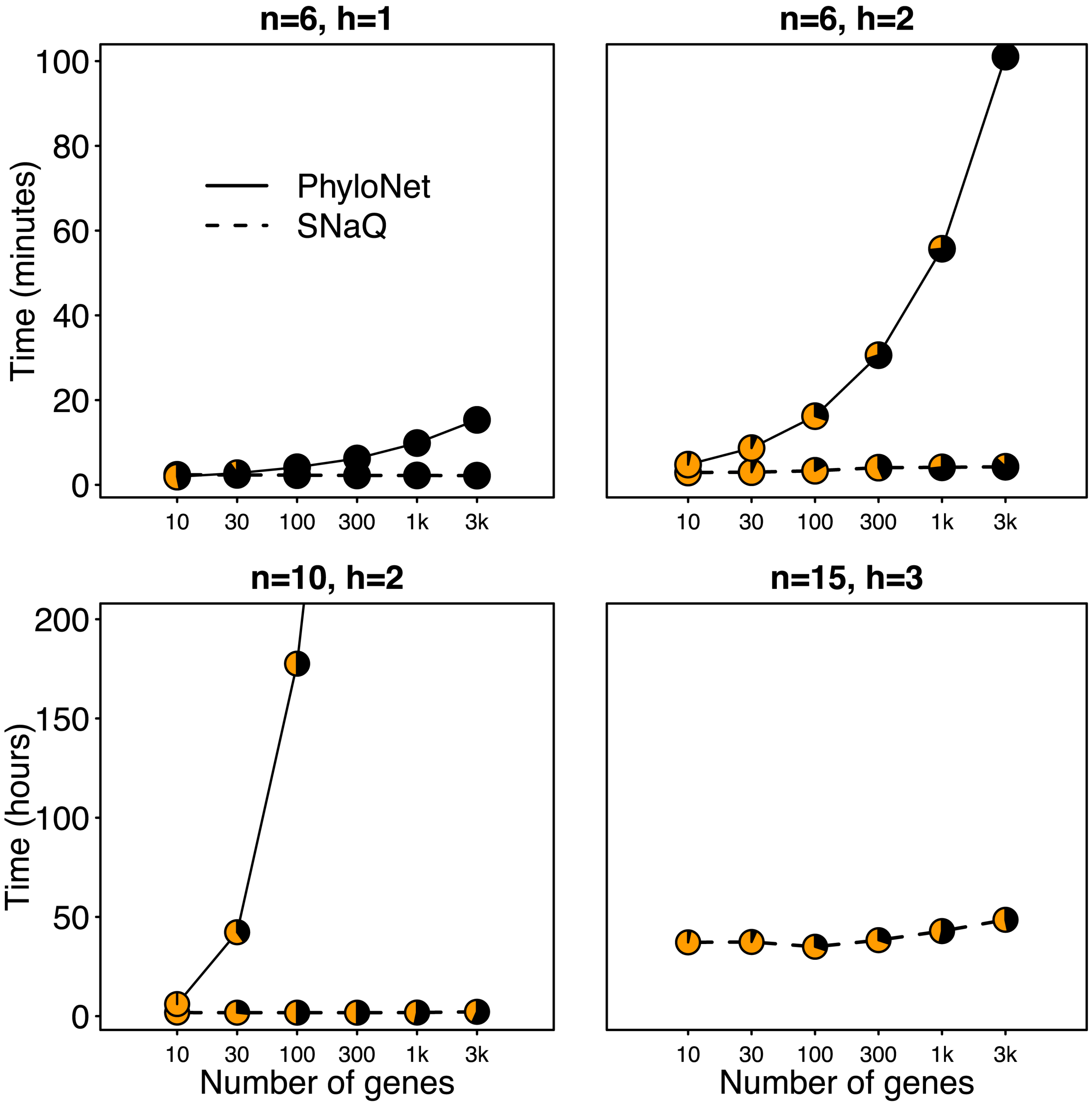


Melisa Olave
SNP2CF

Network challenges

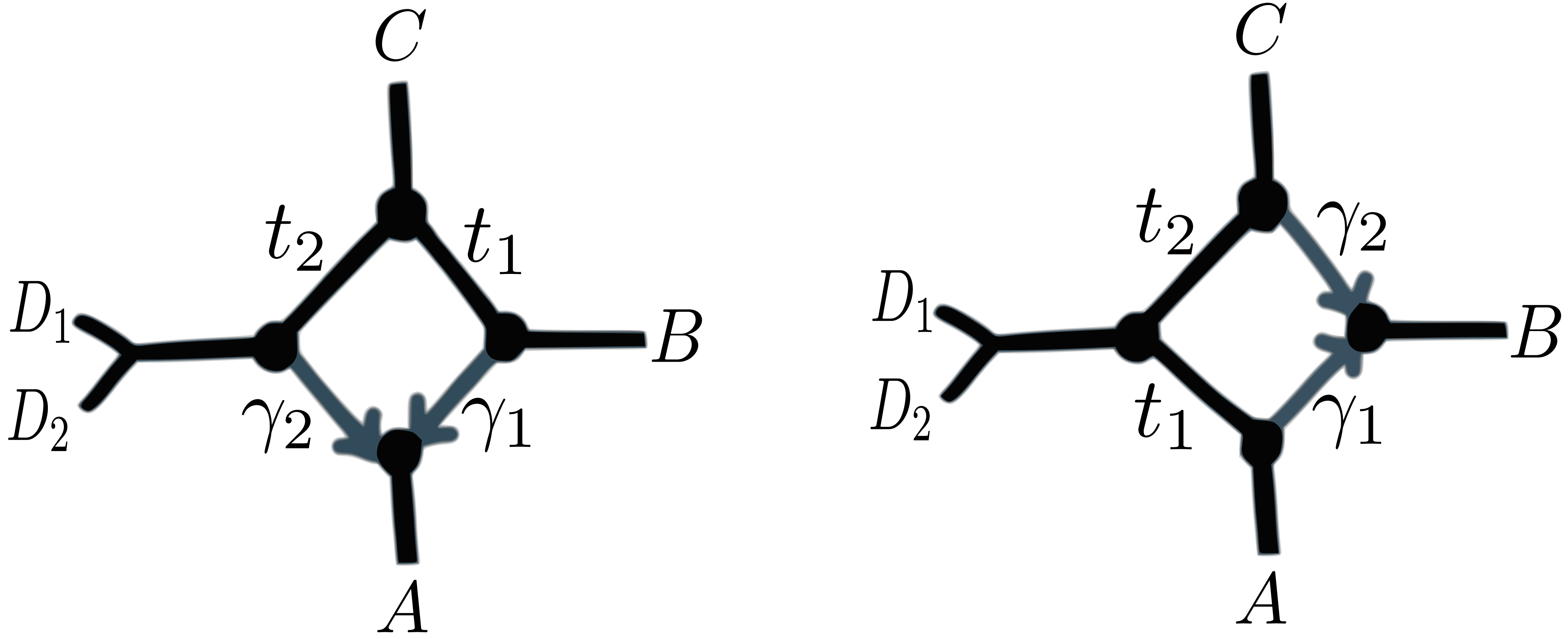
- Scalability
- Identifiability
- Network space
- Network comparison

Scalability gains



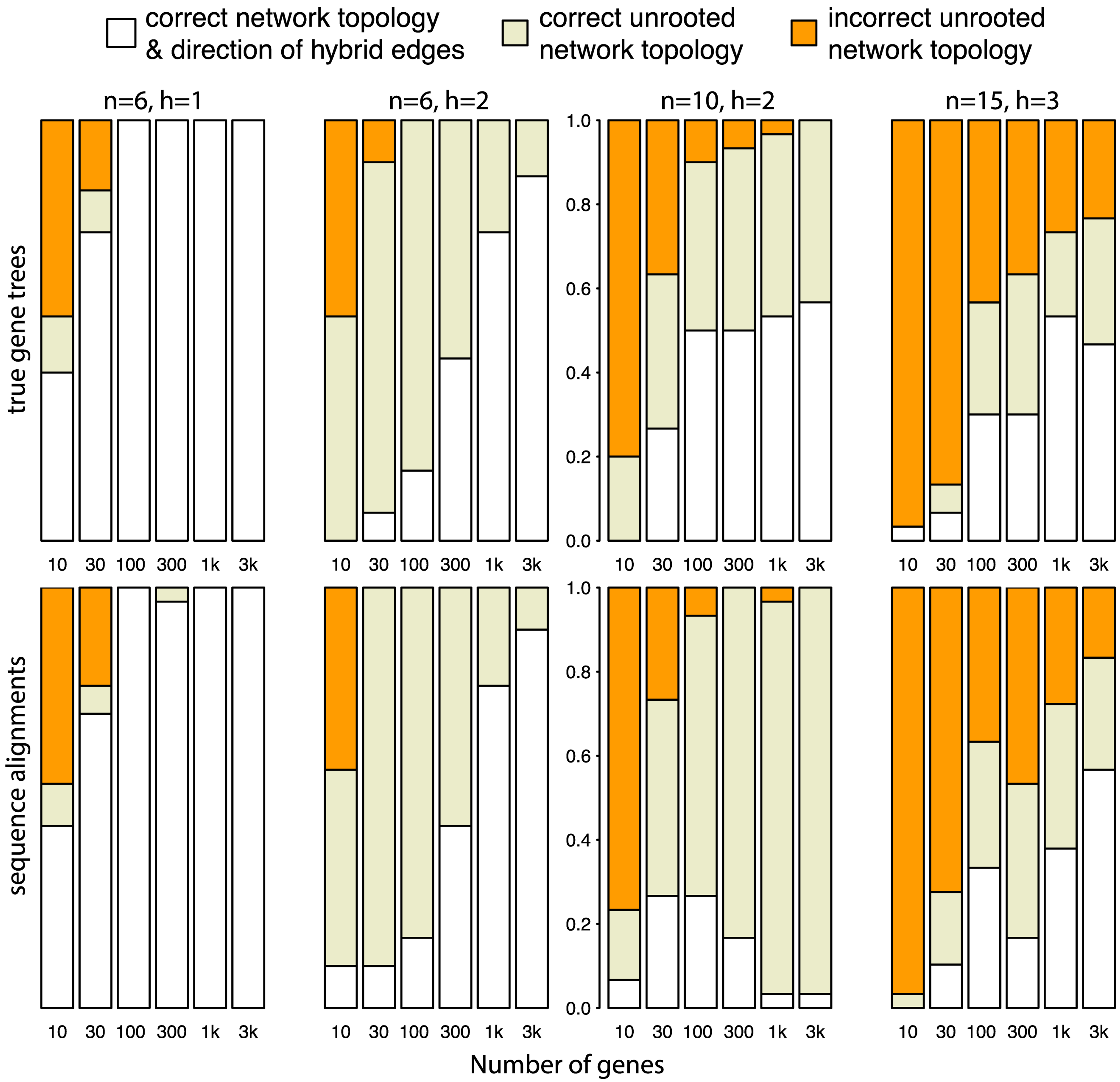
(Solís-Lemus, Ané, 2016, PLoS Genetics)

In practice: flat pseudolikelihood



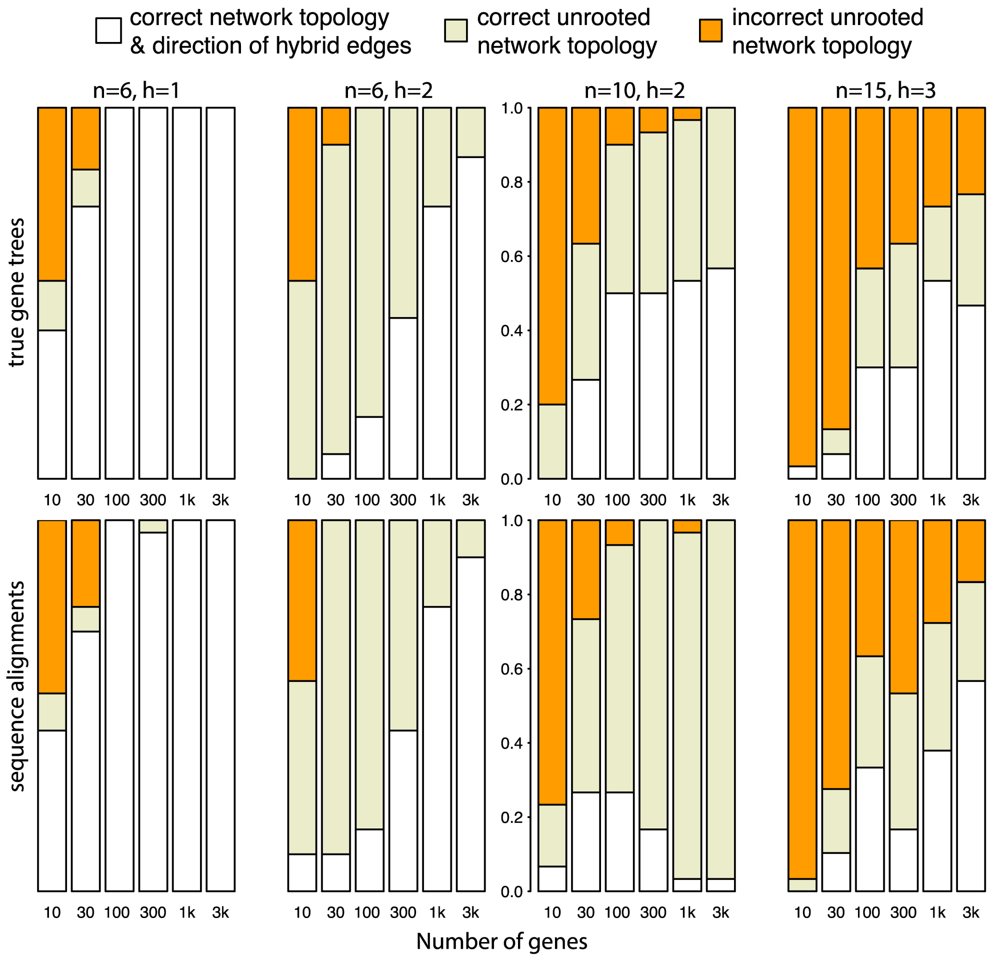
(S.-L., Ané, 2016, PLoS Genetics)

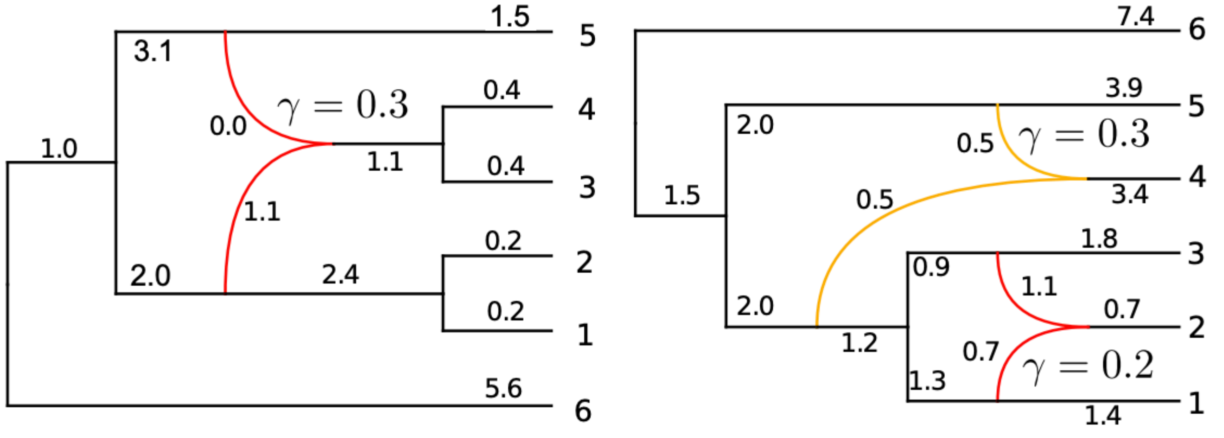
Accuracy



(Solís-Lemus, Ané, 2016, PLoS Genetics)

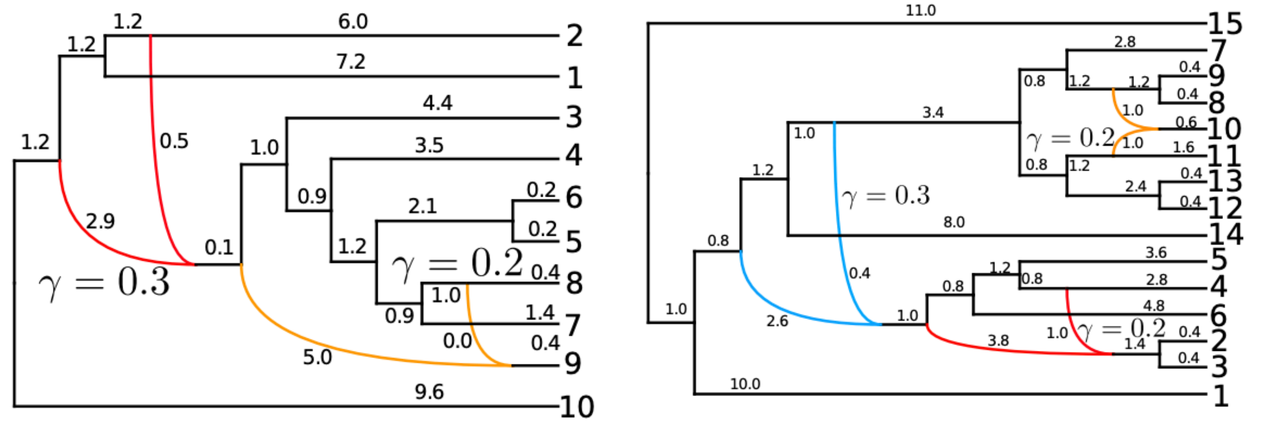
Accuracy





(a) $n = 6$ taxa, $h = 1$ hybridization ($k = 4$)

(b) $n = 6$ taxa, $h = 2$ hybridizations ($k = 4, 4$)

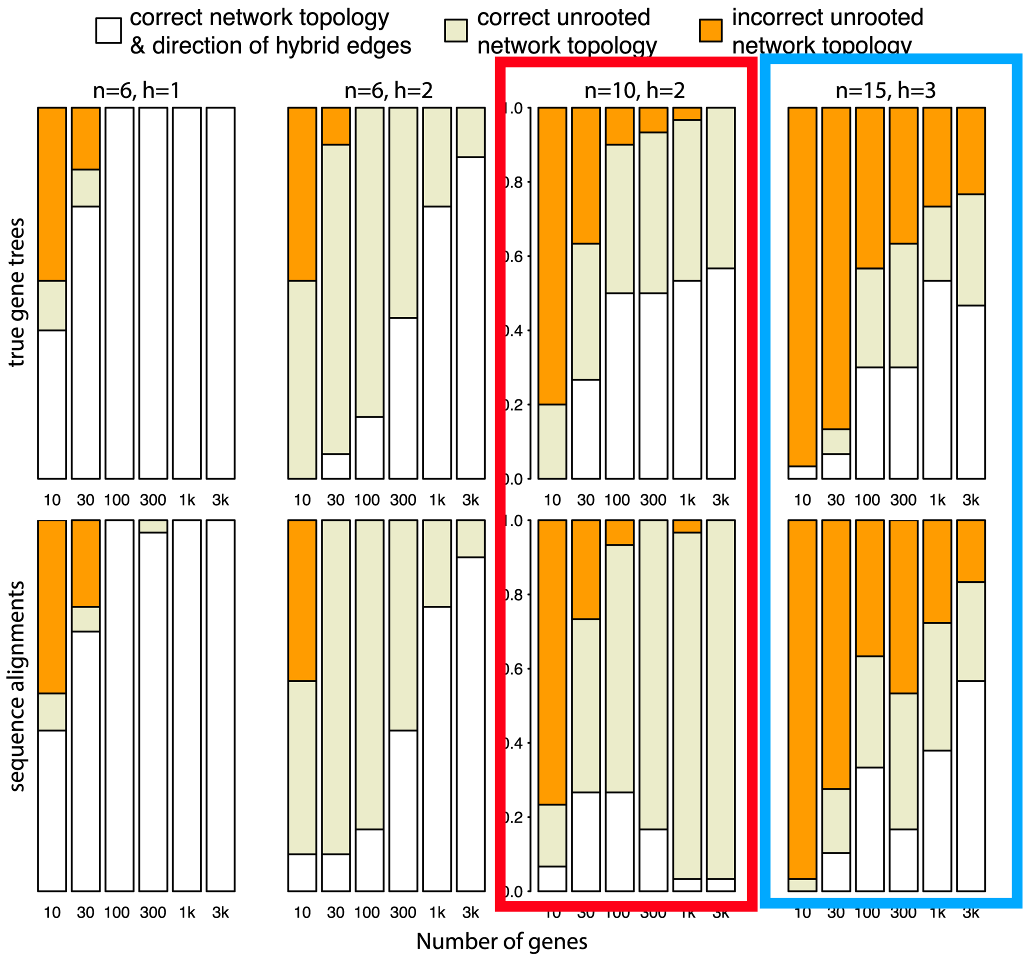


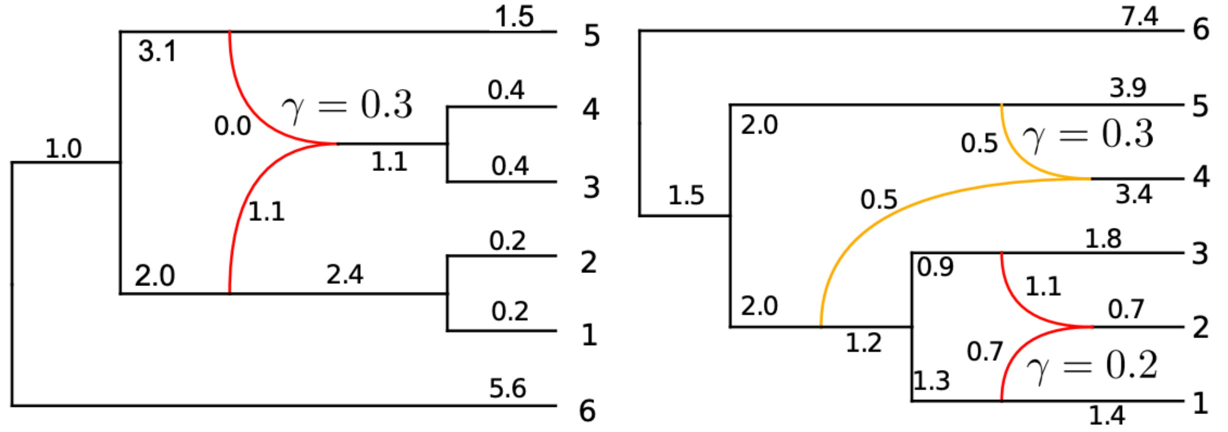
(c) $n = 10$ taxa, $h = 2$ hybridizations ($k = 4, 7$)

(d) $n = 15$ taxa, $h = 3$ hybridizations ($k = 4, 5, 6$)

(Solís-Lemus, Ané, 2016, PLoS Genetics)

Accuracy





(a) $n = 6$ taxa, $h = 1$ hybridization ($k = 4$)

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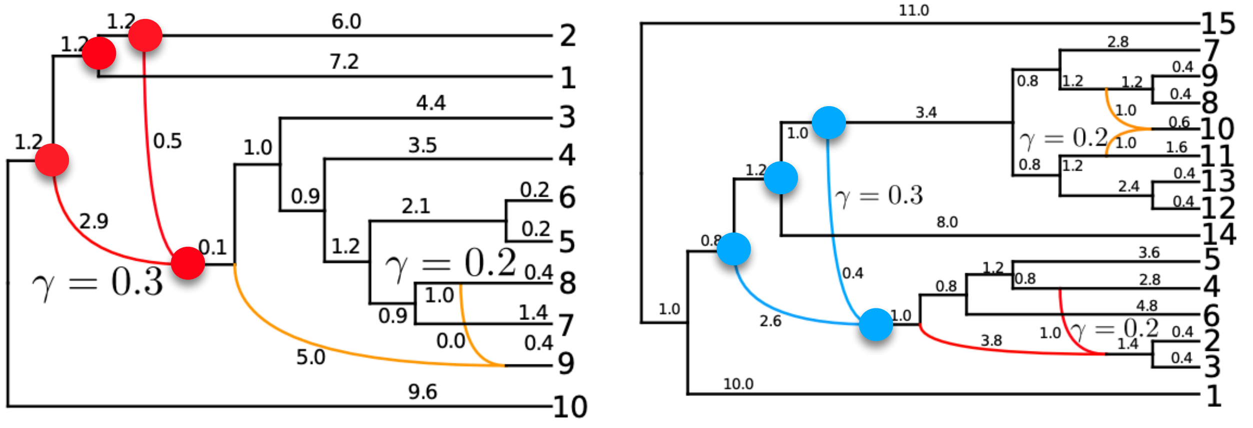
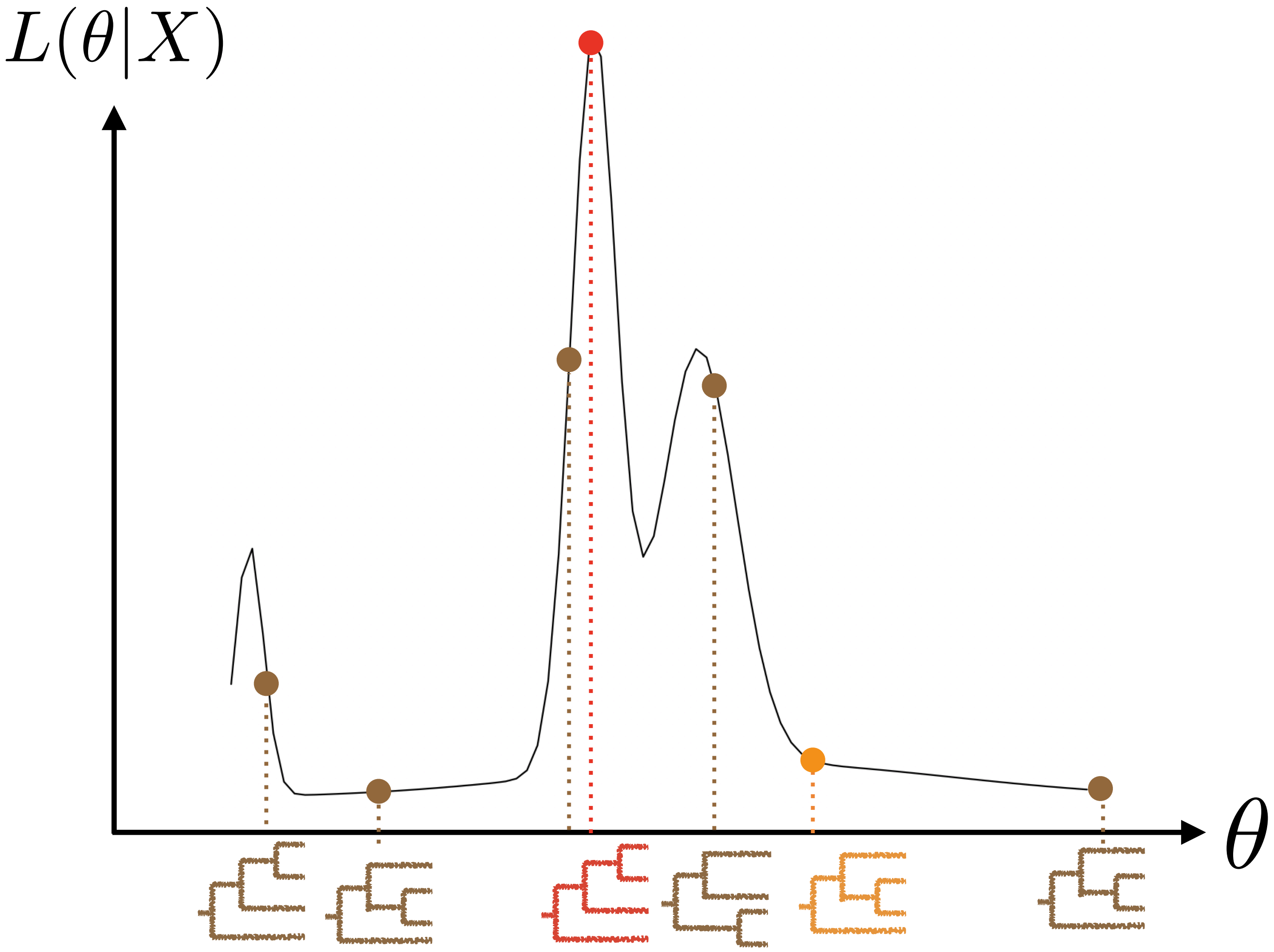


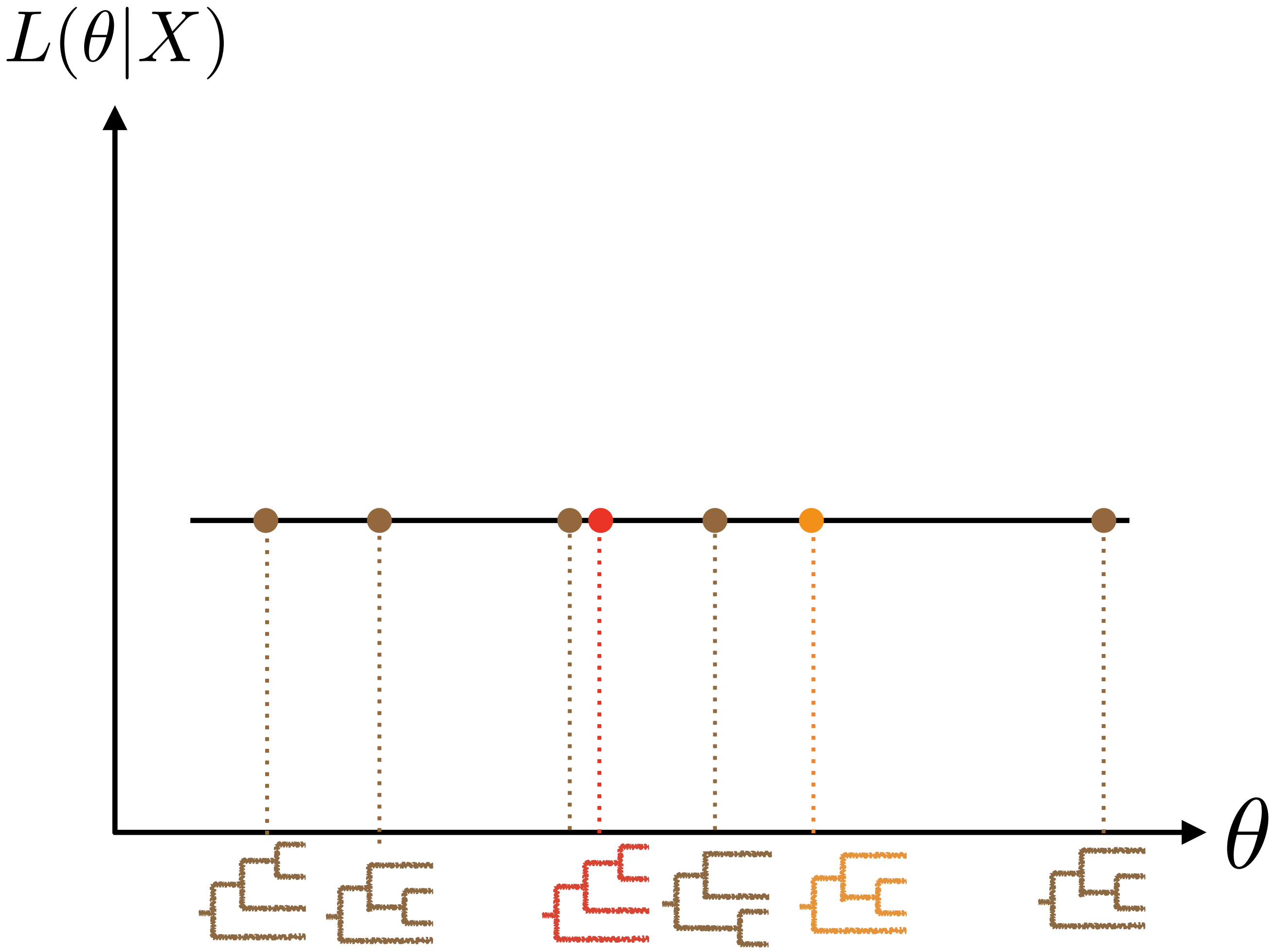
(c) $n = 10$ taxa, $h = 2$ hybridizations ($k = 4, 7$)

(d) $n = 15$ taxa, $h = 3$ hybridizations ($k = 4, 5, 6$)

(Solís-Lemus, Ané, 2016, PLoS Genetics)

Identifiability





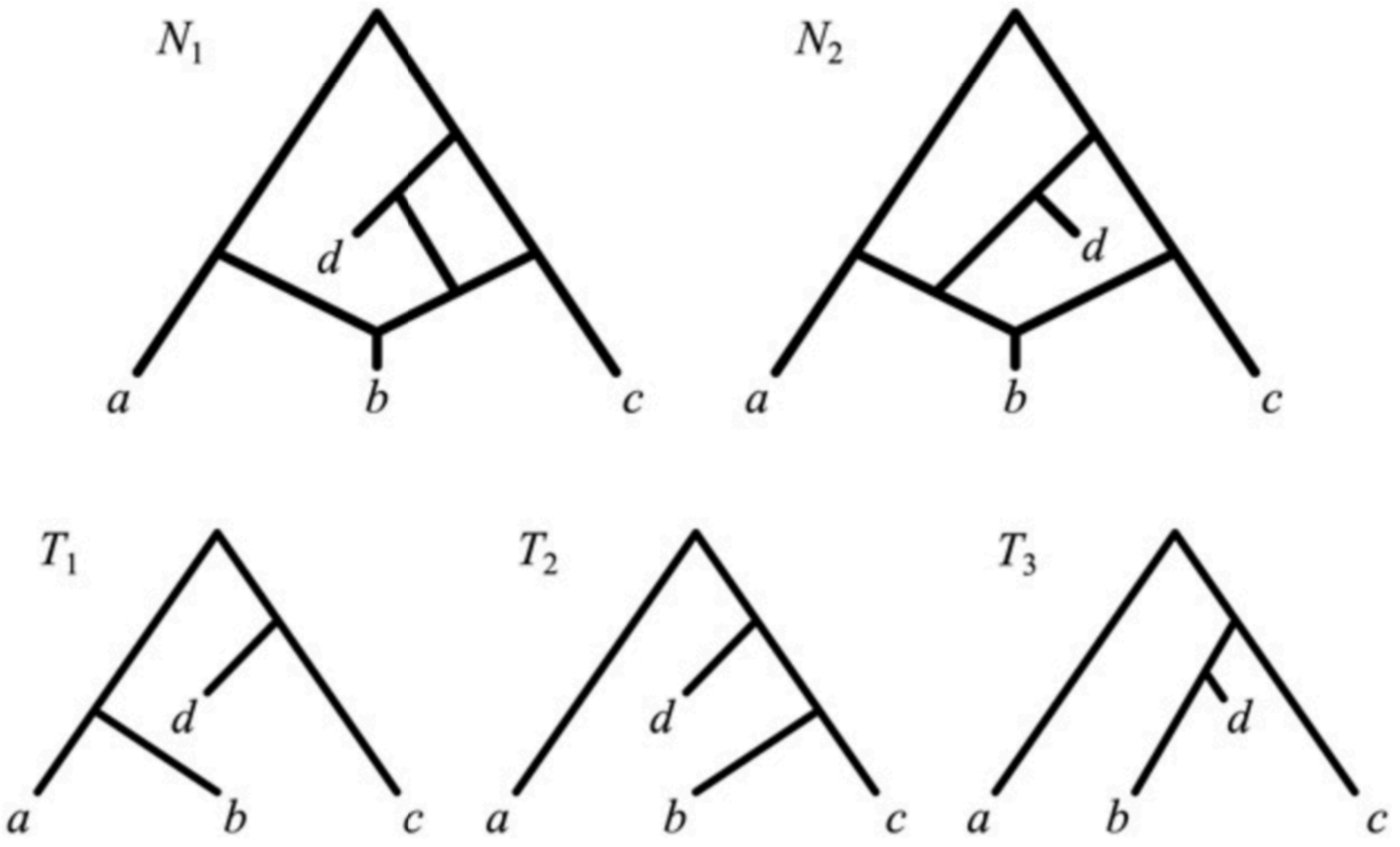
PLOS | COMPUTATIONAL BIOLOGY

RESEARCH ARTICLE

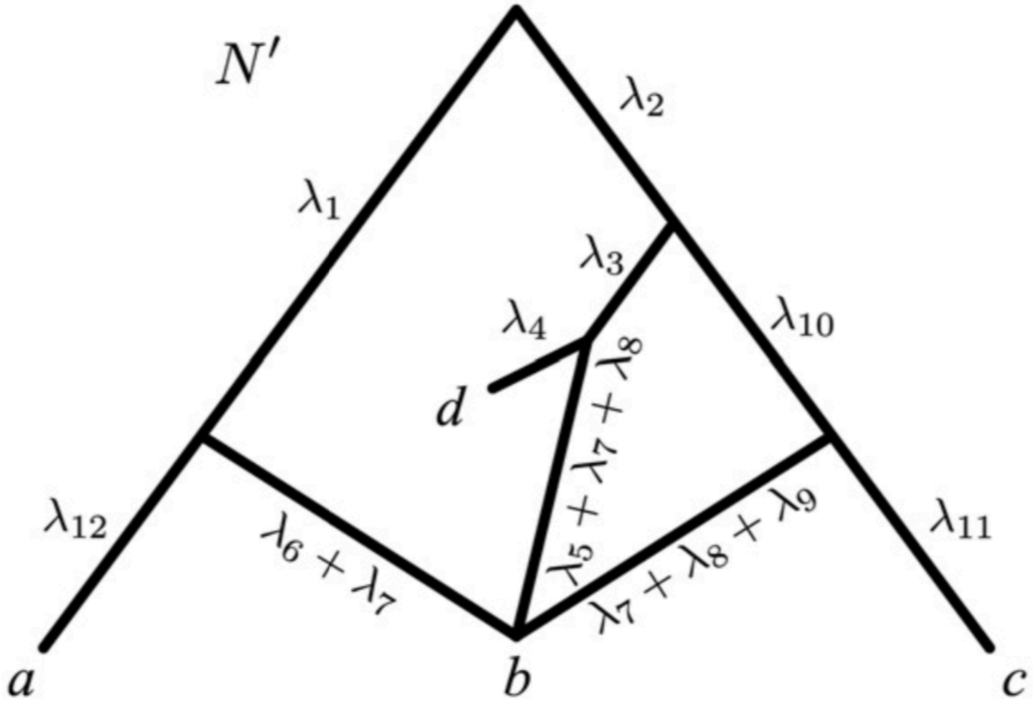
Reconstructible Phylogenetic Networks: Do Not Distinguish the Indistinguishable

Fabio Pardi[1,3]*, **Celine Scornavacca**[2,3]

1 Laboratoire d'Informatique, de Robotique et de Microélectronique de Montpellier (LIRMM, UMR 5506) CNRS, Université de Montpellier, France, **2** Institut des Sciences de l'Evolution de Montpellier (ISE-M, UMR 5554) CNRS, IRD, Université de Montpellier, France, **3** Institut de Biologie Computationnelle, Montpellier, France



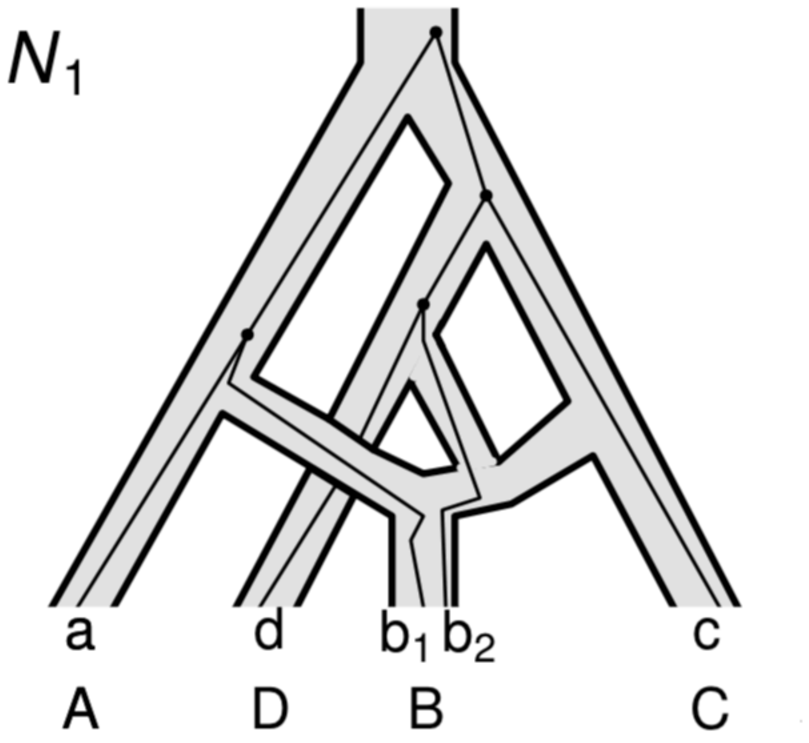
Undistinguishable with the “displayed trees” criterion

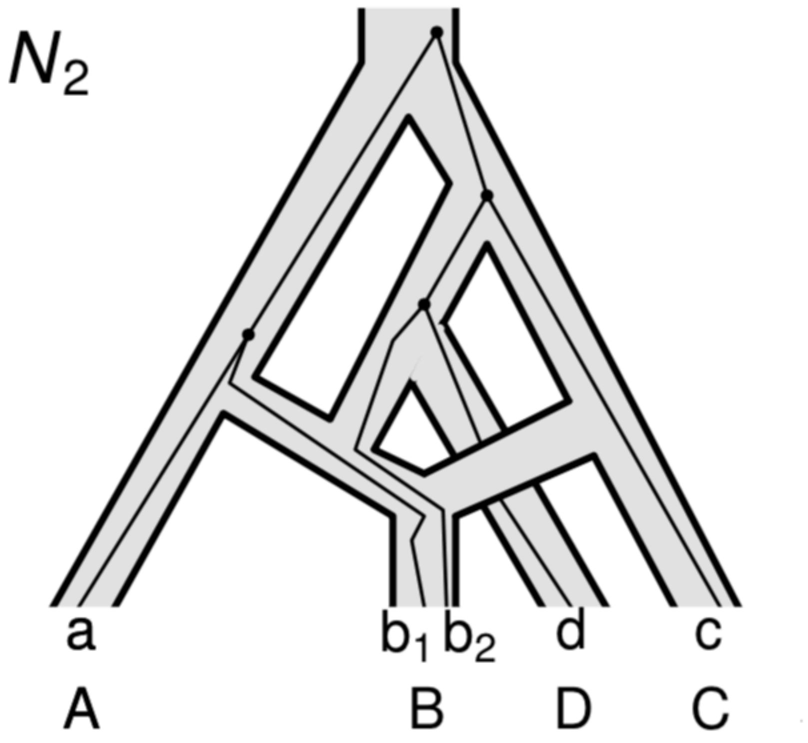


Solution: Canonical network (“unzipped”)

Displayed Trees Do Not Determine Distinguishability Under the Network Multispecies Coalescent

Sha Zhu[1], James H. Degnan[2]

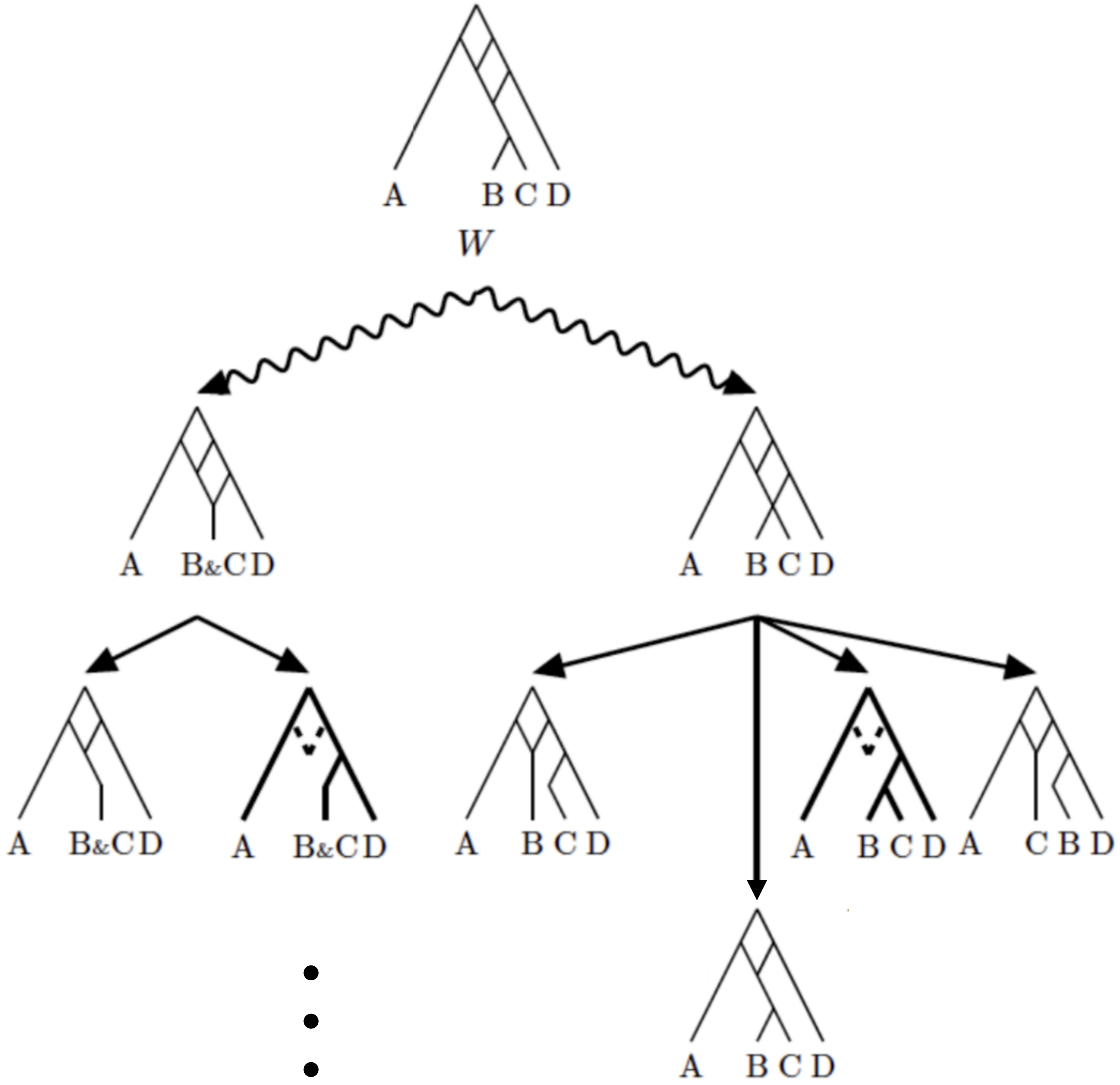




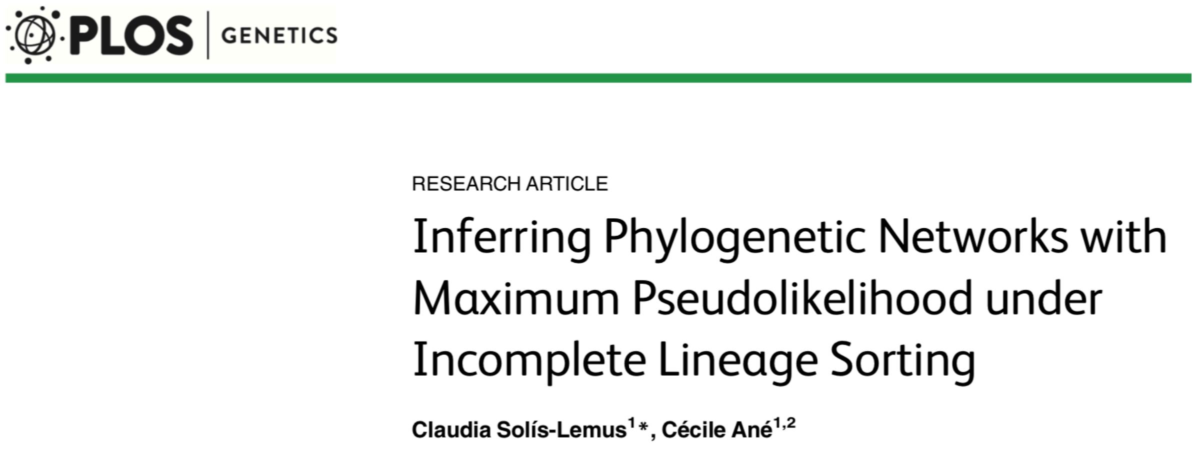
Distinguishable under the MSC

Displayed Trees Do Not Determine Distinguishability Under the Network Multispecies Coalescent

Sha Zhu[1], James H. Degnan[2]



Decomposing network in **parental** trees



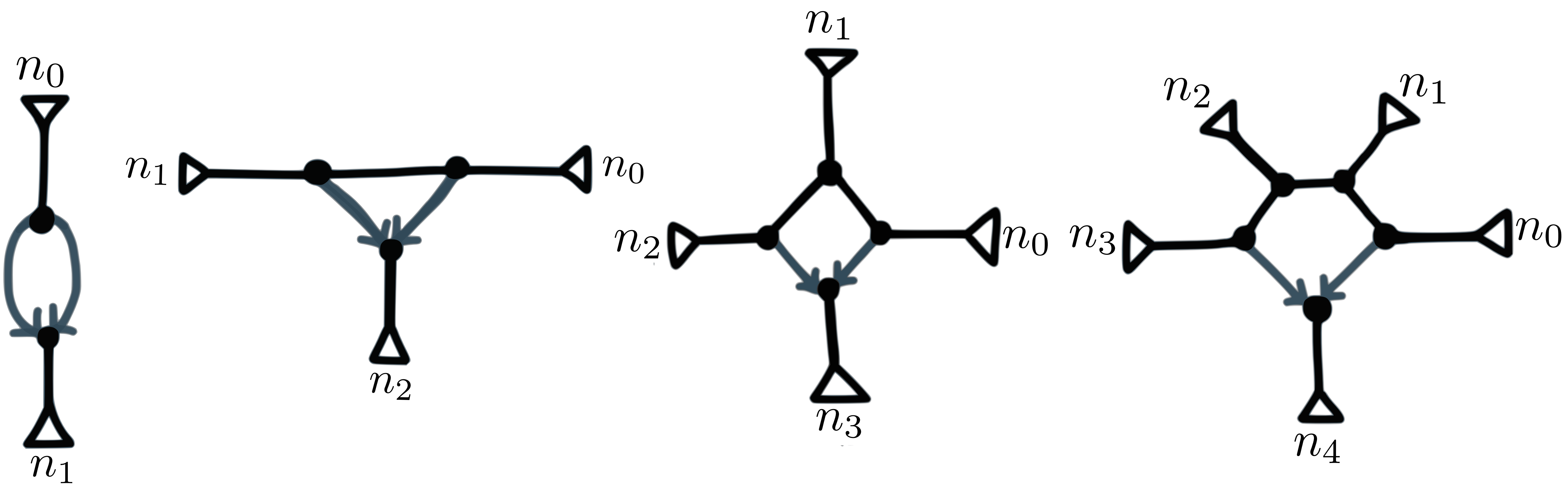
PLOS | GENETICS

RESEARCH ARTICLE

Inferring Phylogenetic Networks with Maximum Pseudolikelihood under Incomplete Lineage Sorting

Claudia Solís-Lemus[1]*, Cécile Ané[1,2]

Can we detect the presence of hybridization in level-1 networks?



No

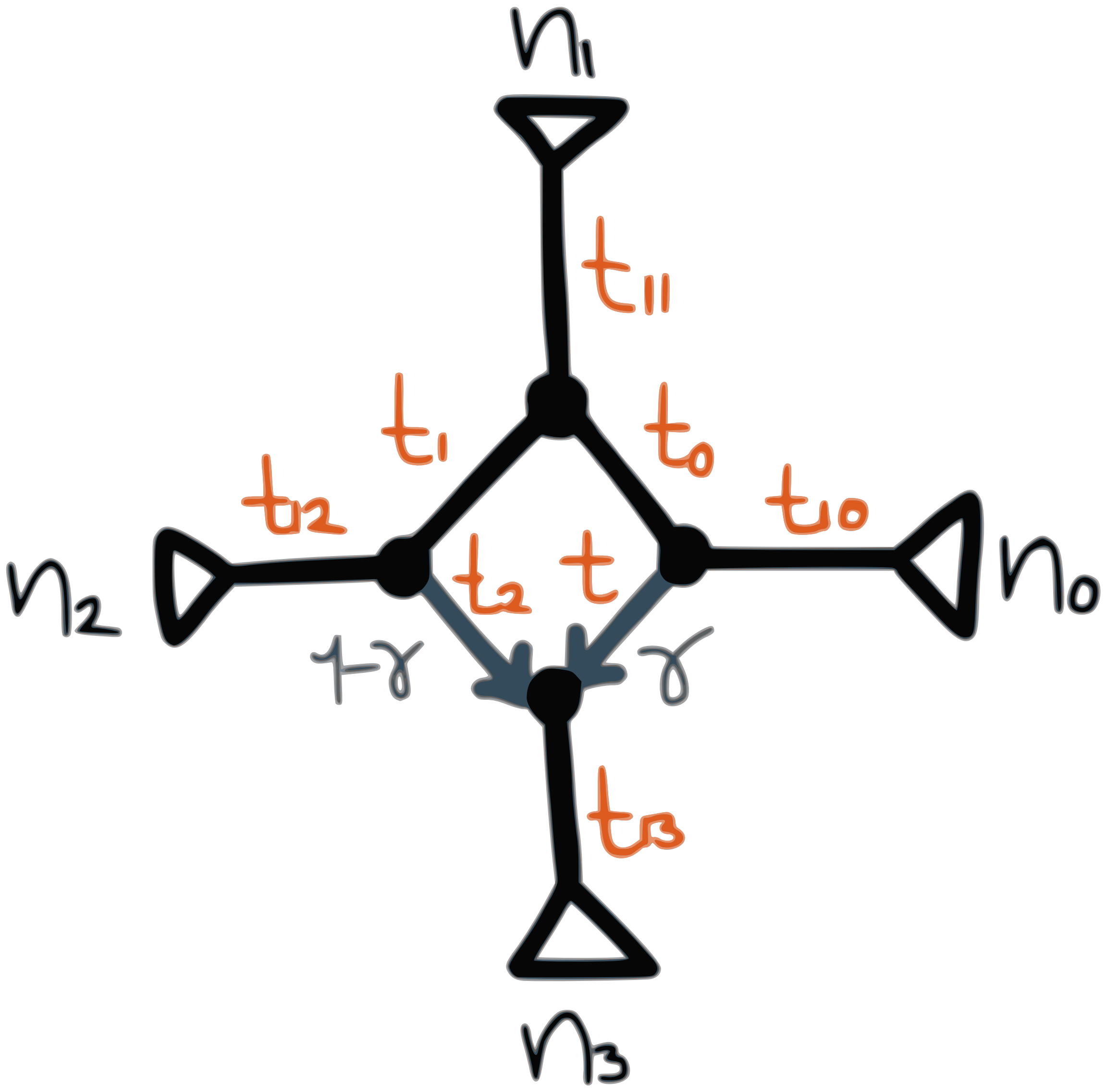
Yes $(n_i, n_j \geq 2)$

Yes $(n_i \geq 2)$

Yes

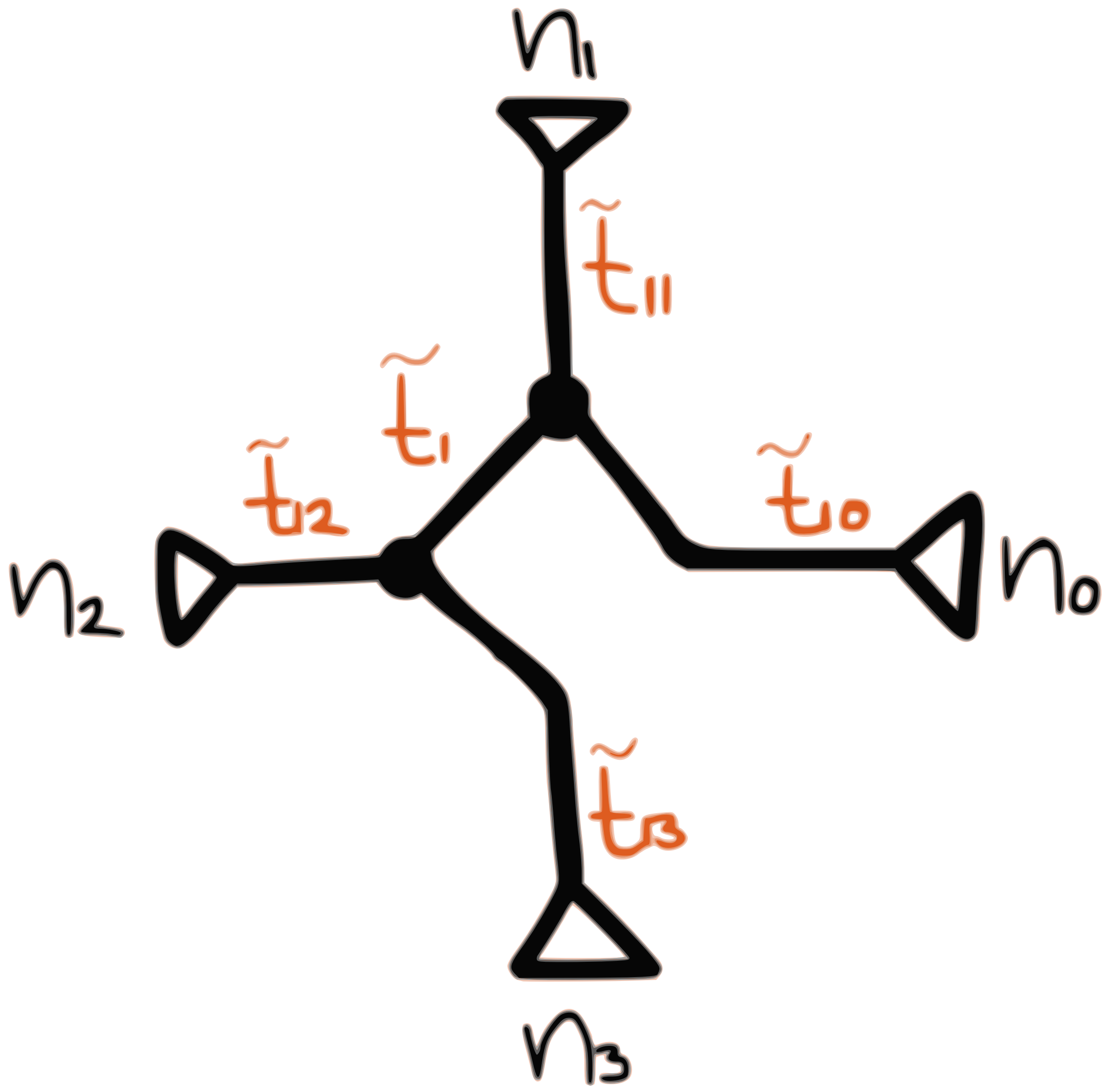
Generic Identifiability $t_i \in (0, \infty), \gamma \in (0, 1)$

Idea of proof of identifiability: hybridization



System of equations

$\{CF_{network}\}$



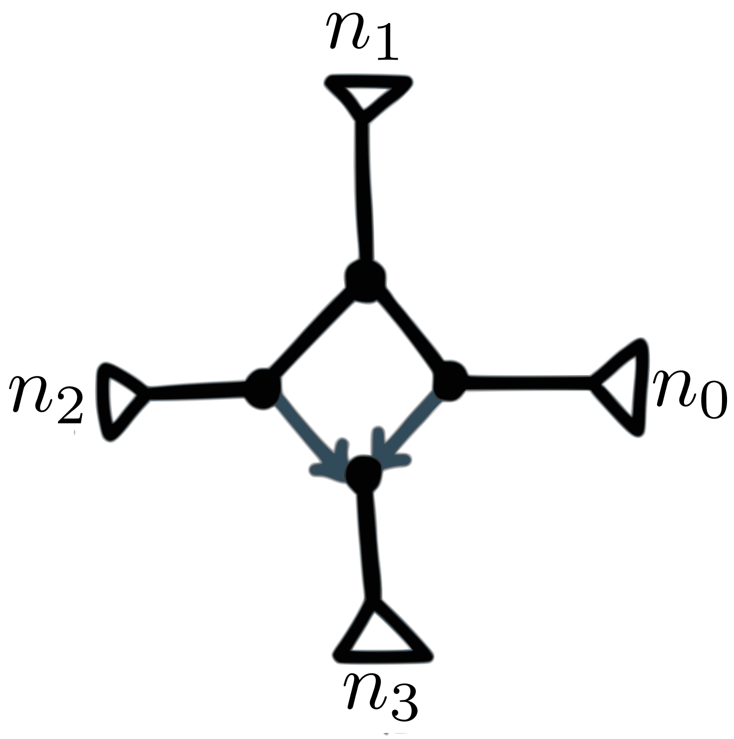
System of equations

$\{CF_{tree}\}$

(Solís-Lemus & Ané, 2016;
Solís-Lemus et al, 2020)

Can we detect the presence of hybridization in level-1 networks?

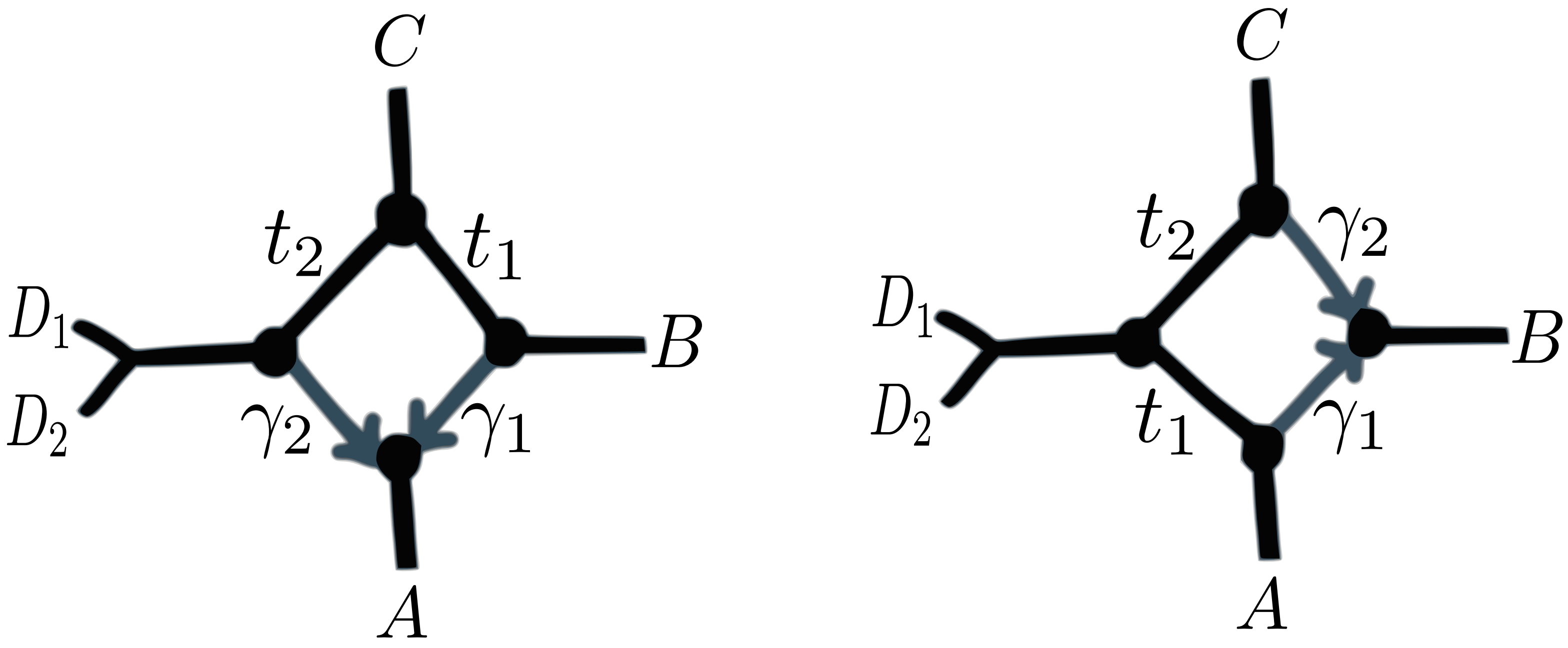
In theory



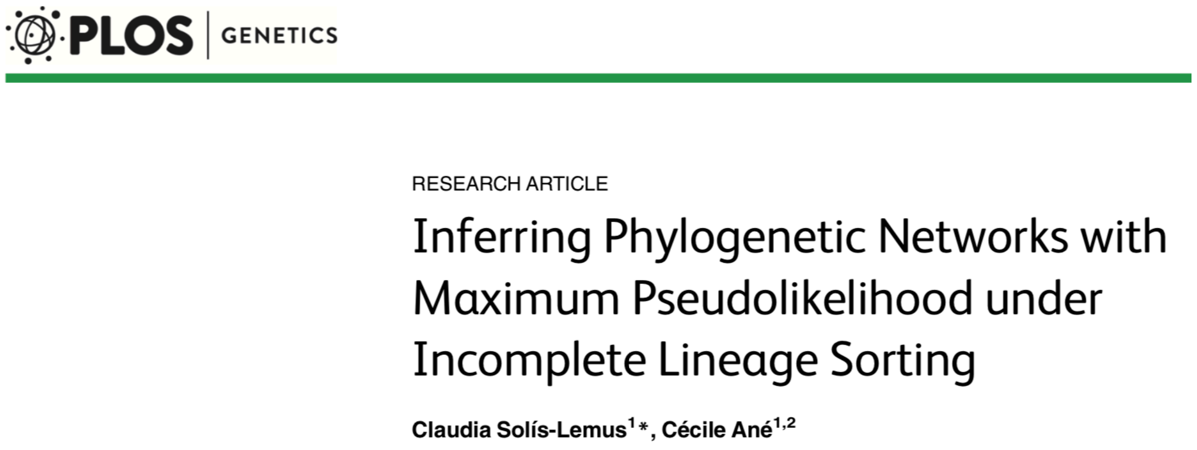
Yes

$(n_i \geq 2)$

In practice



Sometimes

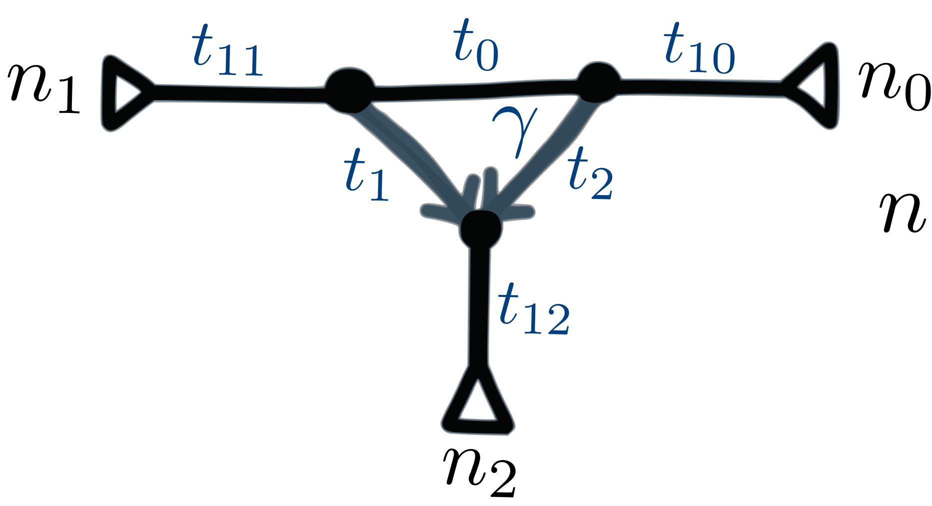

PLOS | GENETICS

RESEARCH ARTICLE

Inferring Phylogenetic Networks with Maximum Pseudolikelihood under Incomplete Lineage Sorting

Claudia Solís-Lemus[1]*, Cécile Ané[1,2]

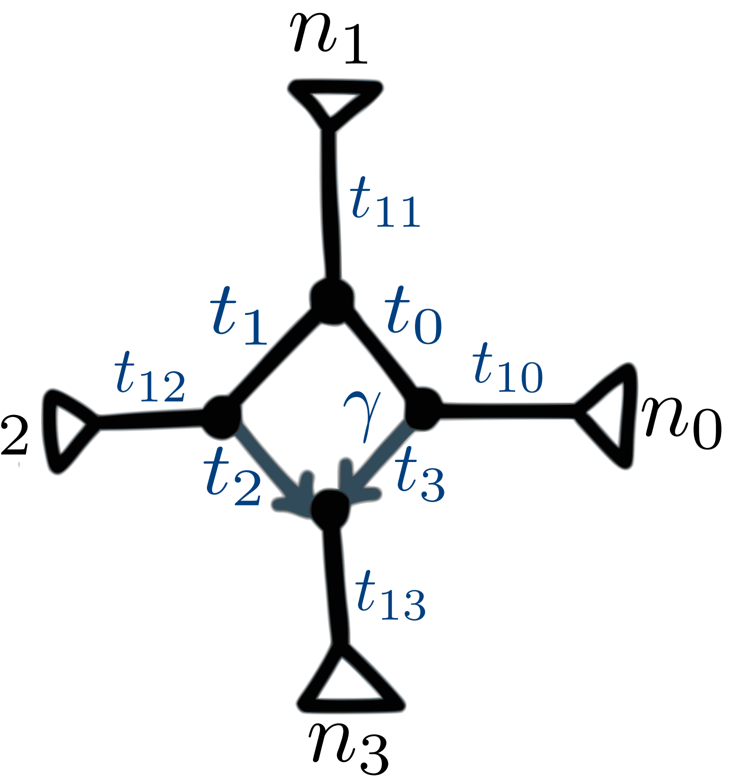
Can we estimate numerical parameters?



No

Good triangle

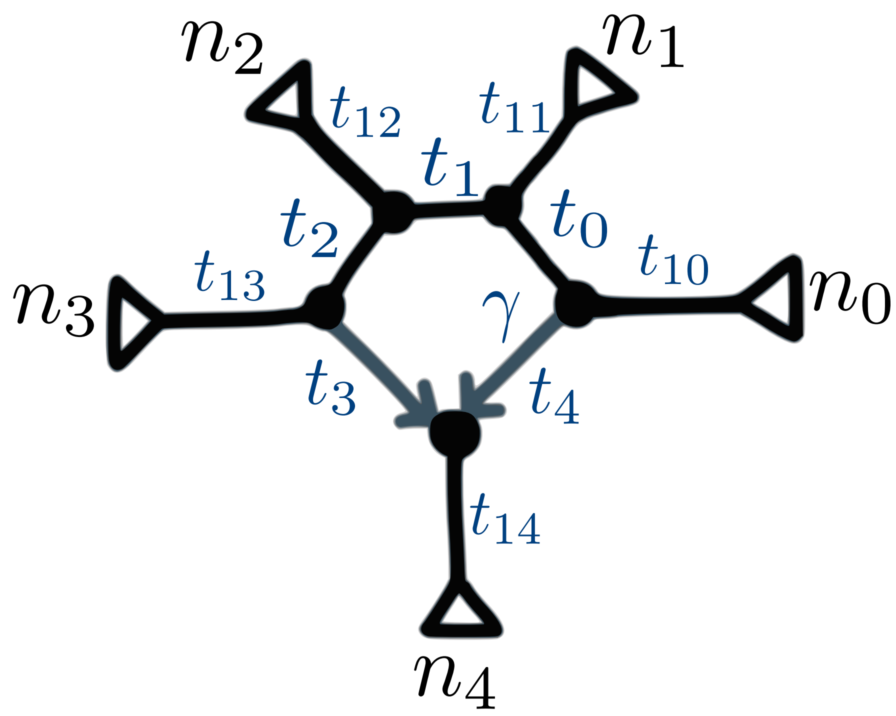
$(t_{12} = 0)$



Yes

Good diamond

$(n_0, n_2 \geq 2)$



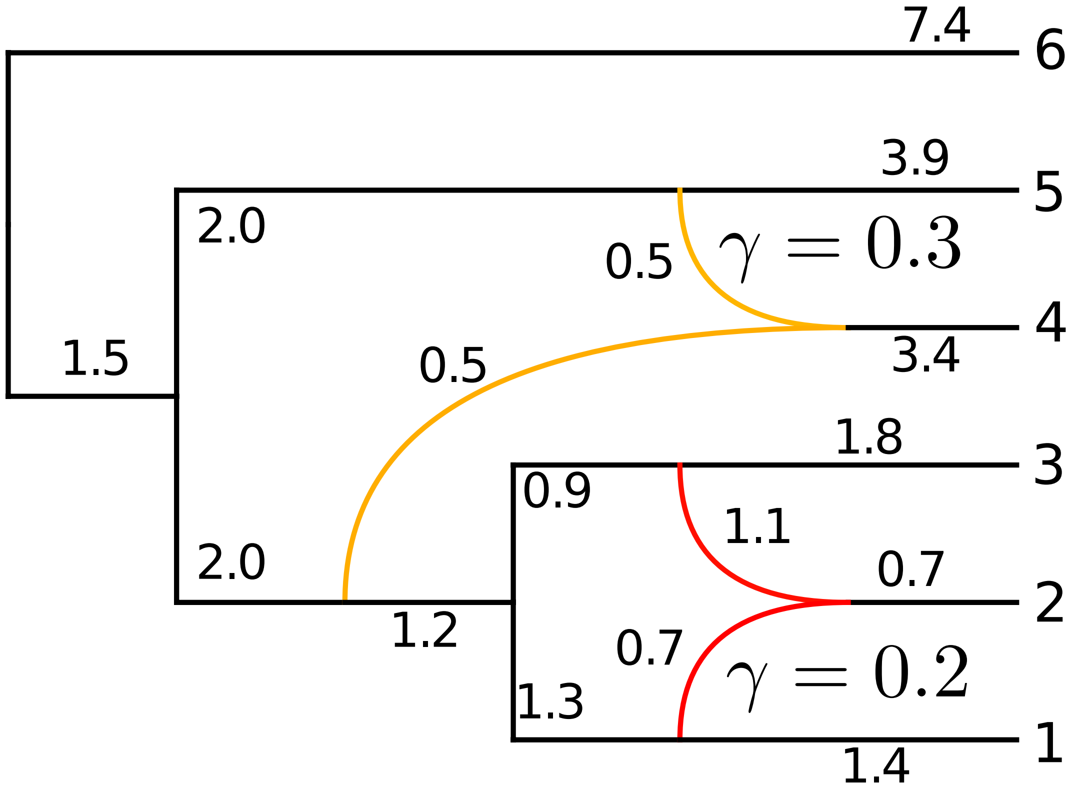
Yes

Generic Identifiability

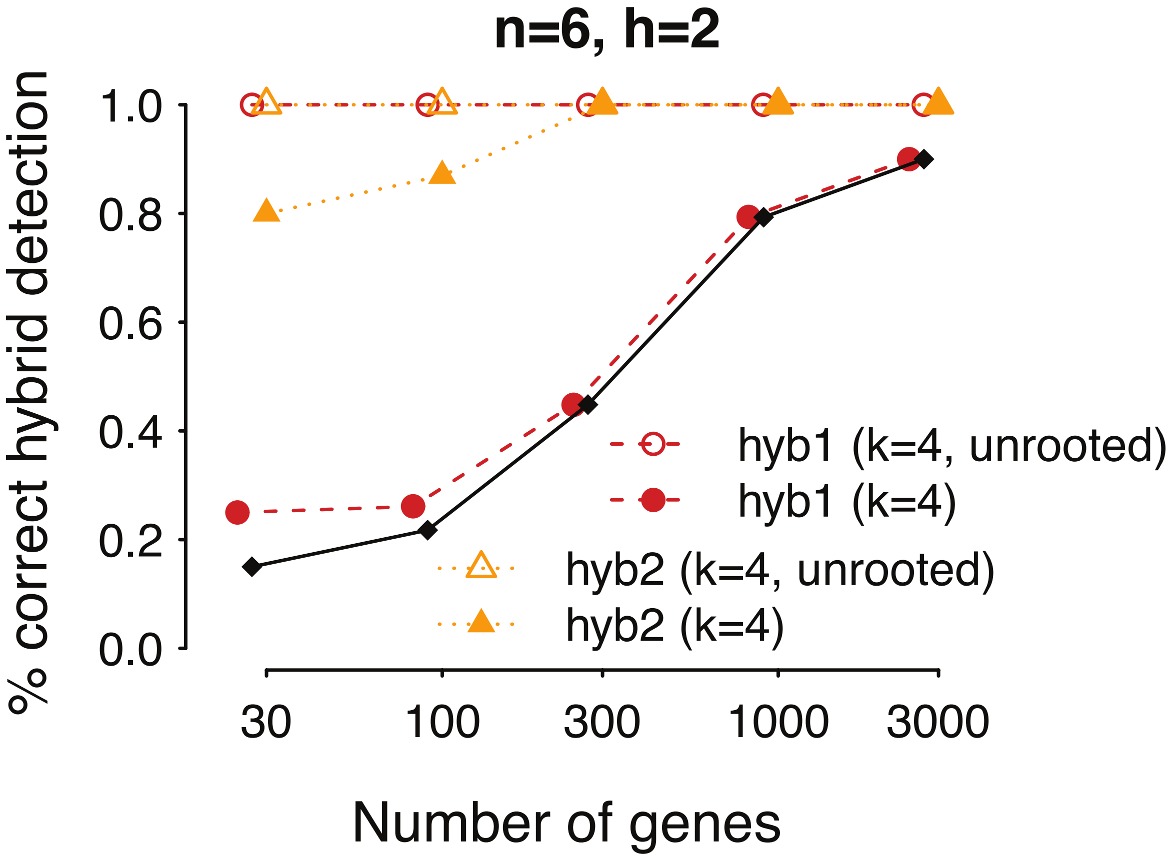
$t_i \in (0, \infty), \gamma \in (0, 1)$

Identifiability matters: SNaQ performance

Good diamond



Bad diamond



(S.-L., Ané, 2016, PLoS Genetics)

Network challenges

- Scalability
- Identifiability
- Network space
- Network comparison

Displayed vs Parental trees
Level-1 semi-directed networks
Hybridizations: case by case
Missing: likelihood, level-k semi-directed

Network challenges

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K. Huber, V. Moulton, C. Scornavacca,...
Missing: path through tree space, semi-directed

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Level-1 semi-directed networks
Hybridizations: case by case
Missing: likelihood, level-k semi-directed

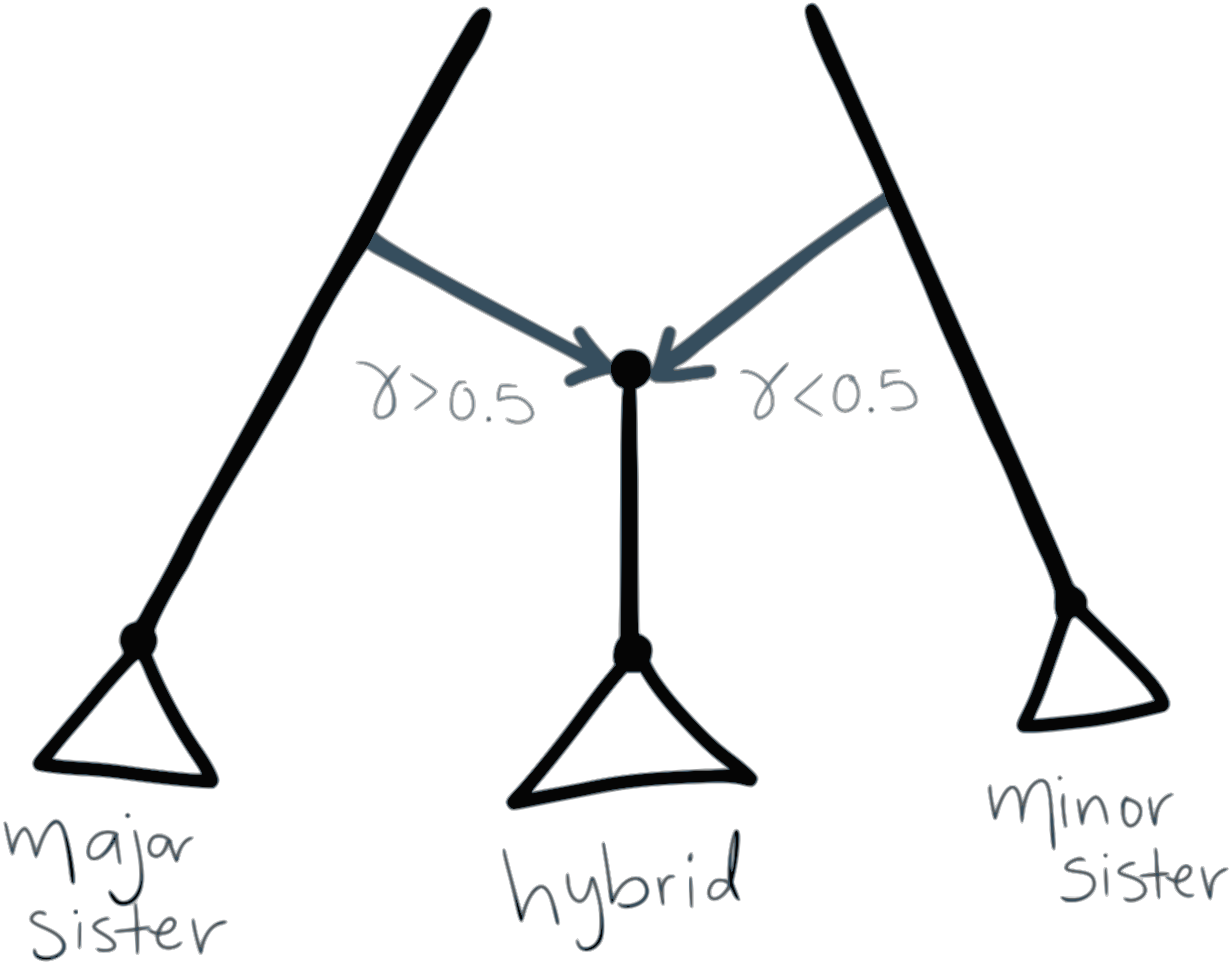
- Network space

K. Huber, V. Moulton, C. Scornavacca,…
Missing: path through tree space, semi-directed

- Network comparison

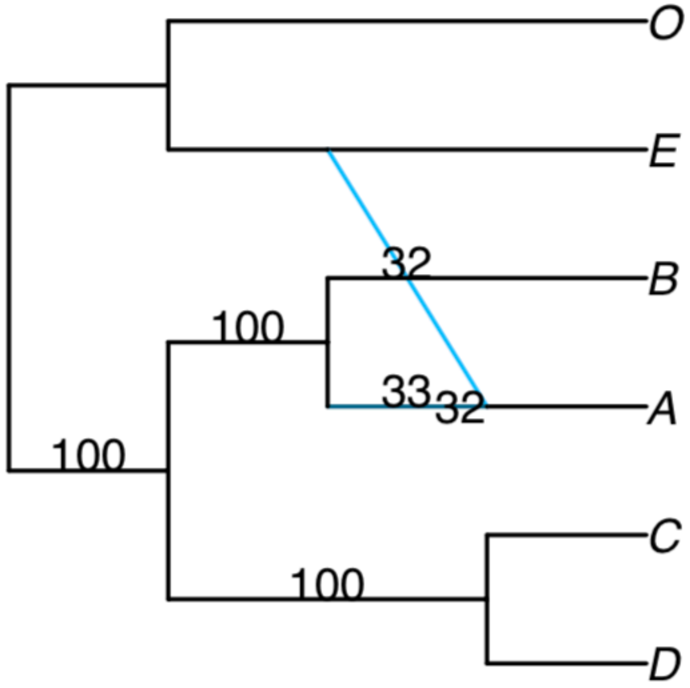
Missing: distance function
Hardwired-cluster distance only for rooted networks
Summary of networks: clades!

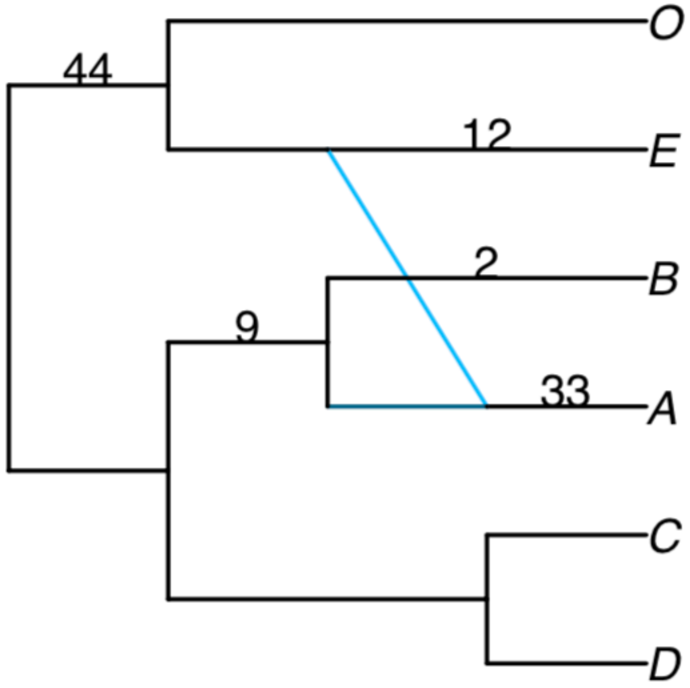
Network summary



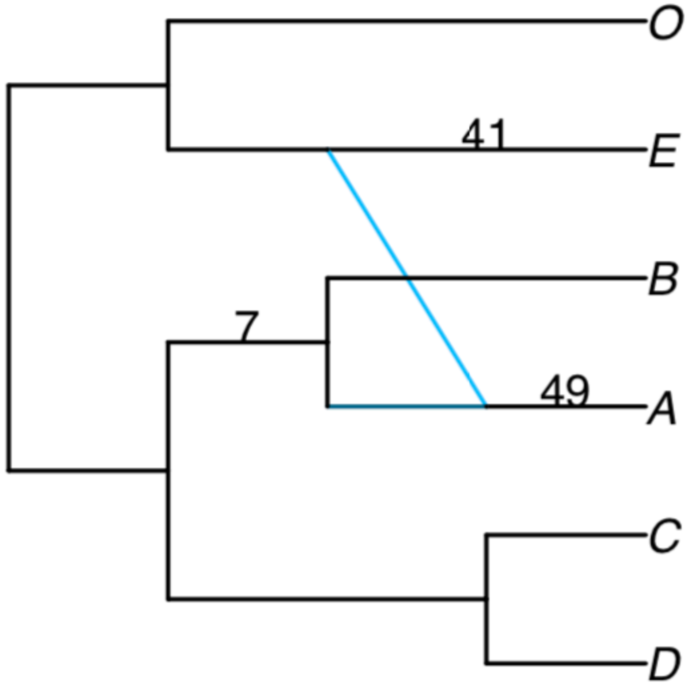
(S.-L. et al, 2017, MBE)

Network summary





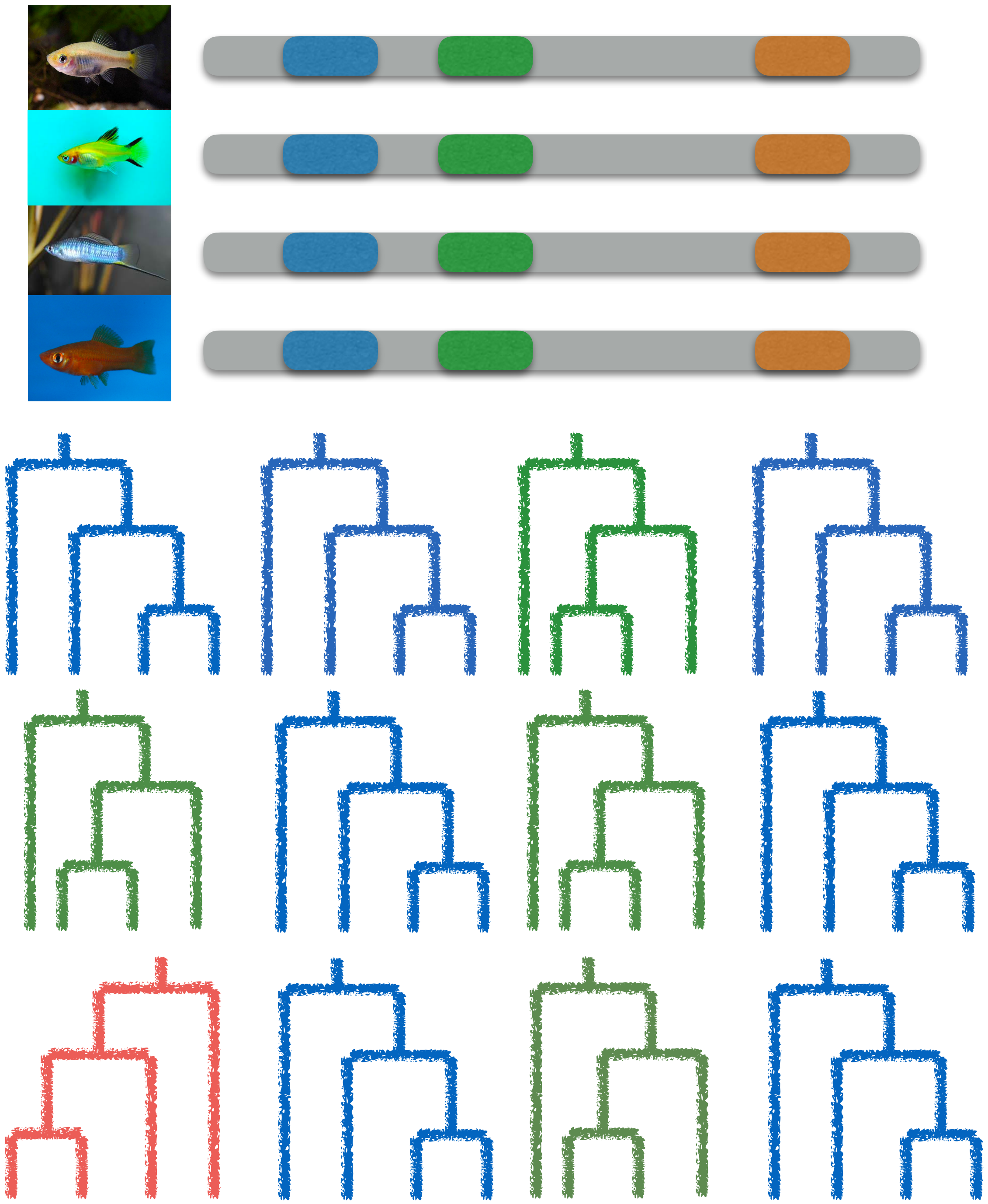
Hybrid clades



Minor sister clades

When?

Phylogenetic network



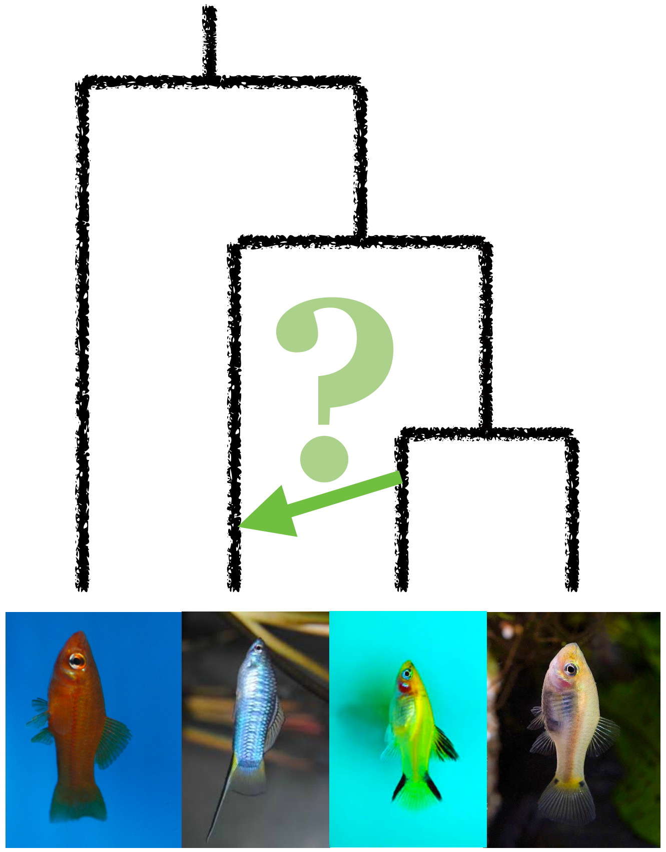
Data

Goodness-of-fit test

Hypothesis test:
Is a tree a good fit?

TICR

GitHub



`https://github.com/nstenz/TICR`

(Stenz et al, 2015, Syst Bio)

Practical advice

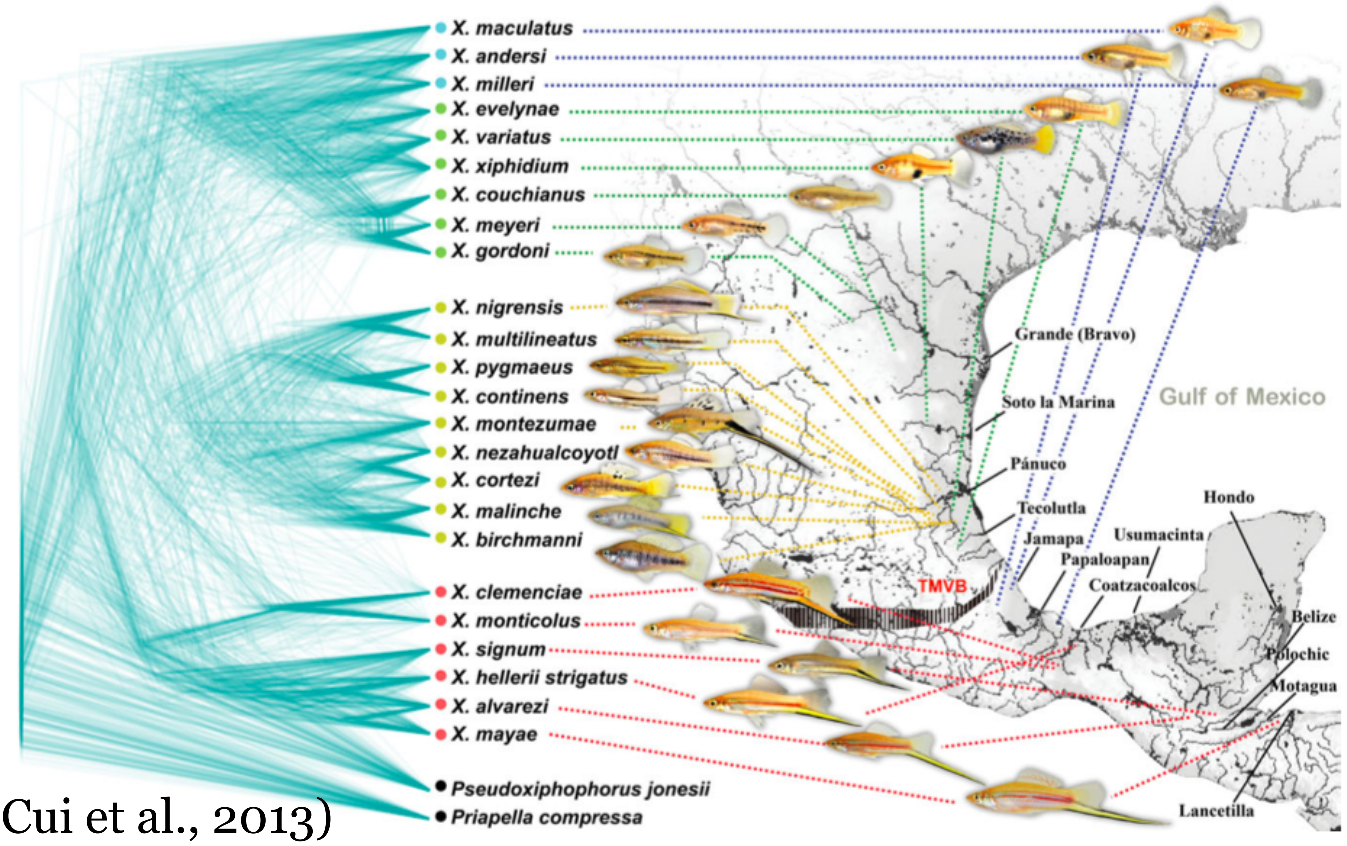
- Do multiple runs
- Do bootstrap
- Check the .networks output file (especially if hybridization conflicts with outgroup)
    - Choice of outgroup important!
- What is the quality of my input data (gene trees/CFs)?

Practical advice

- Do multiple runs
- Do bootstrap
- Check the .networks output file (especially if hybridization conflicts with outgroup)
  - Choice of outgroup important!
- What is the quality of my input data (gene trees/CFs)?

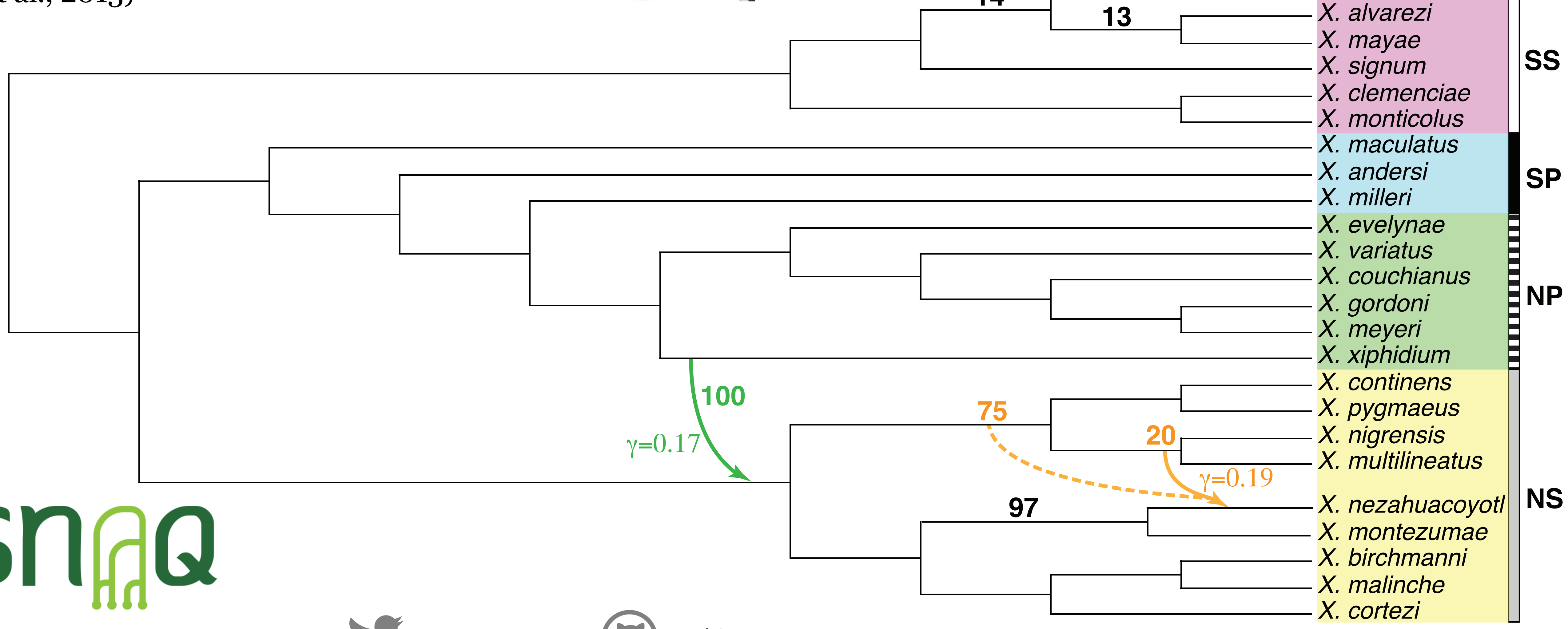
When to stop?
(Cai and Ané, 2020)

1183 genes, 24 swordtails and platyfish



(Cui et al., 2013)

Xiphophorus fish data

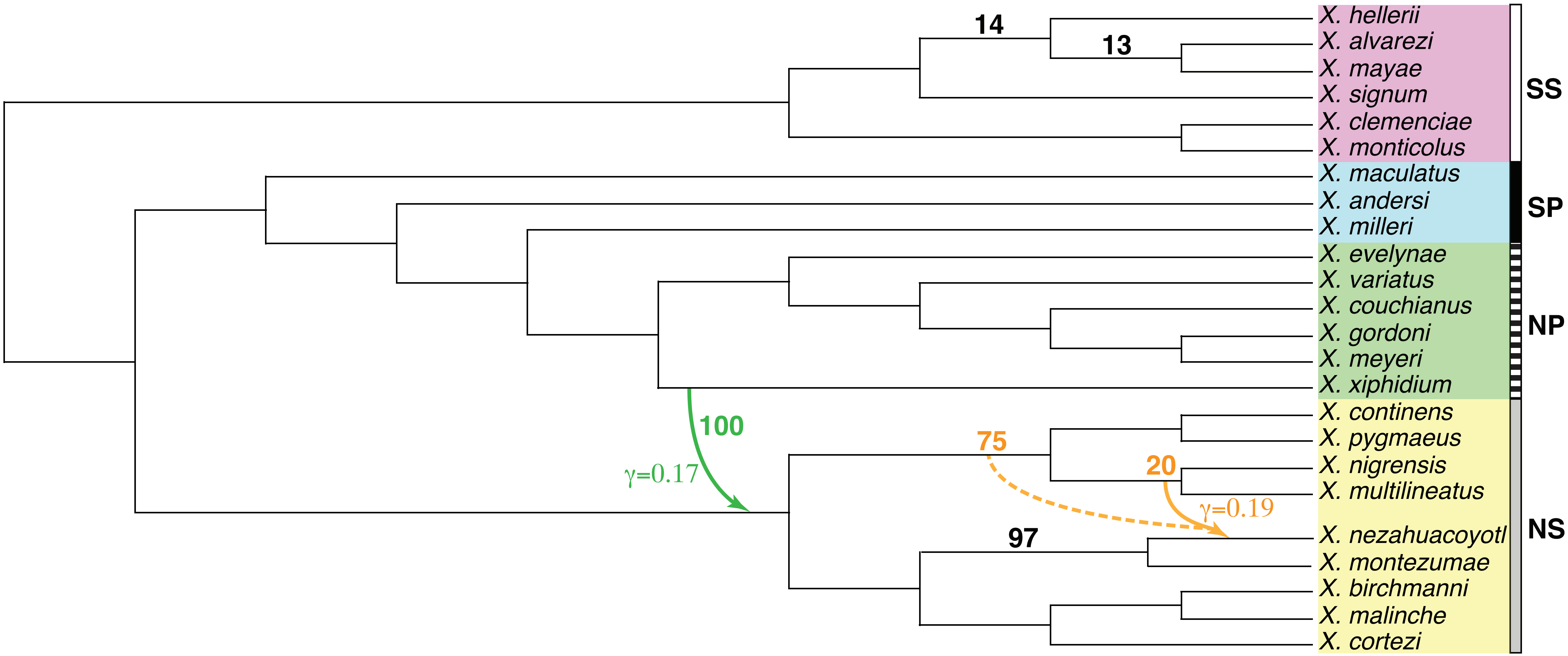


(Solís-Lemus, Ané, 2016, PLoS Genetics)

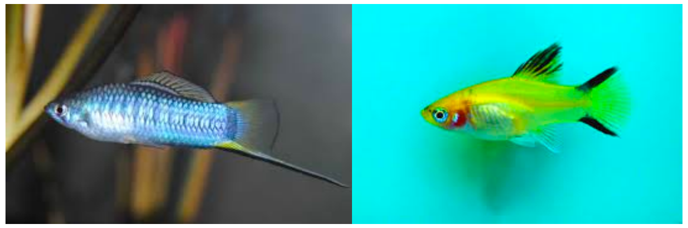
http://solislemuslab.github.io/ @solislemuslab crsl4

Part II

I have the network, now what?



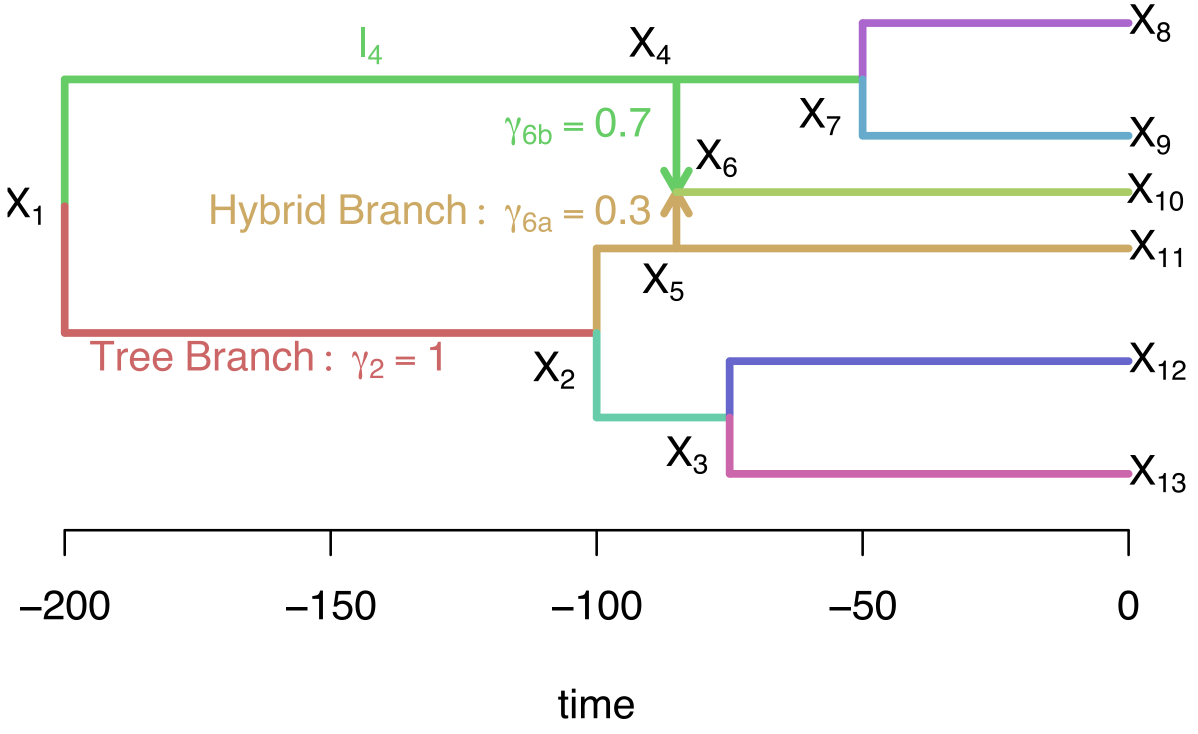
- Sword index
- Female preference

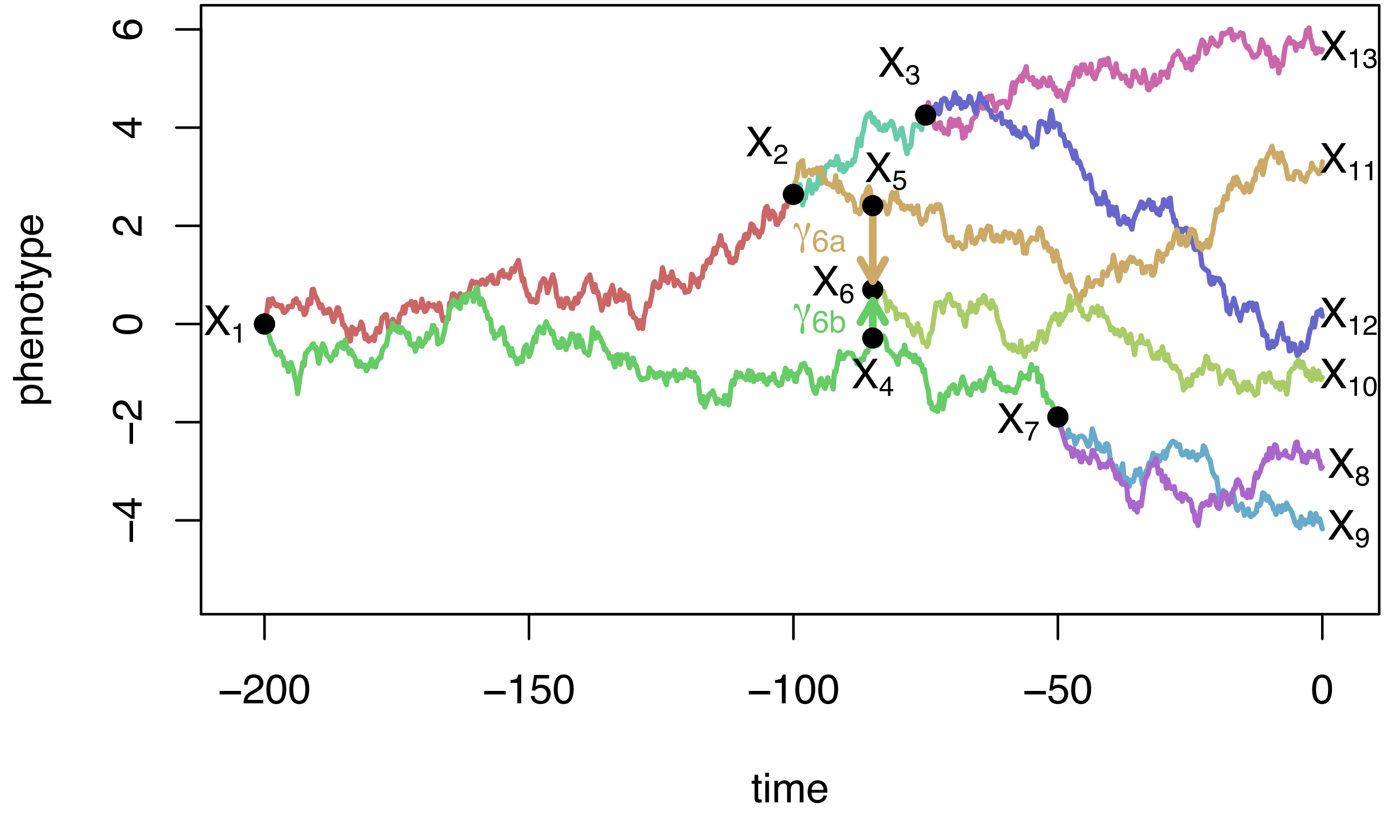


(Cui et al., 2013)

(Solís-Lemus, Ané, 2016, PLoS Genetics)

Trait models of evolution in networks





Brownian Motion
\+ weighted
average in hybrid

$$X_h = \gamma_1 X_{p_1} + \gamma_2 X_{p_2}$$

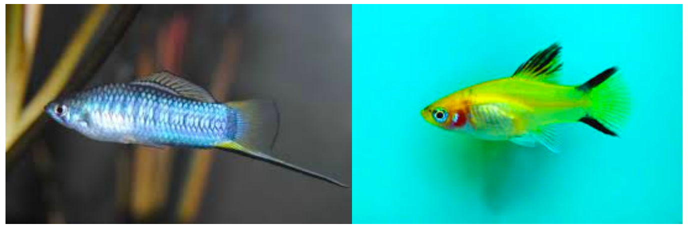
(Bastide et al, 2018, Syst Bio)

$$\mathbf{X} \sim N(X_{root}, \sigma^2 \mathbf{V})$$

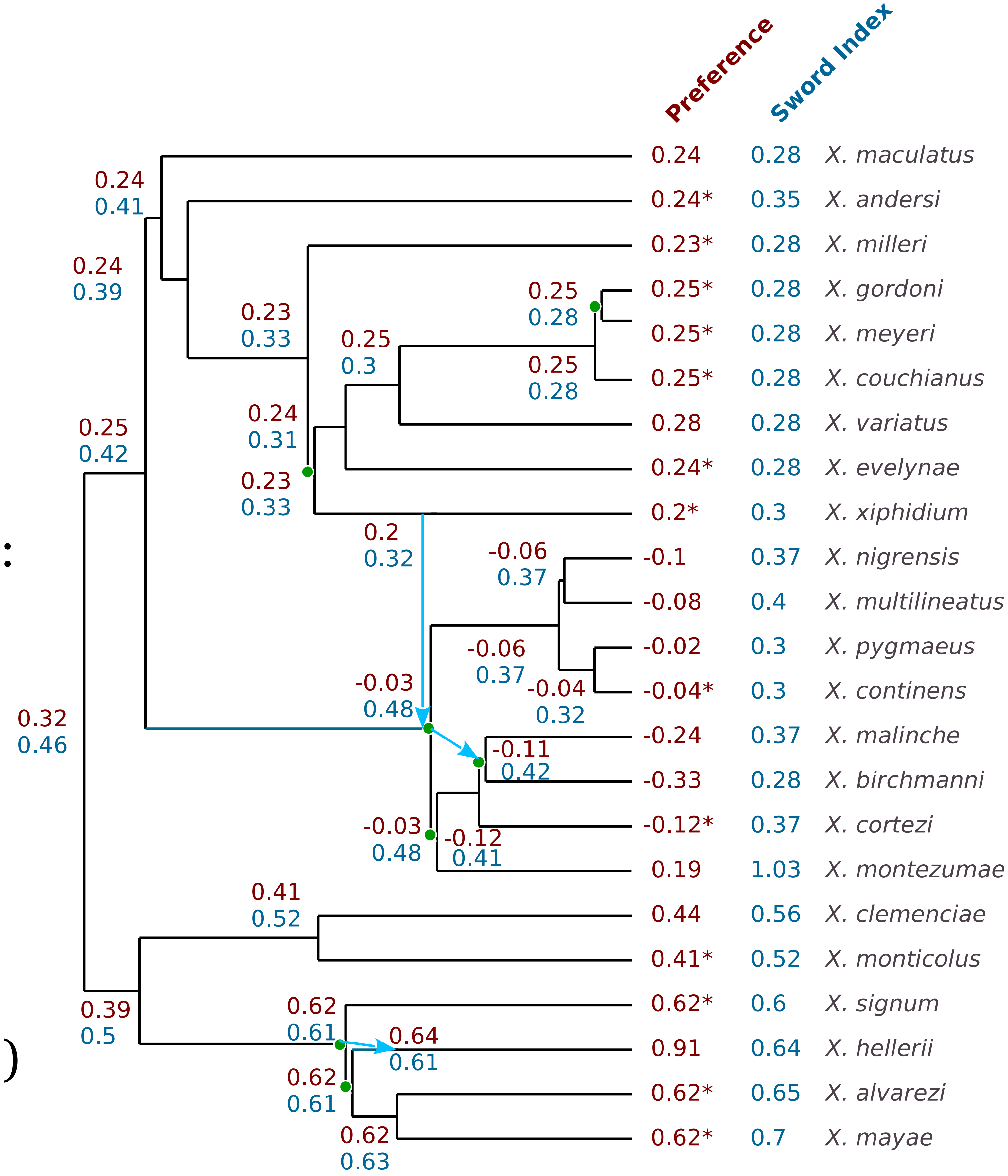
- Phylogenetic signal
- Ancestral reconstruction
- Phylogenetic regression
- Phylogenetic ANOVA

www.github.com/CRSL4/PhyloNetworks

- Sword index
- Female preference

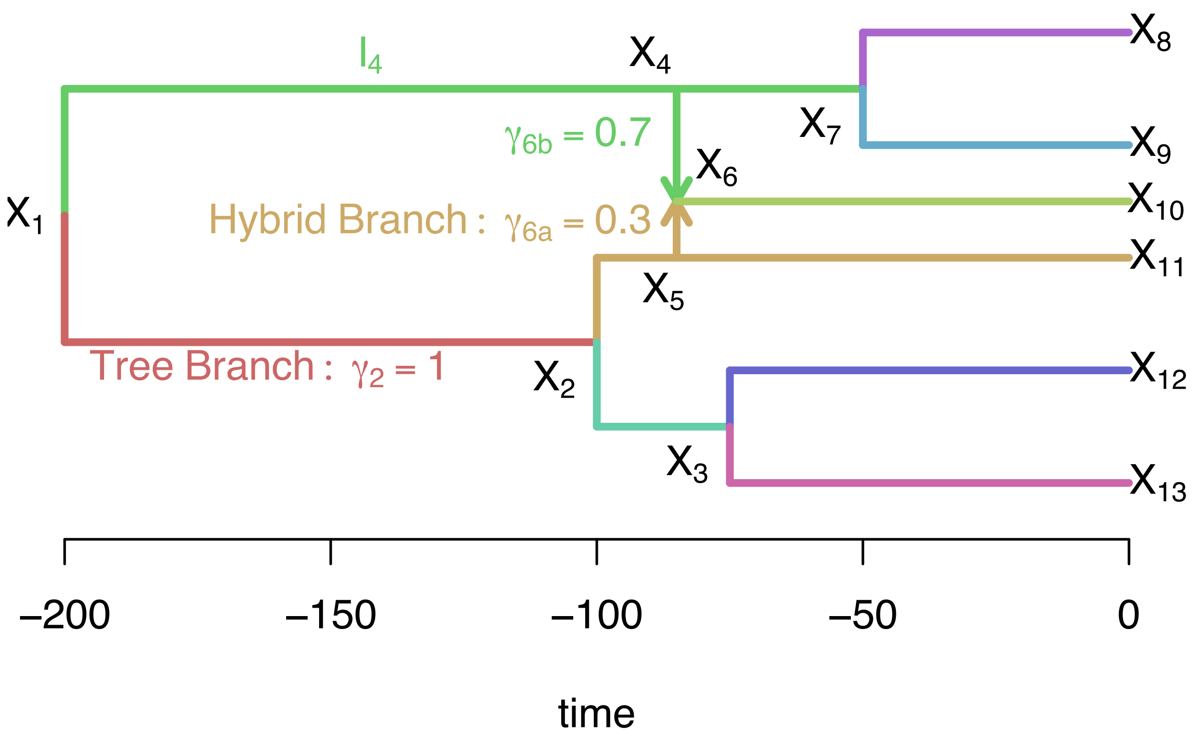


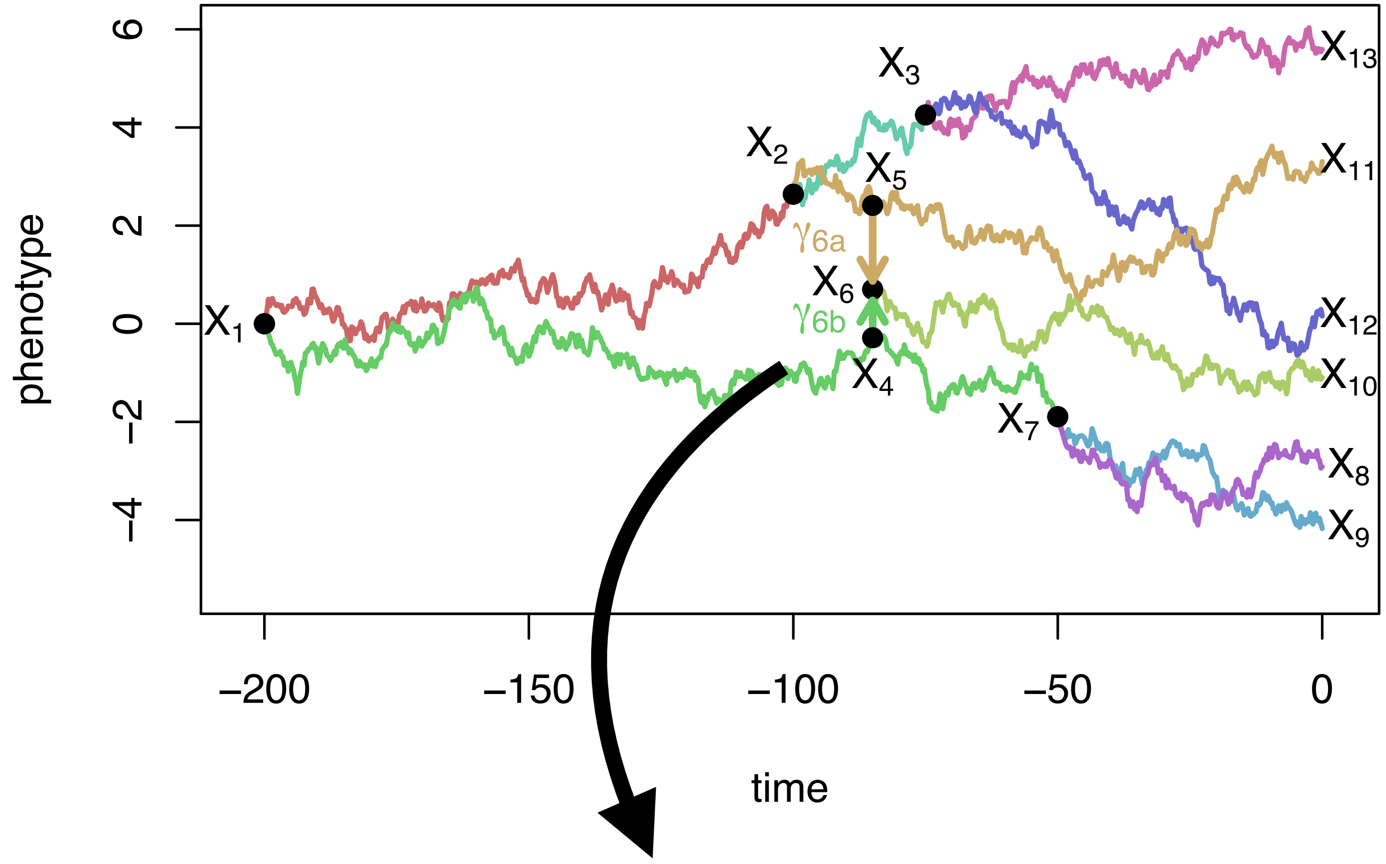
- **Ancestral reconstruction**: common ancestor likely had sword
- **Phylogenetic regression:** positive association between sword index and female preference but not significant ($p = 0.106$)



Test for transgressive evolution

$$X_h = \gamma_1 X_{p_1} + \gamma_2 X_{p_2} + \Delta_h$$





$\Delta_h = 0$ No transgressive evolution

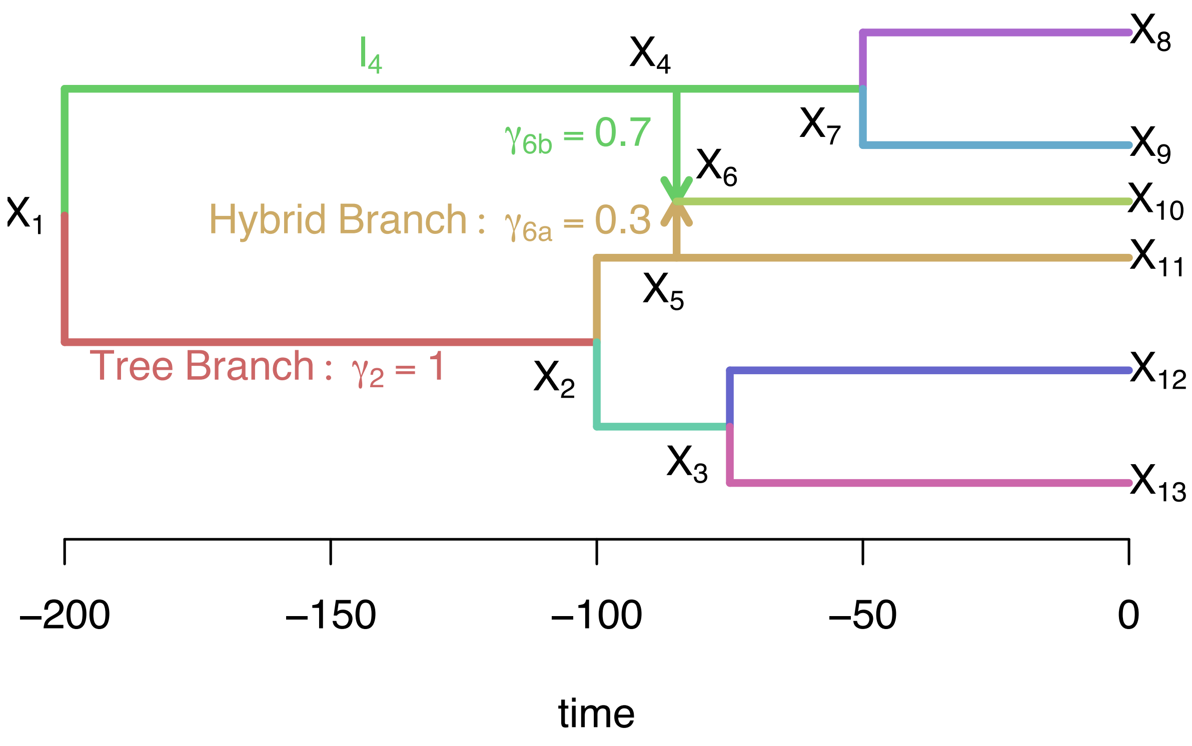
$\Delta_h = \Delta$ Single-effect transgressive evolution

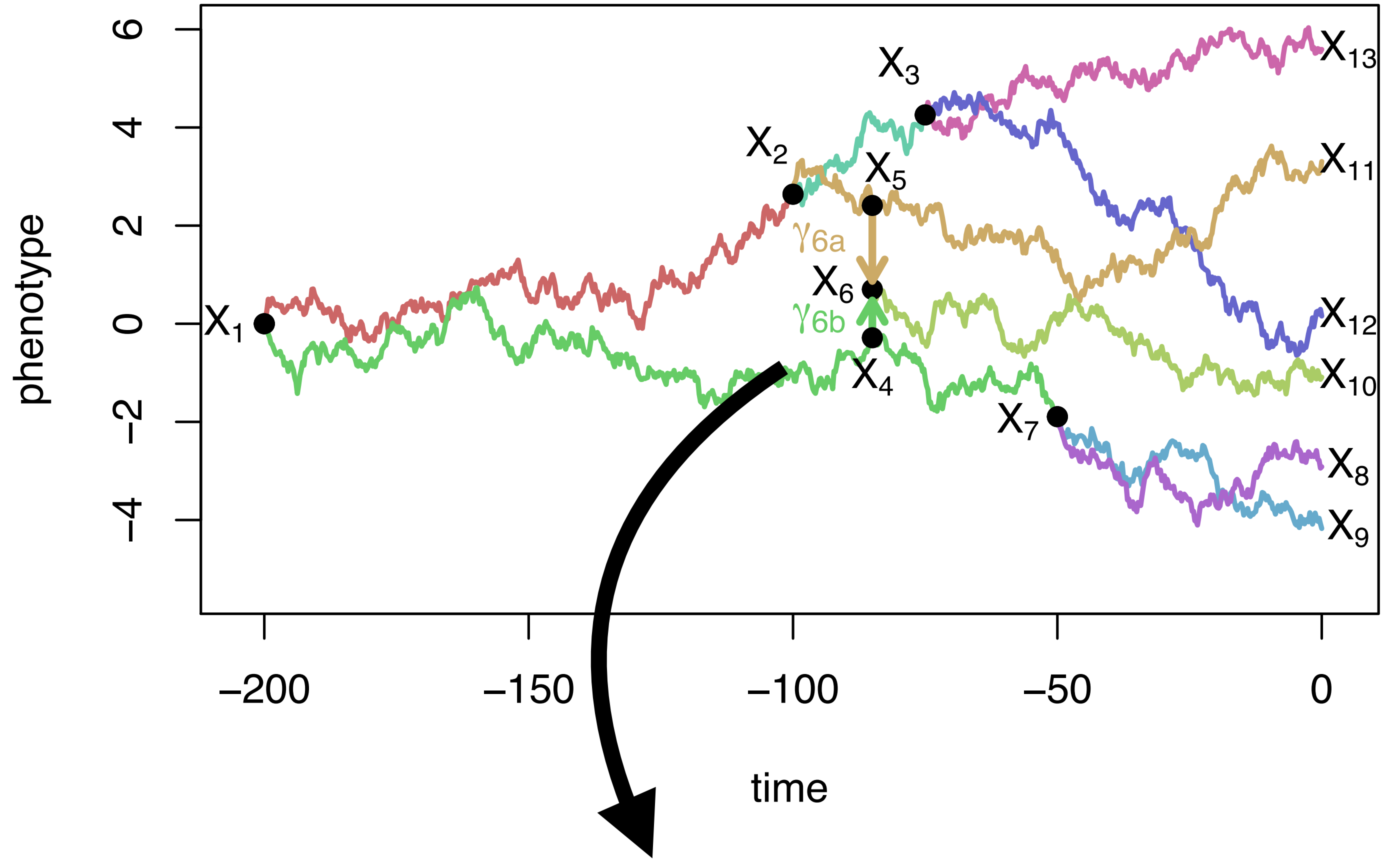
Δ_h Multi-effect transgressive evolution

F tests

Hybrid value:
shift from
parents range

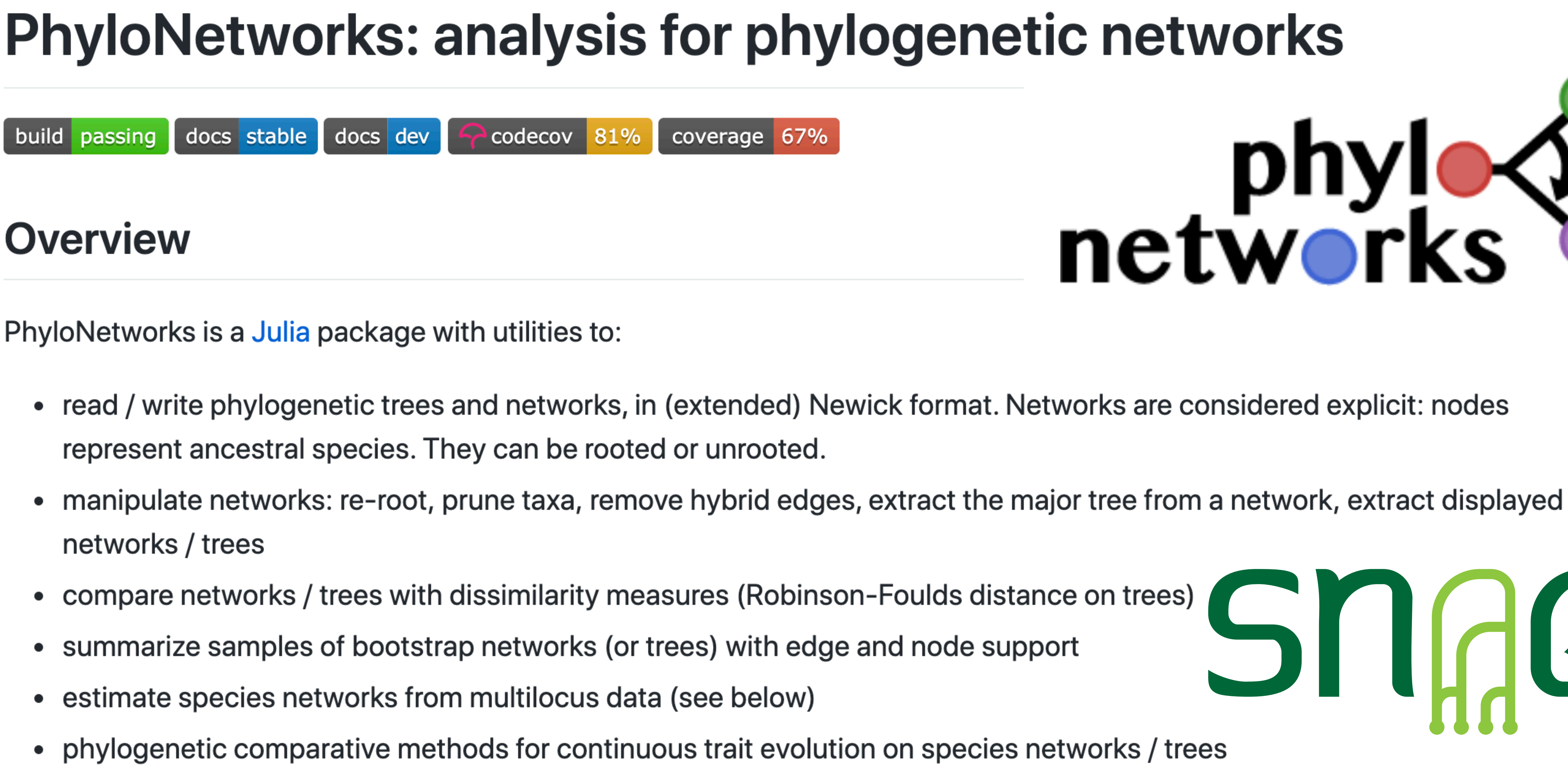
Test for transgressive evolution





- Sword index: p=0.55
- Female preference: p=0.0064

Hybrid value:
shift from
parents range



PhyloNetworks: analysis for phylogenetic networks

Overview

PhyloNetworks is a Julia package with utilities to:

- read / write phylogenetic trees and networks, in (extended) Newick format. Networks are considered explicit: nodes represent ancestral species. They can be rooted or unrooted.
- manipulate networks: re-root, prune taxa, remove hybrid edges, extract the major tree from a network, extract displayed networks / trees
- compare networks / trees with dissimilarity measures (Robinson-Foulds distance on trees)
- summarize samples of bootstrap networks (or trees) with edge and node support
- estimate species networks from multilocus data (see below)
- phylogenetic comparative methods for continuous trait evolution on species networks / trees

GitHub

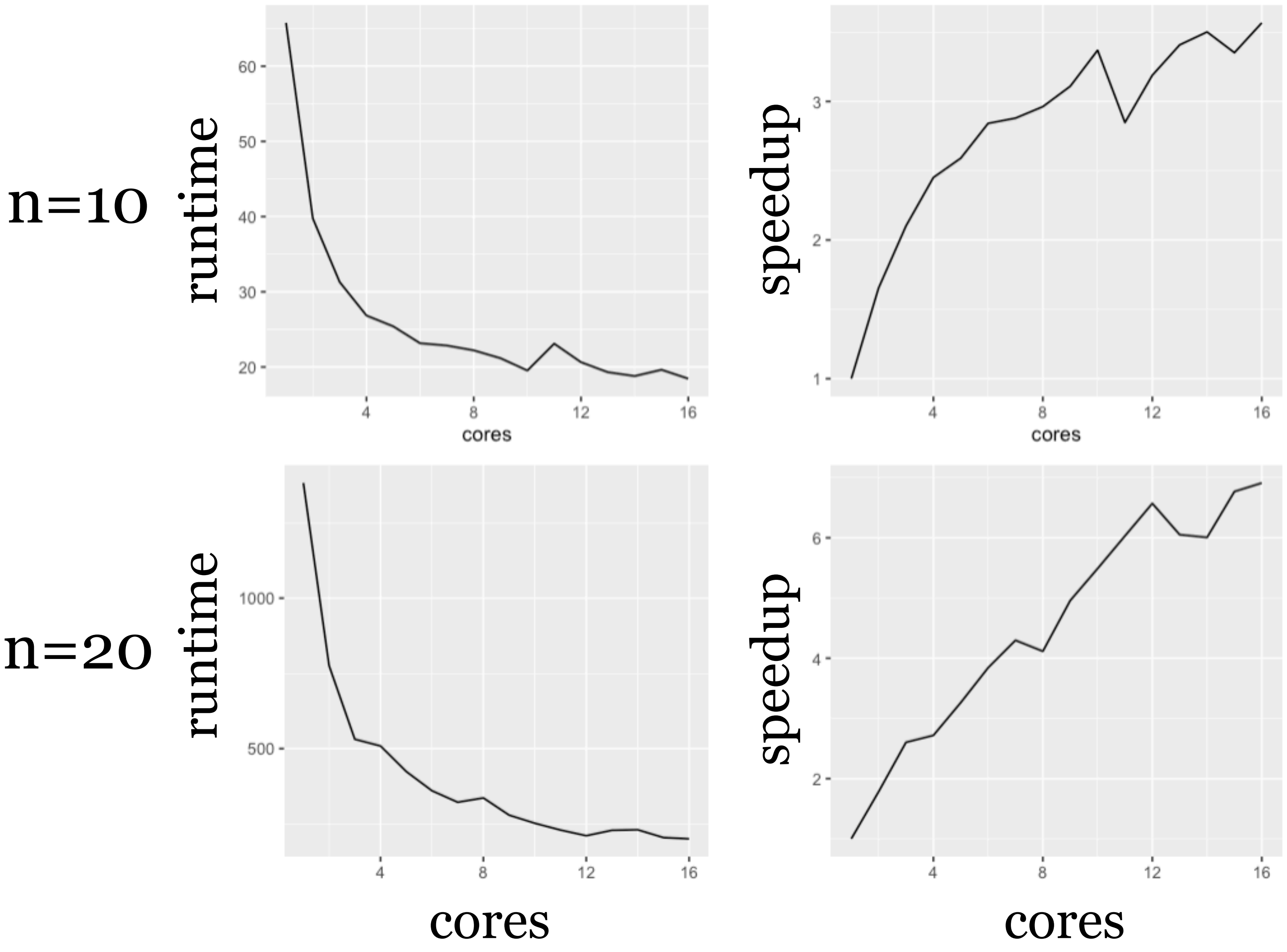
- Step-by-step tutorial
- Online documentation
- Google user group

(Solis-Lemus & Ane, 2016; Solis-Lemus. et al, 2017)

https://solislemuslab.github.io/ @solislemuslab crsl4 @thestatistician

Phylogenetic network inference: Ongoing projects

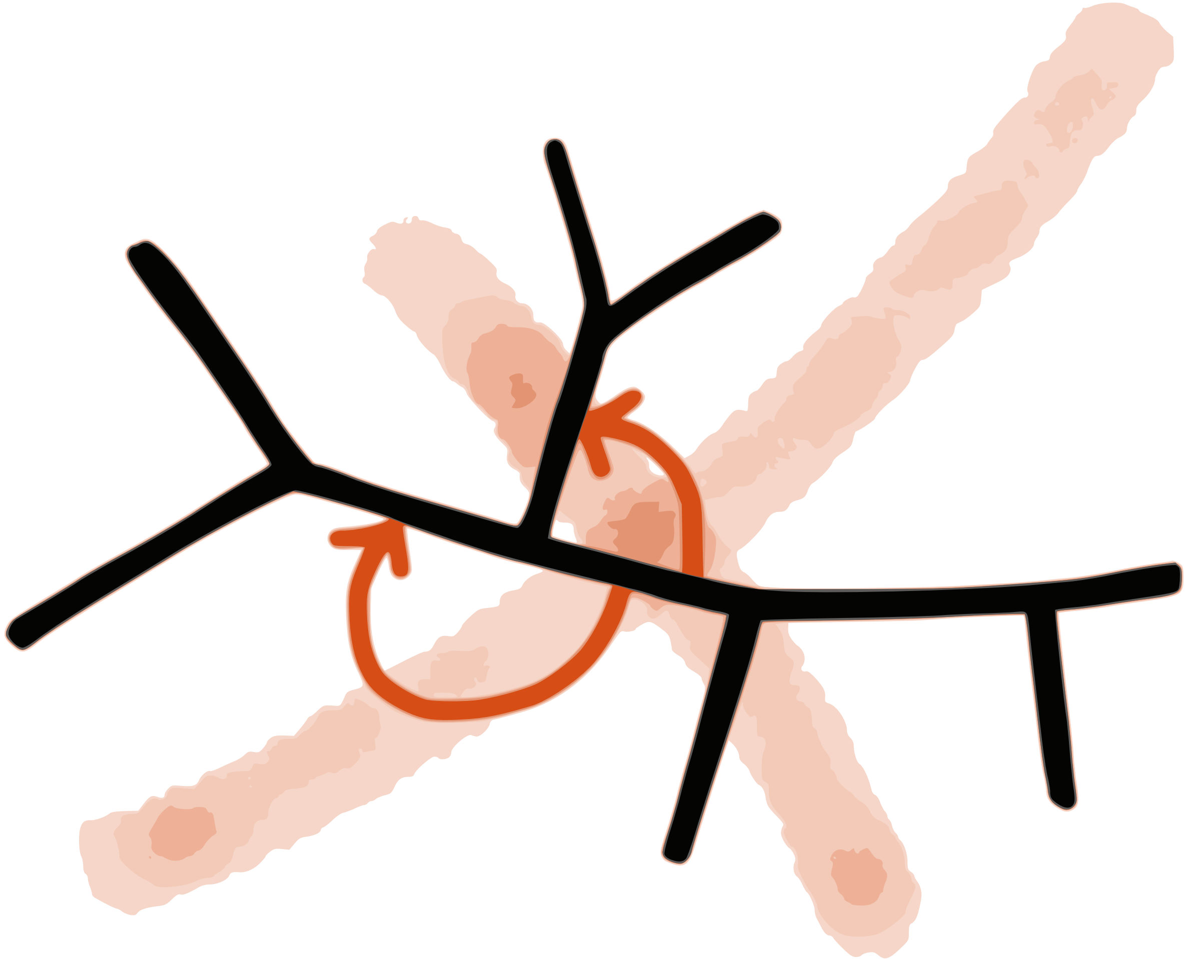
SNaQ is faster, but is it fast?

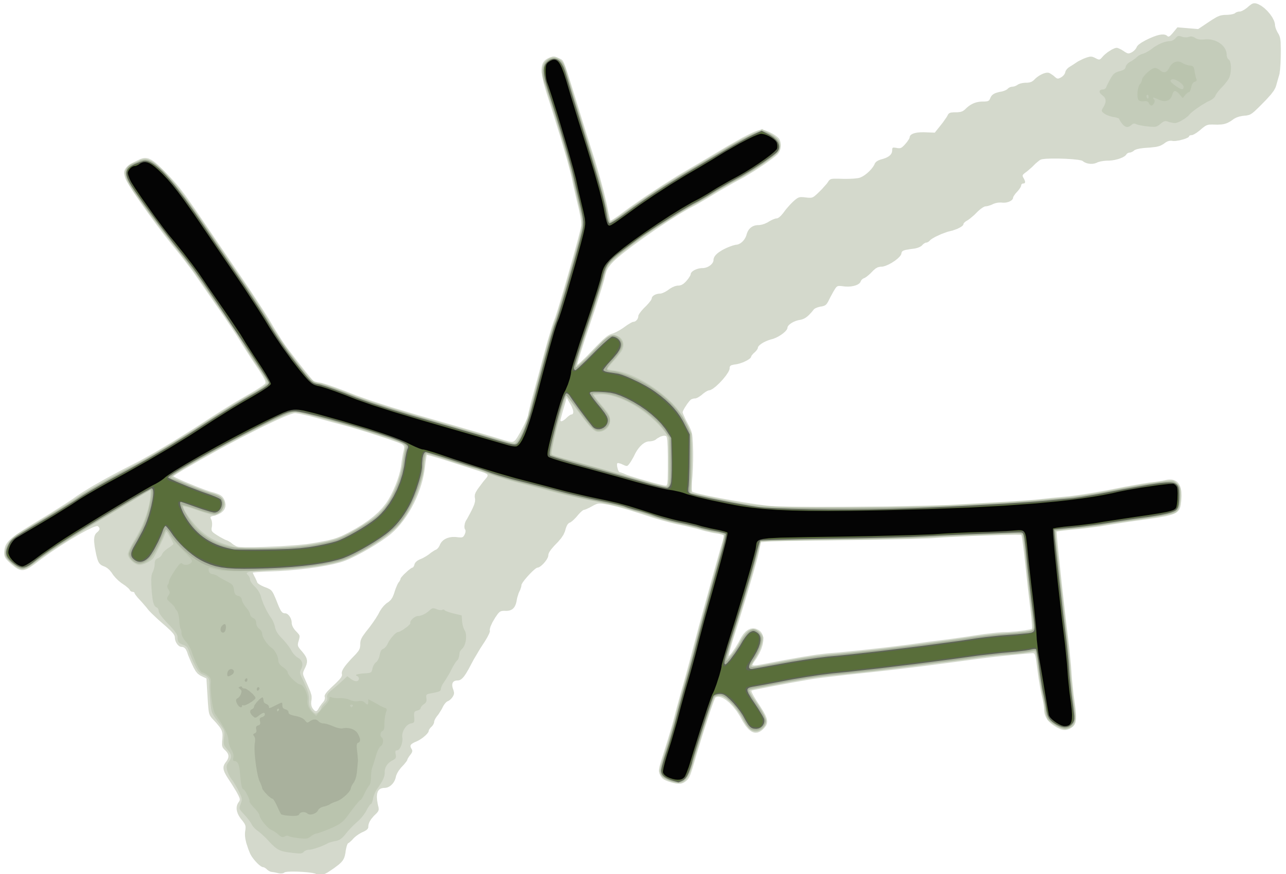


- Parallel quartet likelihood computation
- Weights to quartets: deviations from expected CFs
- Sampling of quartets without biasing inference

Work led by Tyler Chafin
Postdoc: UW-Madison+CU-Boulder

SNaQ limitation: Level-1 networks





Phylogenetic network inference: Ongoing projects

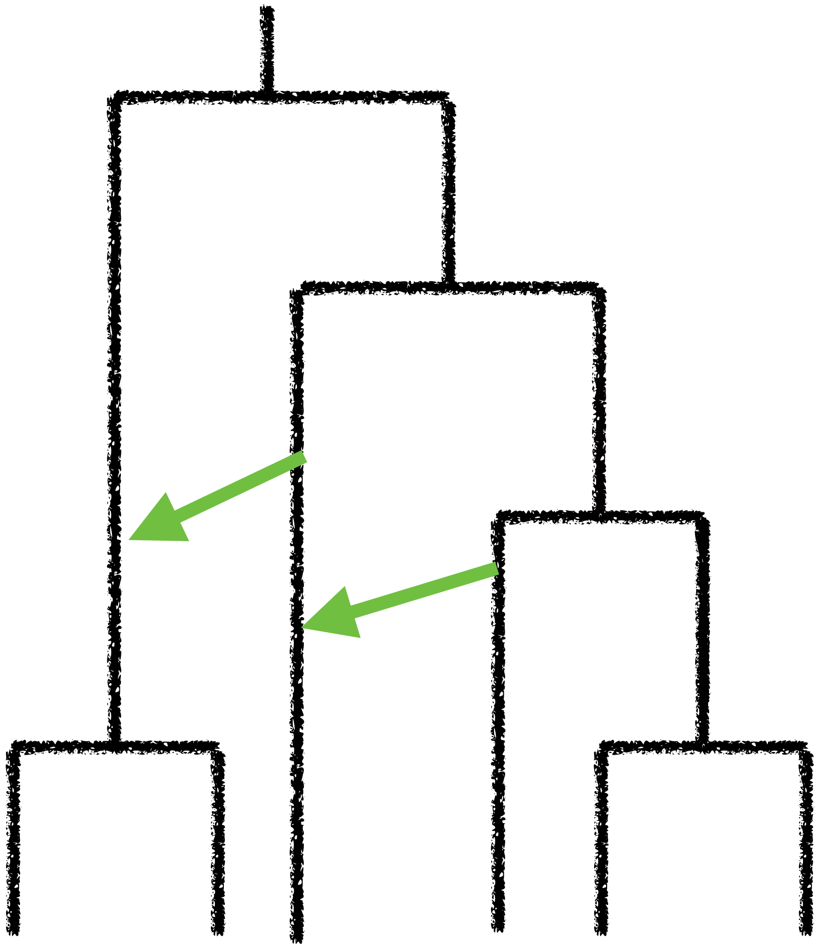
SNaQ Robustness for level-k networks

No results yet

- Simulate networks that are not level-1 with SiPhyNetworks
- Simulate gene trees under those networks with Hybrid-Lambda (Zhu et al, 2015)
- Estimate a level-1 network with SNaQ

Work led by Gustavo Ballen and Carlos Acosta

SNaQ Robustness for level-k networks



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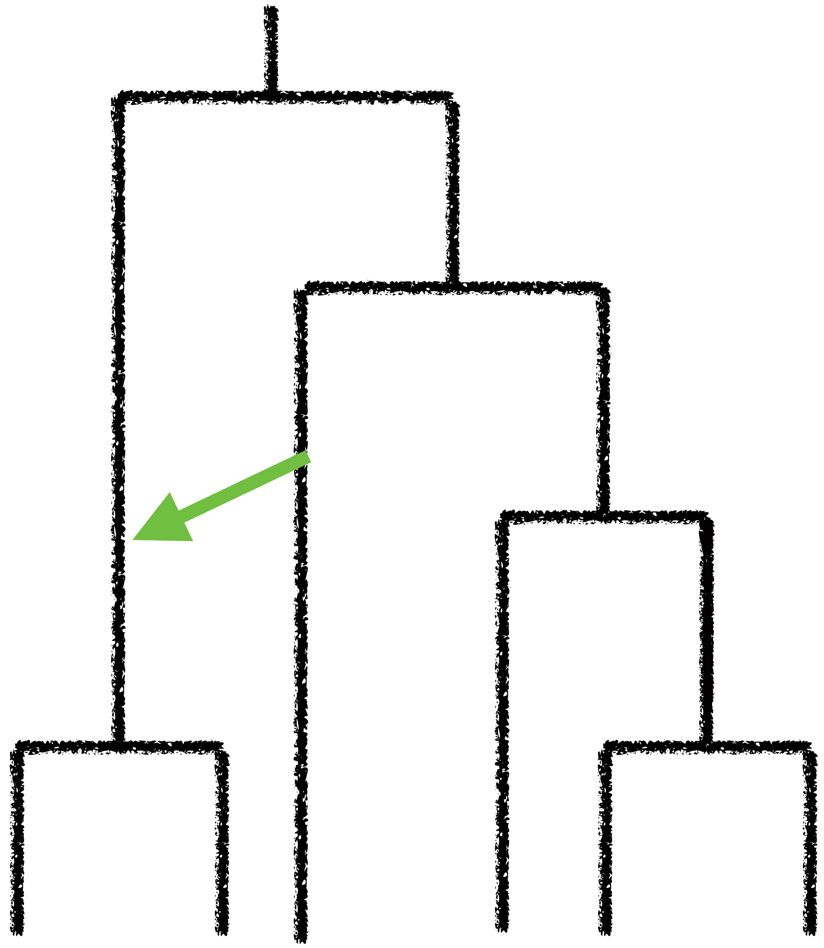

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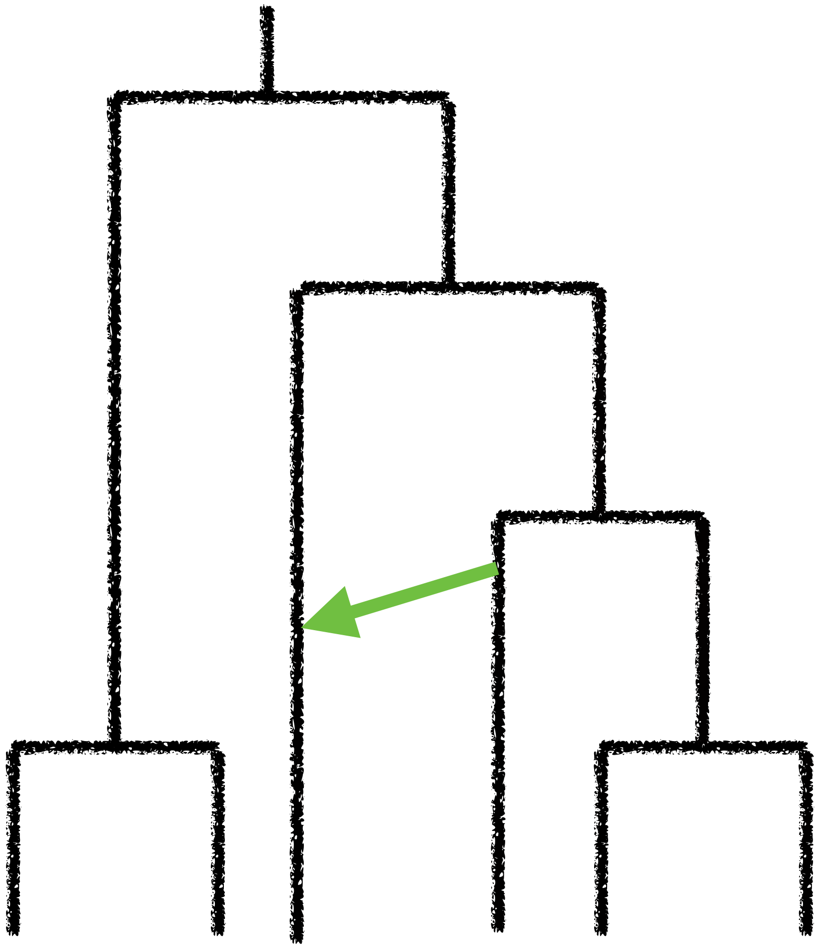

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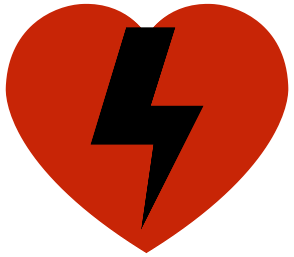

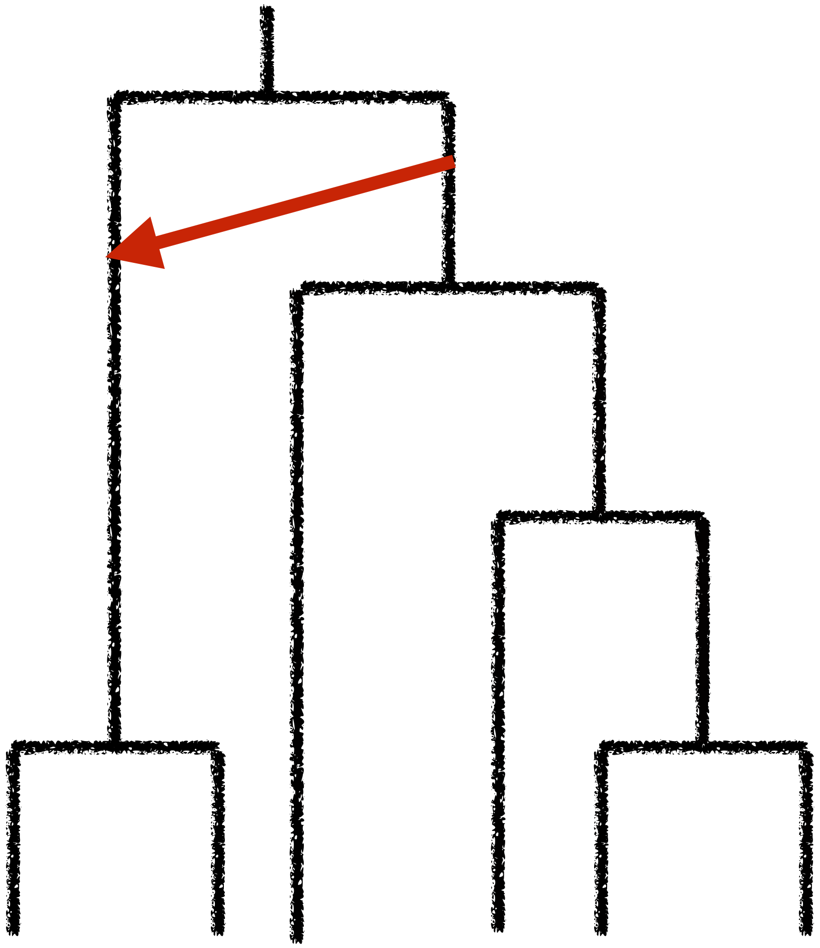

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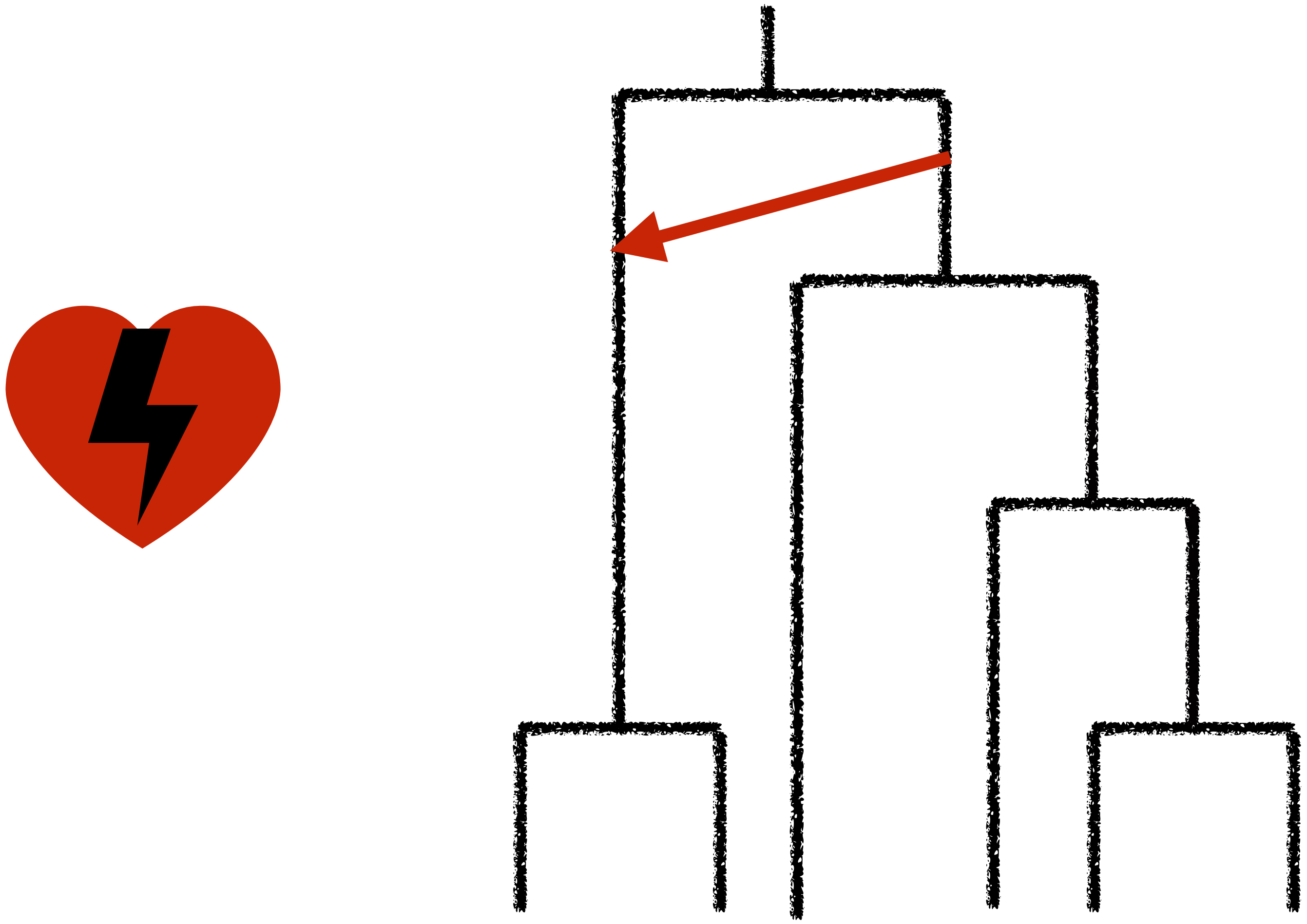

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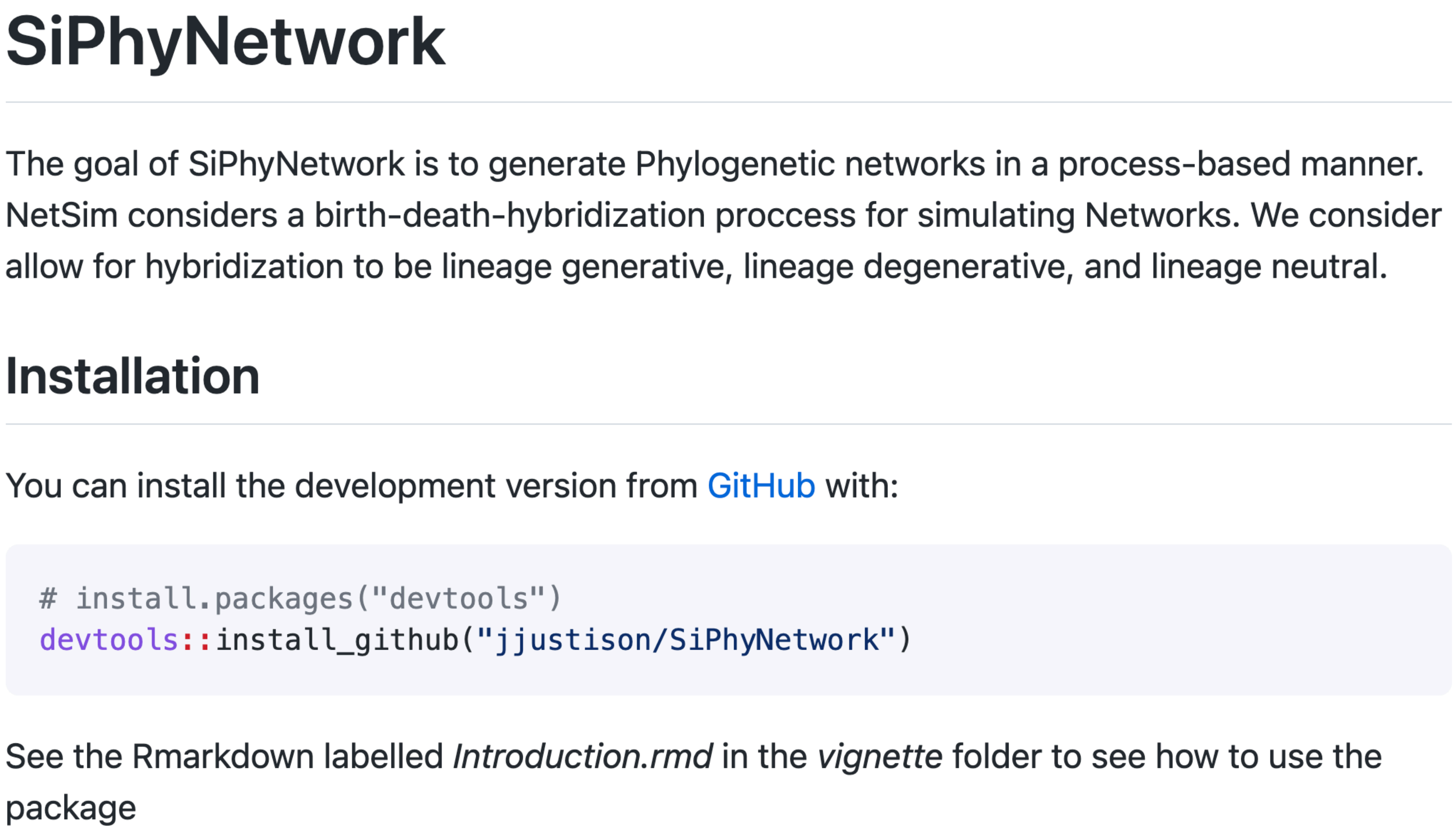

SiPhyNetwork

The goal of SiPhyNetwork is to generate Phylogenetic networks in a process-based manner. NetSim considers a birth-death-hybridization proccess for simulating Networks. We consider allow for hybridization to be lineage generative, lineage degenerative, and lineage neutral.

Installation

You can install the development version from GitHub with:

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# install.packages("devtools")
devtools::install_github("jjustison/SiPhyNetwork")
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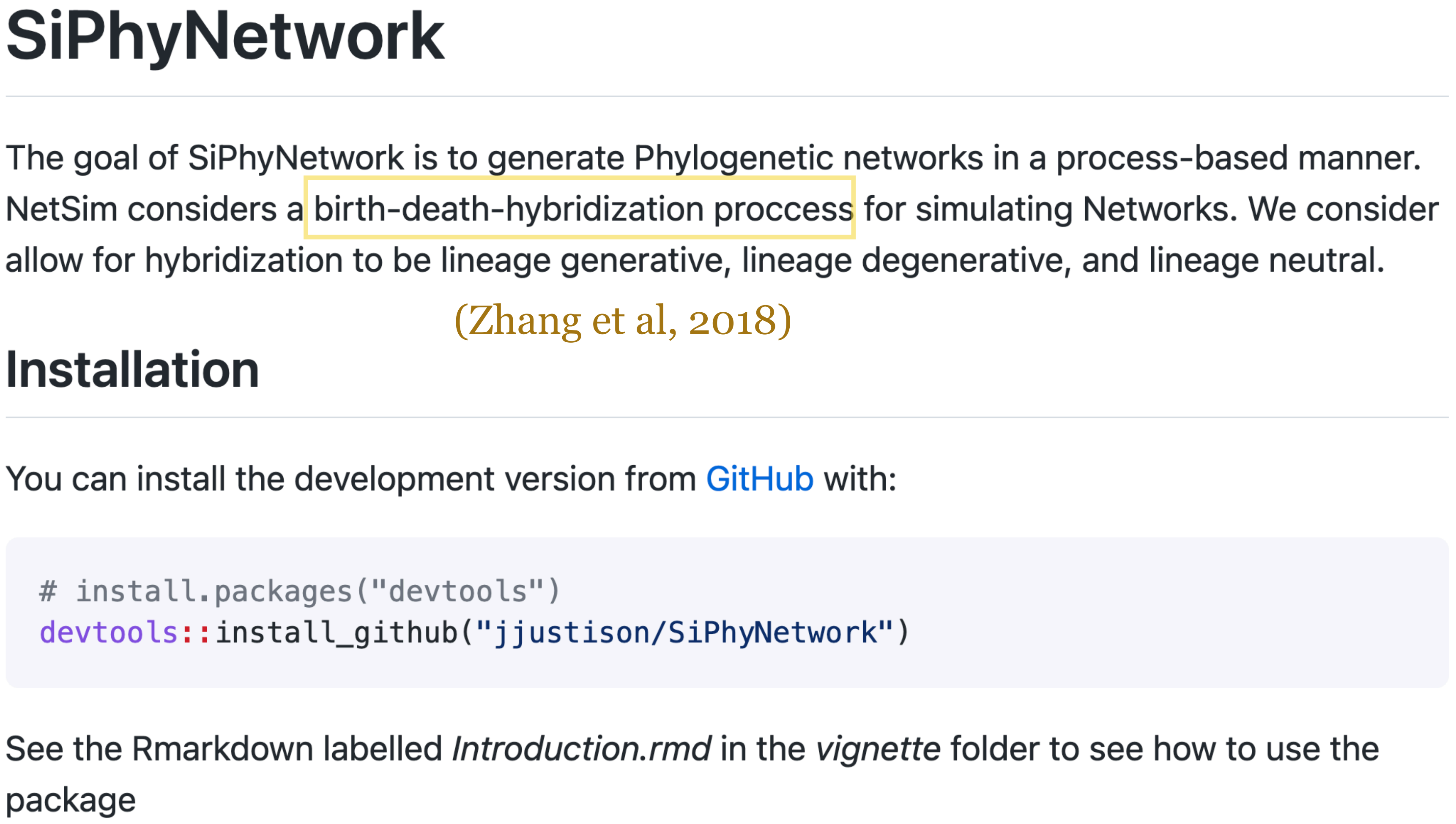
See the Rmarkdown labelled *Introduction.rmd* in the *vignette* folder to see how to use the package

Josh Justison

Tracy Heath

Phylogenetic network inference: Ongoing projects



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(Zhang et al, 2018)

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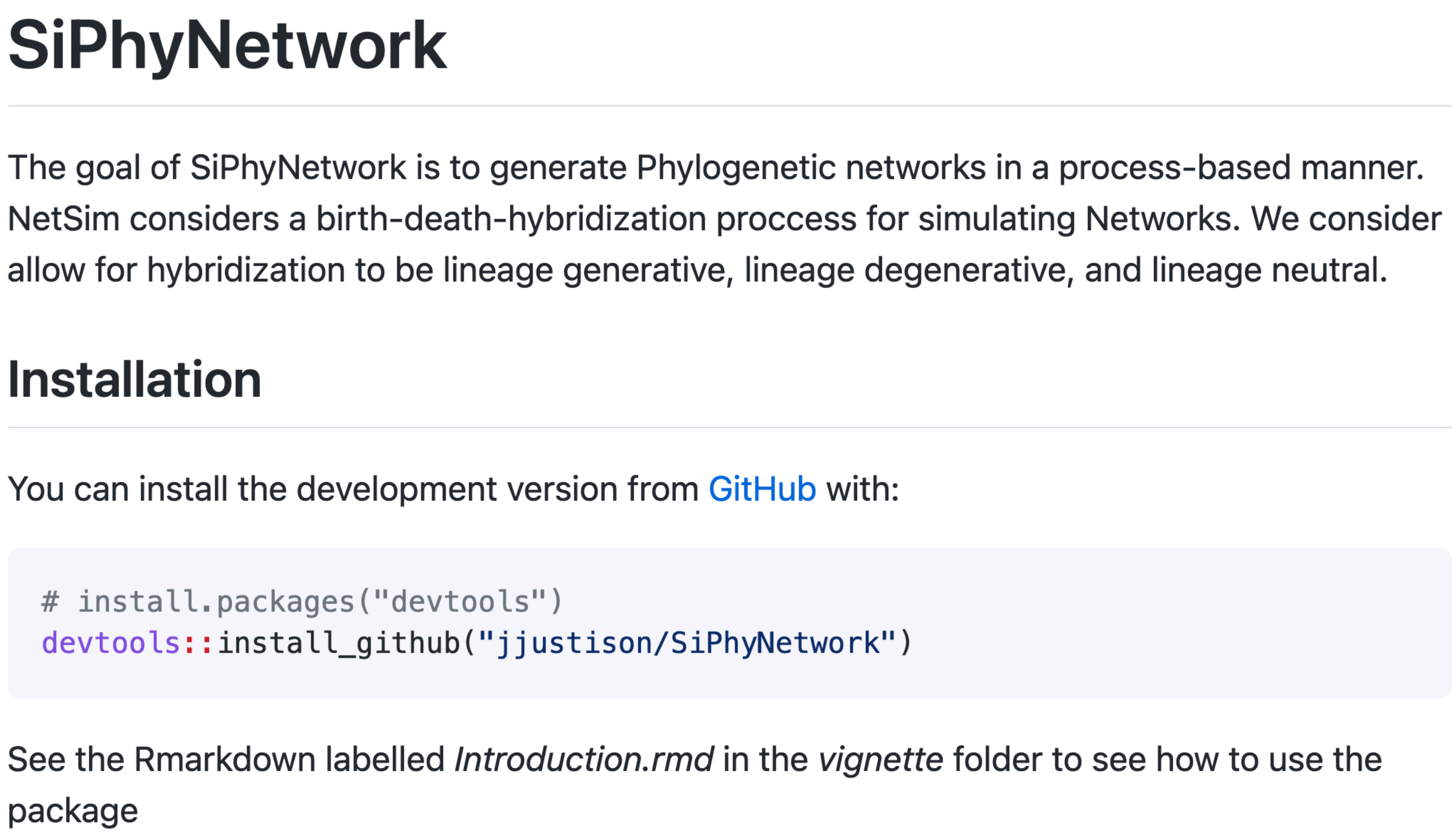

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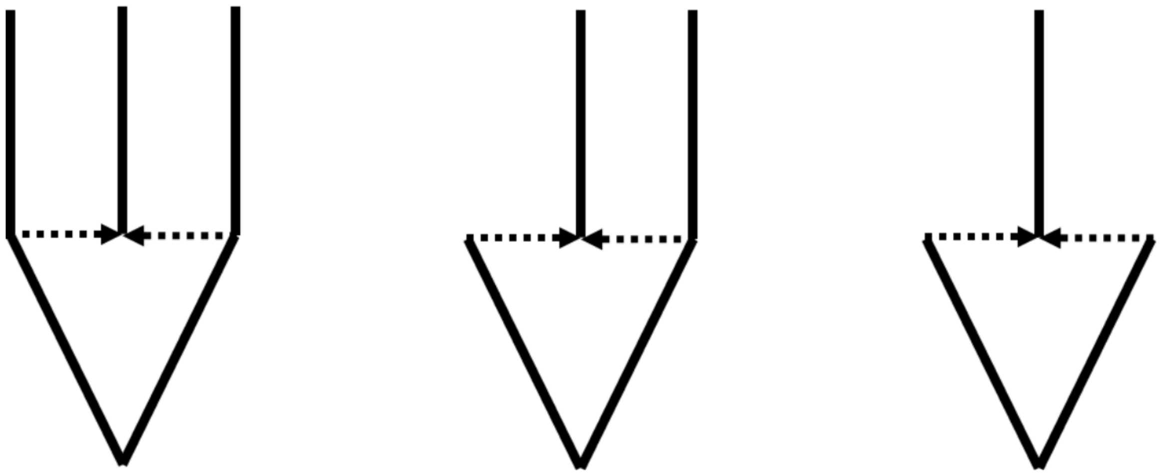
Types of hybridization



Phylogenetic network inference: Ongoing projects

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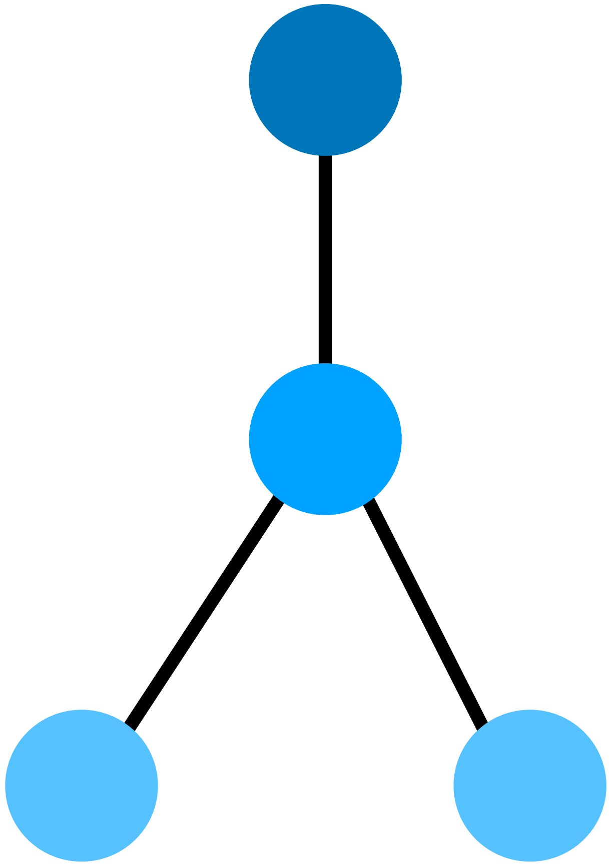
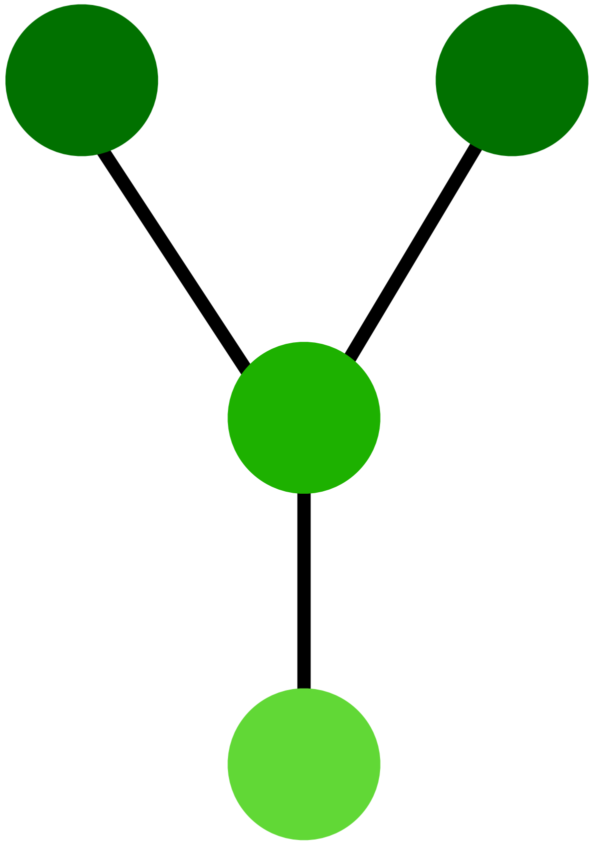
Phylogenetic network inference: Ongoing projects

Extend pseudolikelihood estimation to tree-child networks



Tree node



Hybrid node

Tree-child network: at least one child of every internal node is a tree node

Phylogenetic network inference: Ongoing projects

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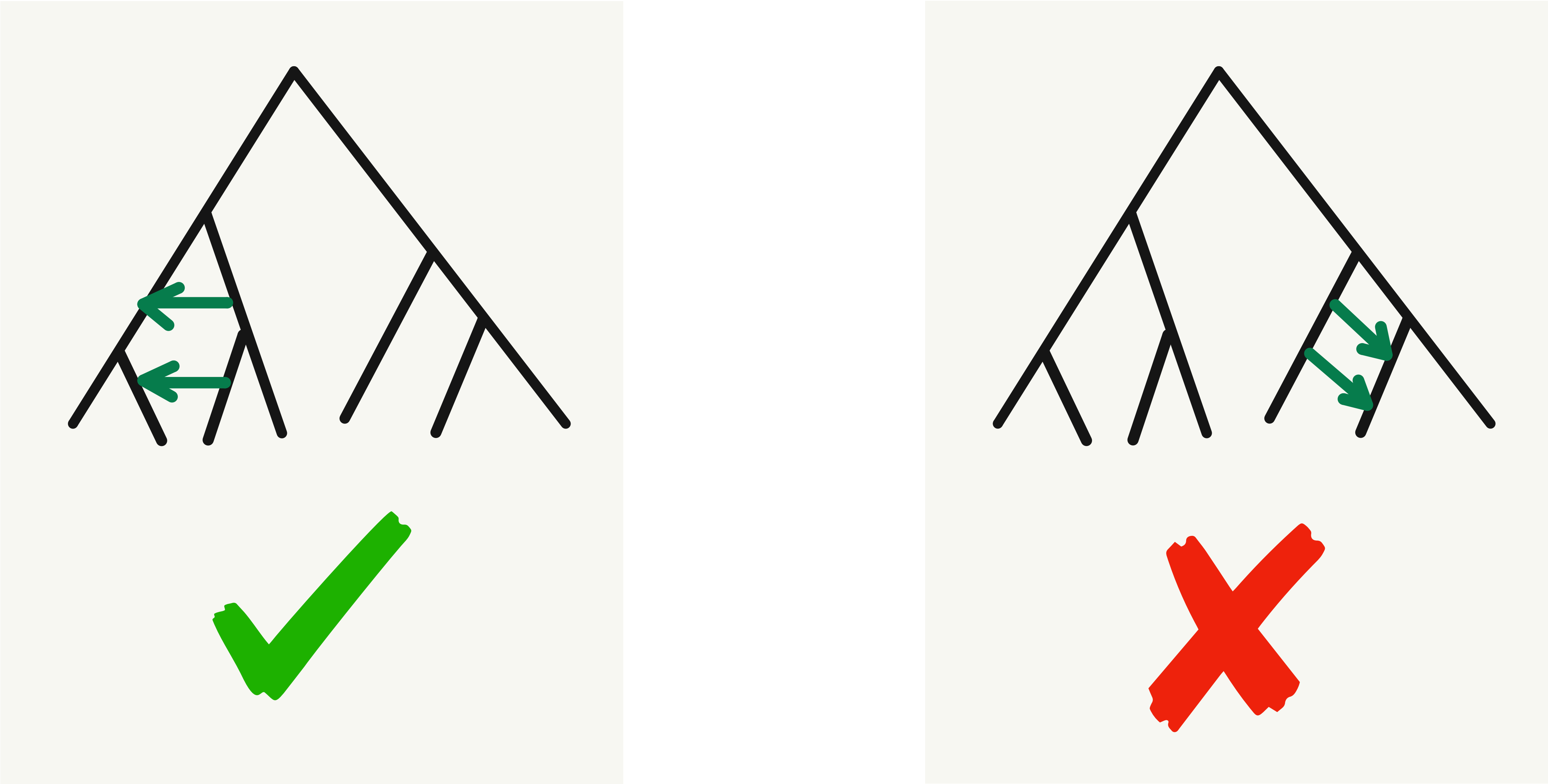

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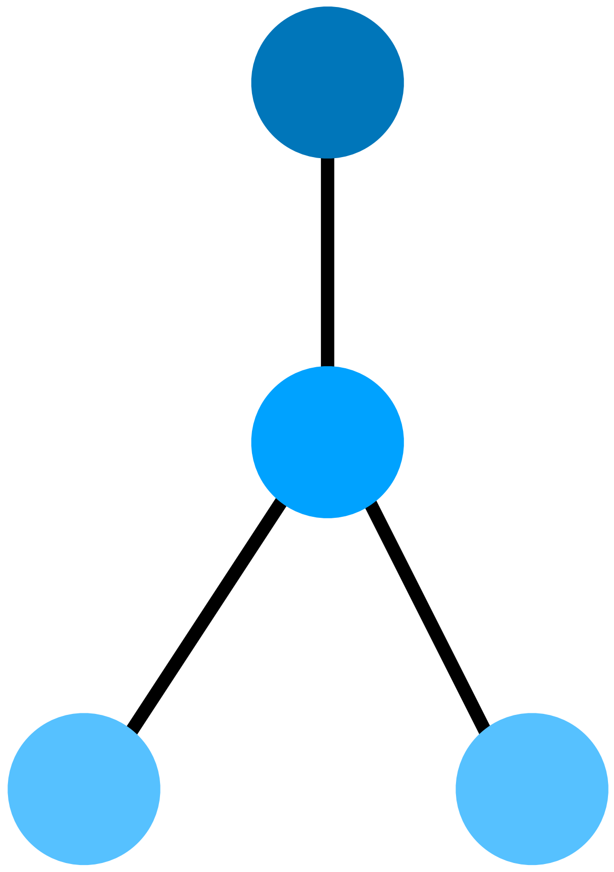

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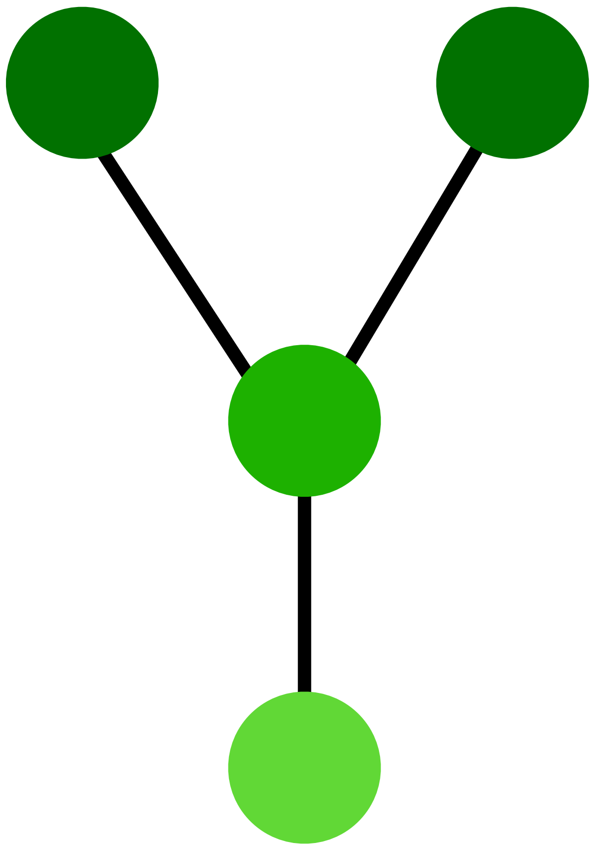

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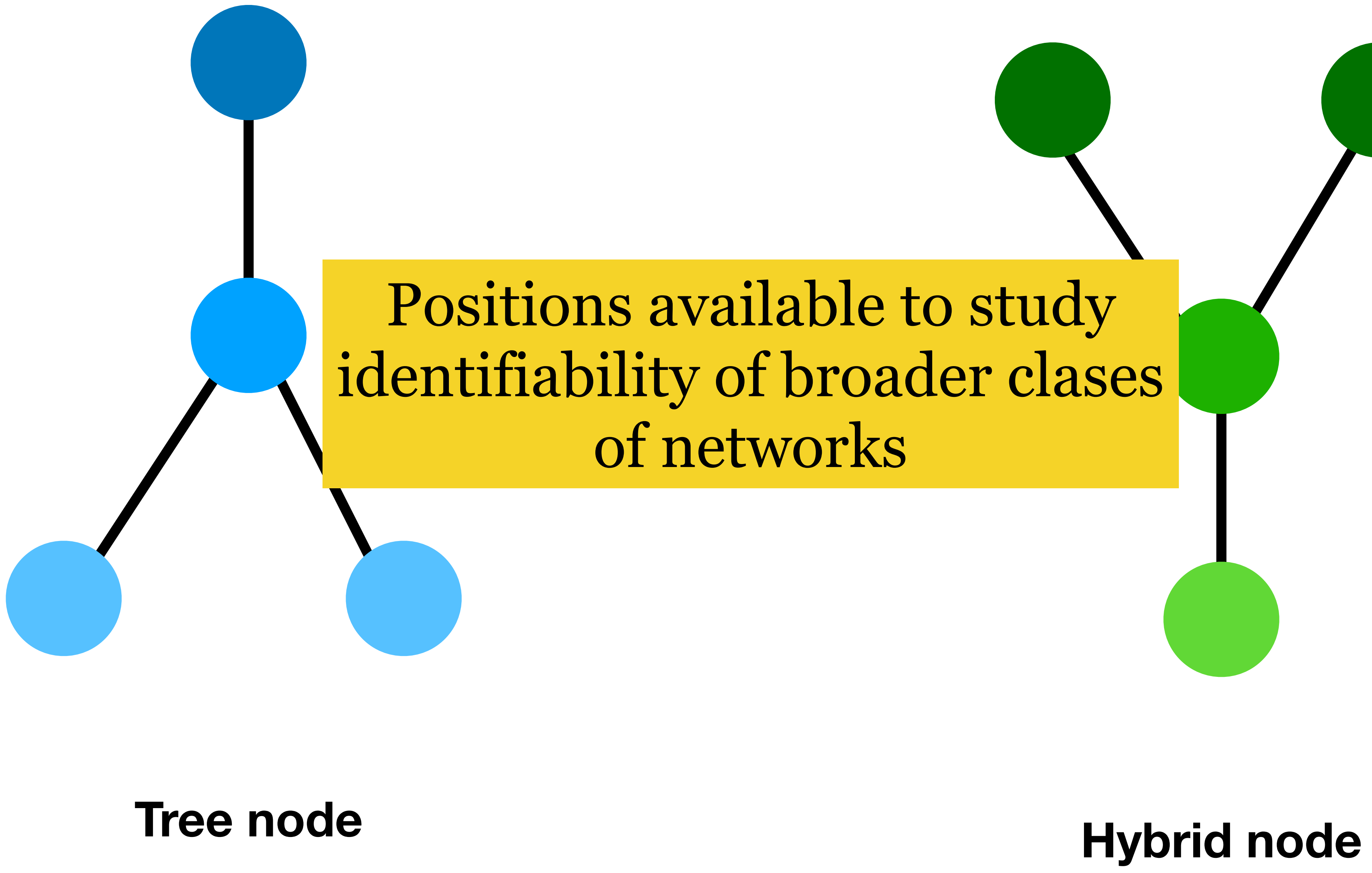

Positions available to study identifiability of broader clases of networks

Nathan Kolbow

Tree-child network: at least one child of every internal node is a tree node

PhyloNetworks: analysis for phylogenetic networks

build passing | docs stable | docs dev | codecov 81% | coverage 67%

Overview

PhyloNetworks is a Julia package with utilities to:

- read / write phylogenetic trees and networks, in (extended) Newick format. Networks are considered explicit: nodes represent ancestral species. They can be rooted or unrooted.
- manipulate networks: re-root, prune taxa, remove hybrid edges, extract the major tree from a network, extract displayed networks / trees
- compare networks / trees with dissimilarity measures (Robinson-Foulds distance on trees)
- summarize samples of bootstrap networks (or trees) with edge and node support
- estimate species networks from multilocus data (see below)
- phylogenetic comparative methods for continuous trait evolution on species networks / trees

GitHub

- Step-by-step tutorial
- Online documentation
- Google user group

(Solis-Lemus & Ane, 2016; Solis-Lemus. et al, 2017)

https://solislemuslab.github.io/ @solislemuslab crsl4 @thestatistician

Questions?