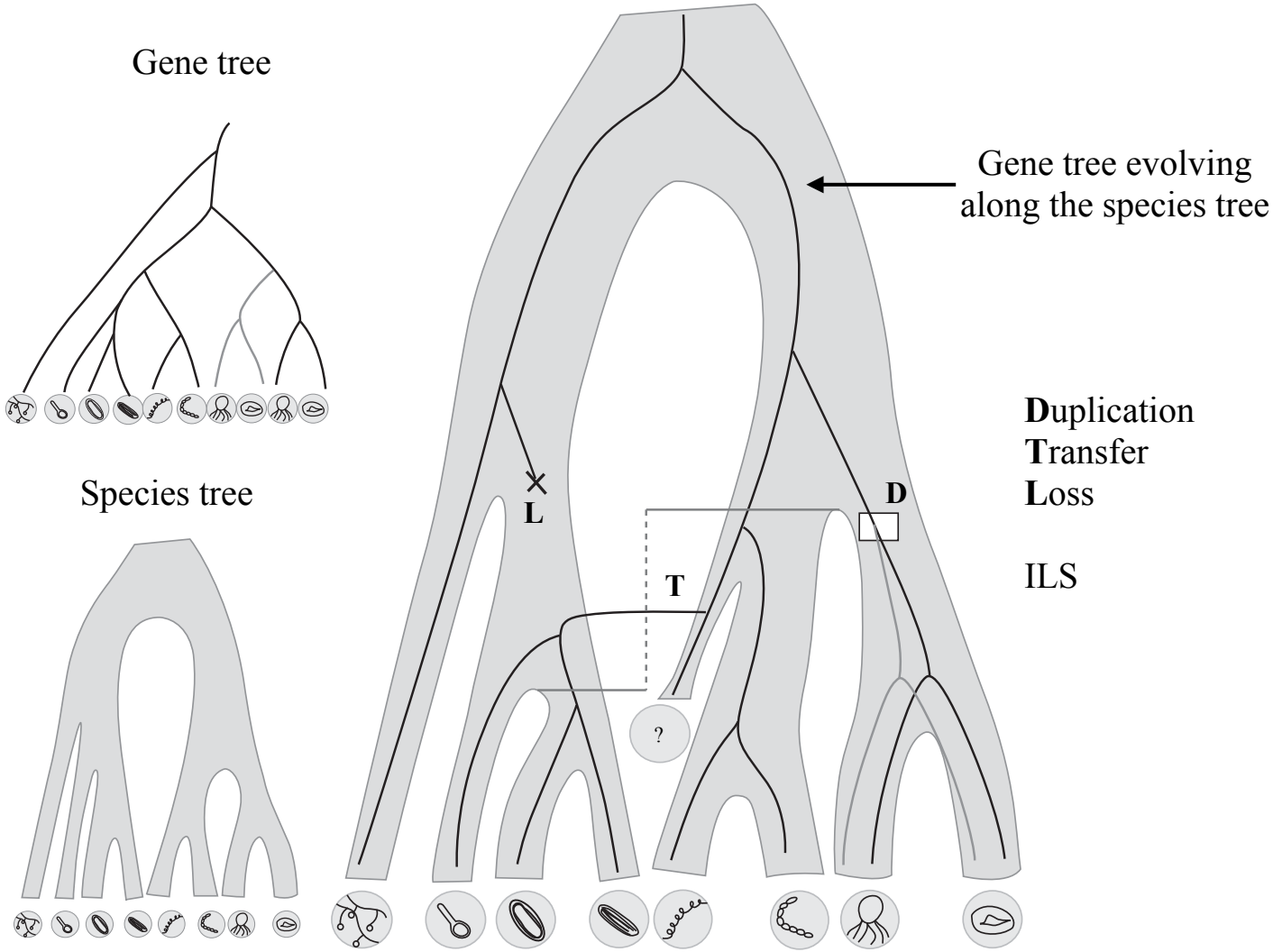
The problem is gene trees are not species trees

A gene tree is a deformation of the species tree through the prism of genome evolution and population genetics processes.

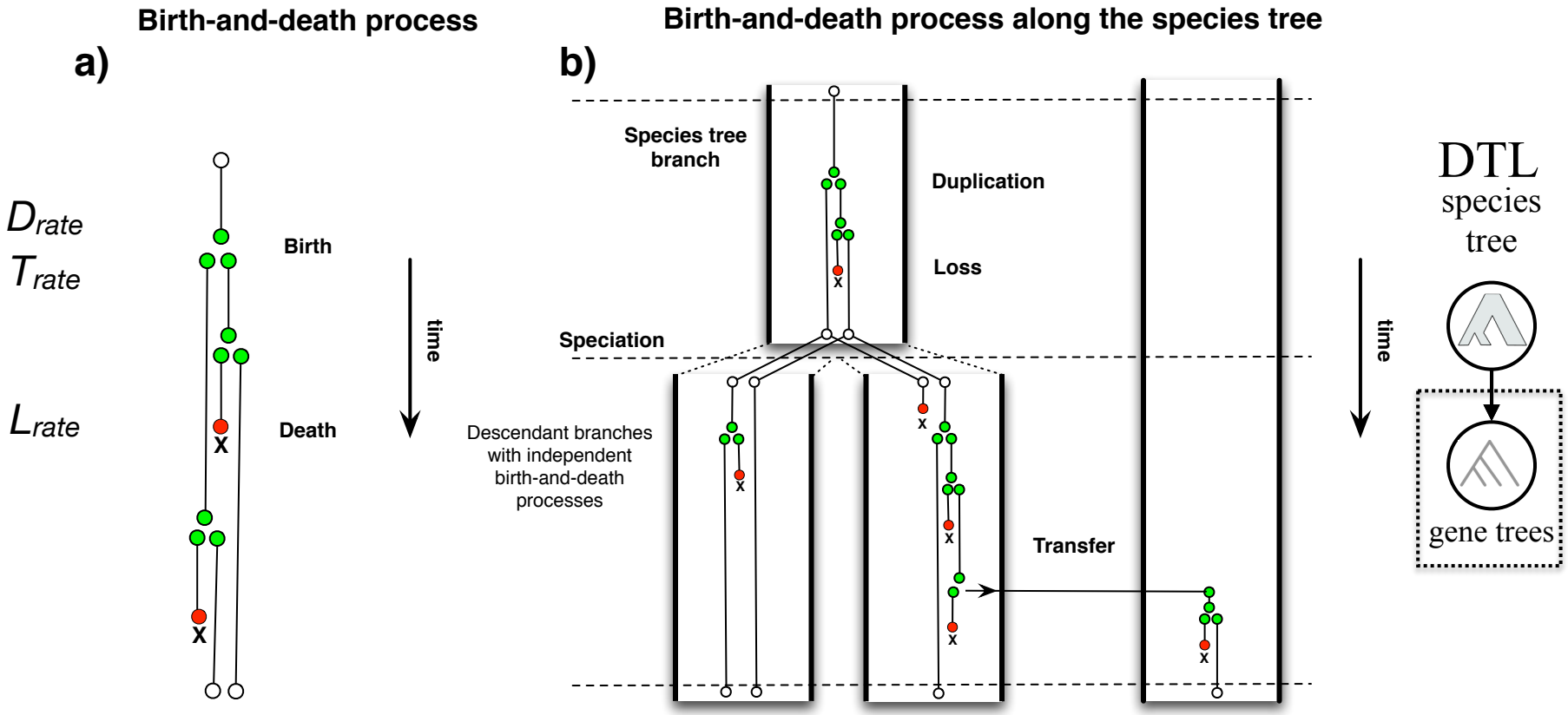


Daubin & Szöllősi 2016

.. gene trees are generated along the species tree

Calculating the likelihood $P(\text{gene tree} \mid \text{species tree})$ requires

summing over all possible ***gene birth and death events*** along a given ***species tree.***

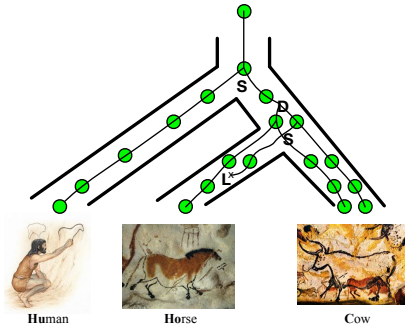


Tofigh *PhD thesis* 2009

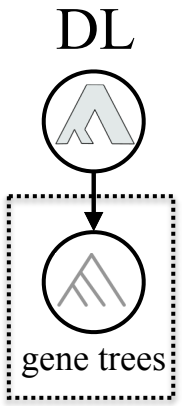
Szöllősi, Boussau, Abby, Tannier & Daubin ***PNAS*** (2012)
Phylogenetic modeling of lateral gene transfer reconstructs the pattern and relative timing of speciations

.. but gene trees are generated along the species tree

If we model the process generating gene trees along the species tree we can hope to infer better gene trees and species trees. To calculate the likelihood of a ***gene tree*** we sum over all possible ***gene birth and death events*** along a given ***species tree.***



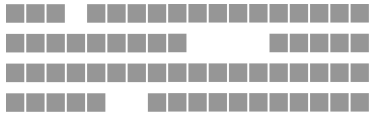
	calculation complexity	**parameters (ML or Bayes)**
DL	~10 × log(#species) × #genes	D&L rates branch lengths, root
DTL	~ 10 × #species^2 × #genes	D,T&L rates dated tree



The solution is to model how gene trees are generated along the species tree

Given the **species tree, which gene tree** produced my **sequences**? ..
and in **what evolutionary context?**

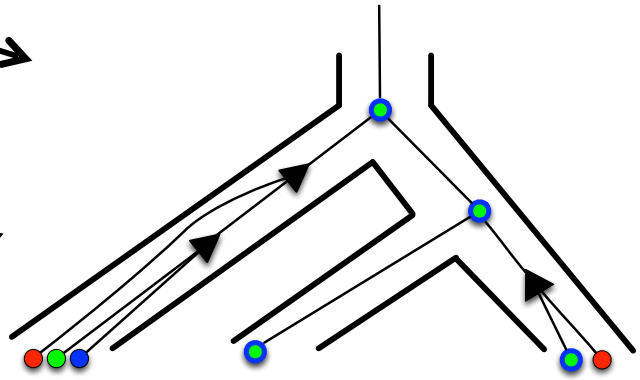
Joint likelihood: $P(\text{sequences} \mid \text{gene tree}) \; P(\text{gene tree} \mid \text{species tree})$

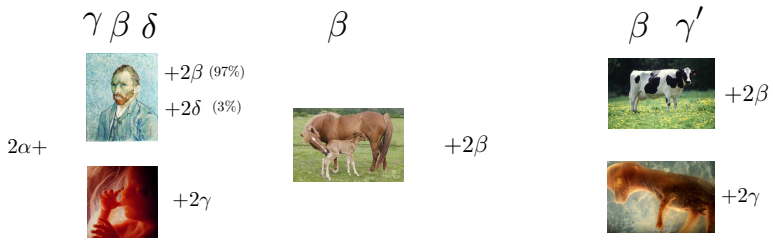


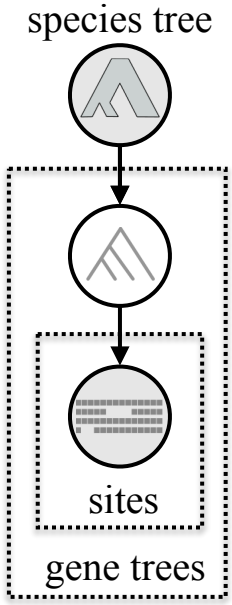
Gene family alignment

Rooted binary species tree

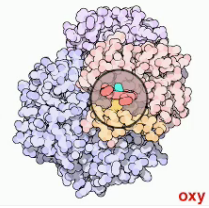
Most likely species tree-aware gene tree







hemoglobin



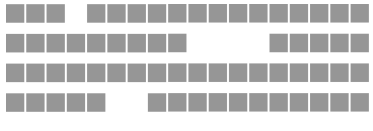
SZÖLLŐSI

gergely.szollosi@oist.jp

The solution is to model how gene trees are generated along the species tree

Given the **species tree, which gene tree** produced my **sequences**? ..
and in **what evolutionary context?**

Joint likelihood: $P(\text{sequences} \mid \text{gene tree}) \; P(\text{gene tree} \mid \text{species tree})$



Gene family alignment

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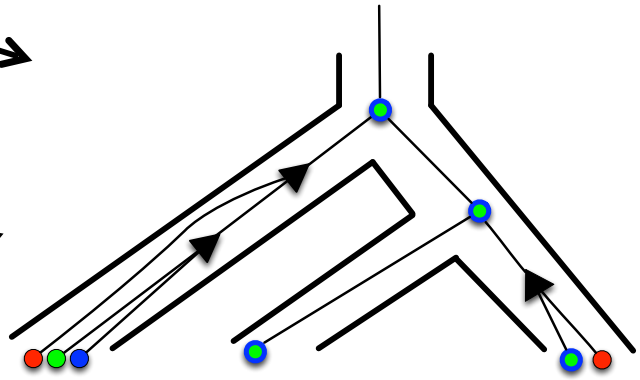
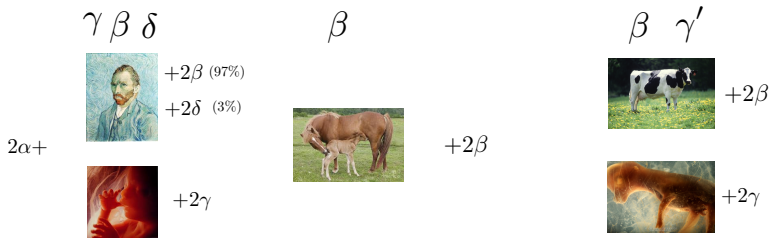
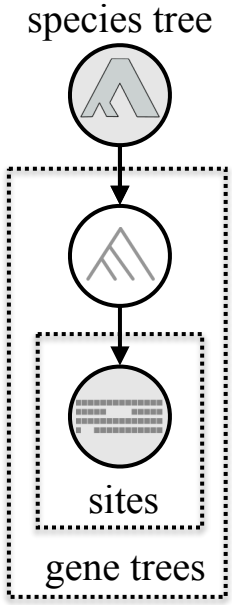
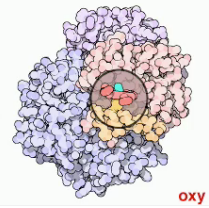
Most likely species tree-aware gene tree







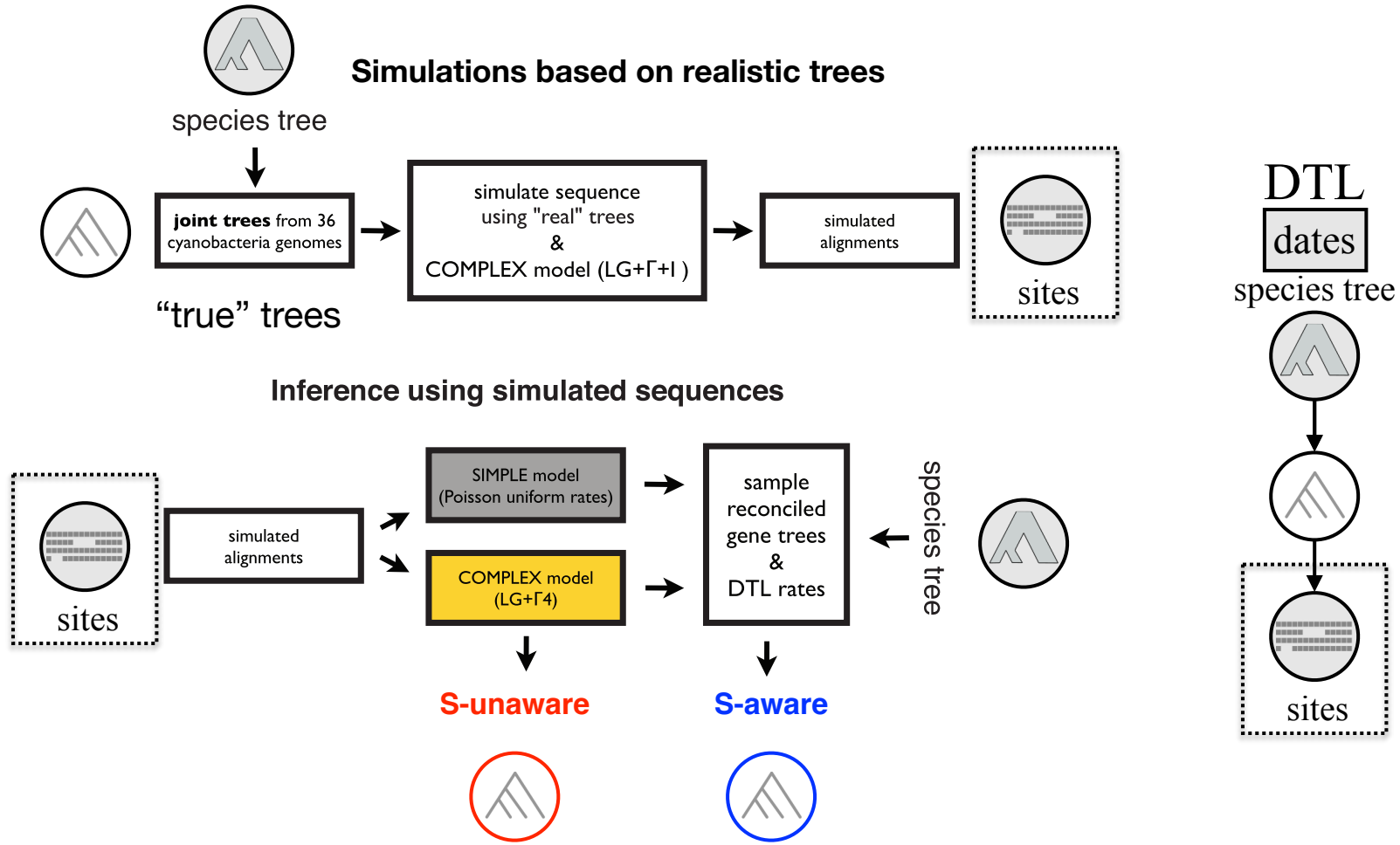
hemoglobin



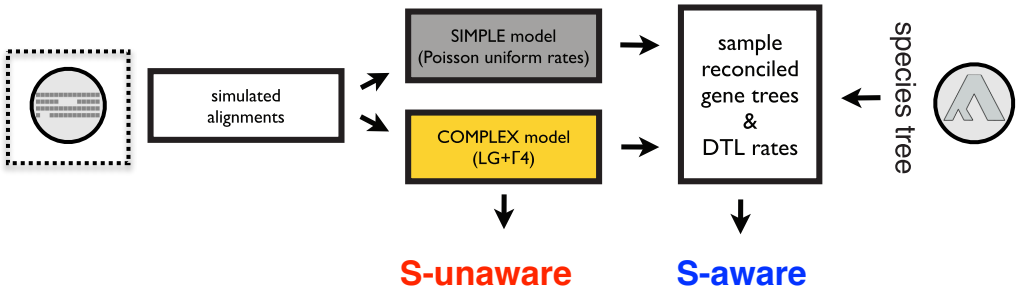
SZÖLLŐSI

gergely.szollosi@oist.jp

"Realistic simulations" suggest S-aware methods are important

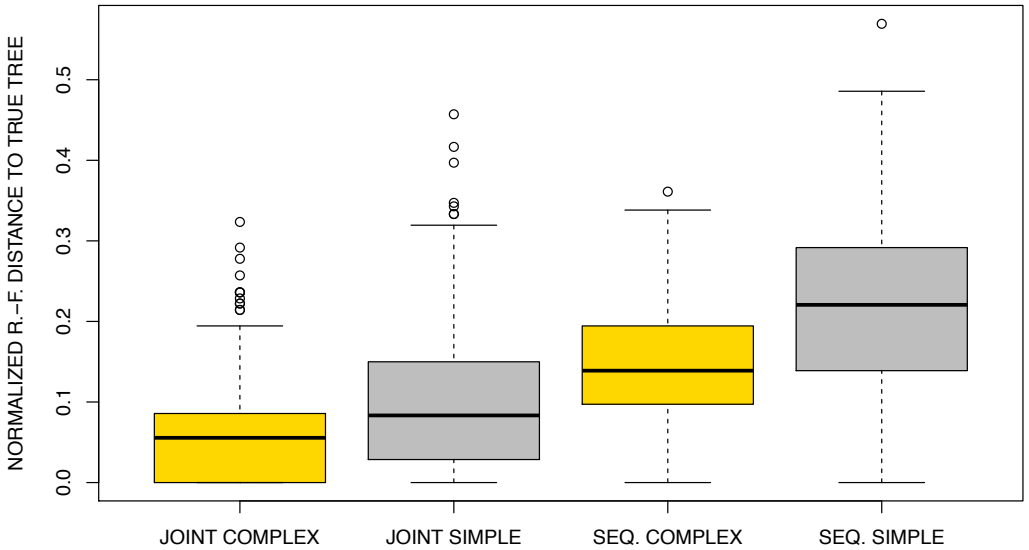


"Realistic simulations" suggest S-aware methods are important

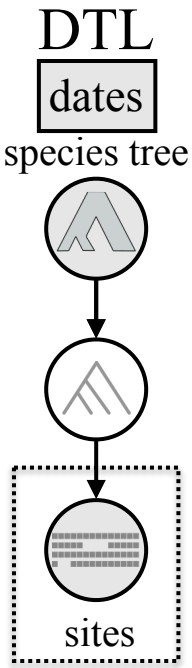


Distance to true tree

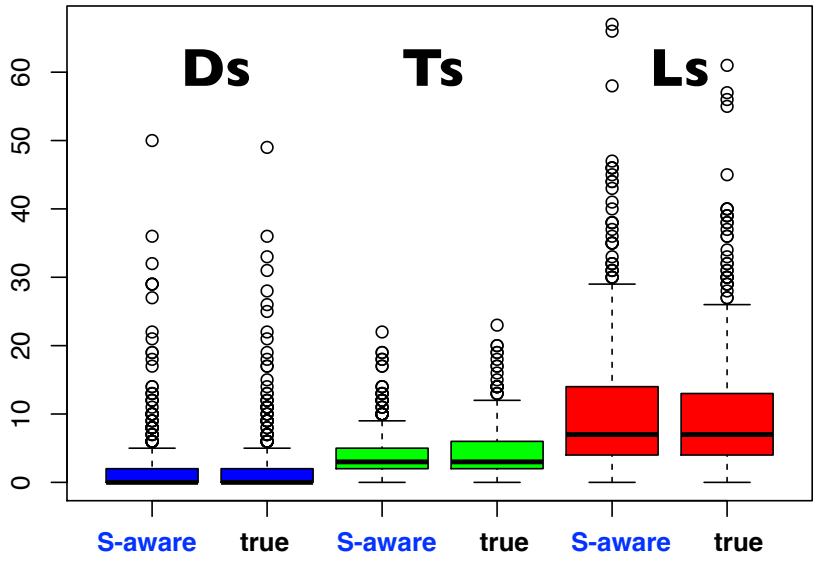
(based on 474 near universal single copy fams.)

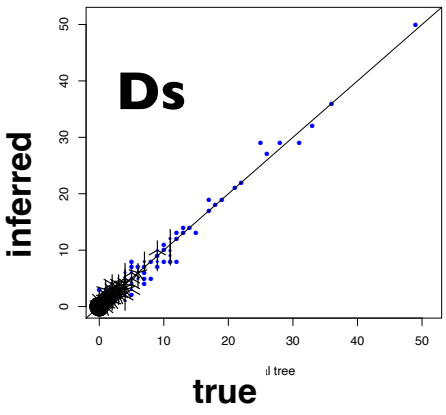


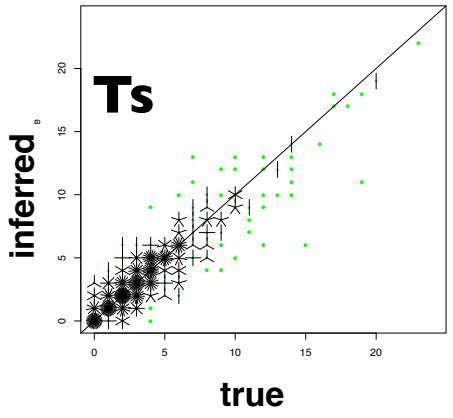
S-aware S-unaware

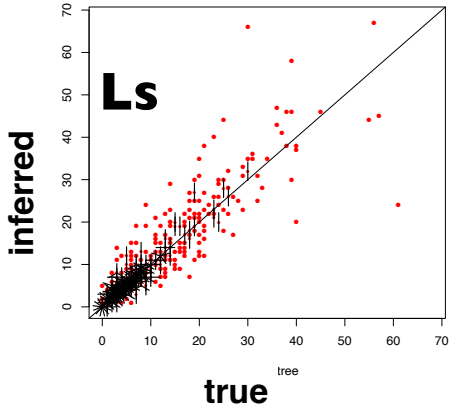


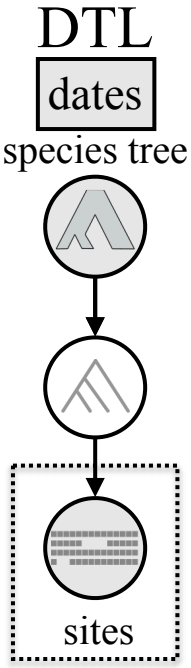
S-aware methods accurately recover number of DTL events





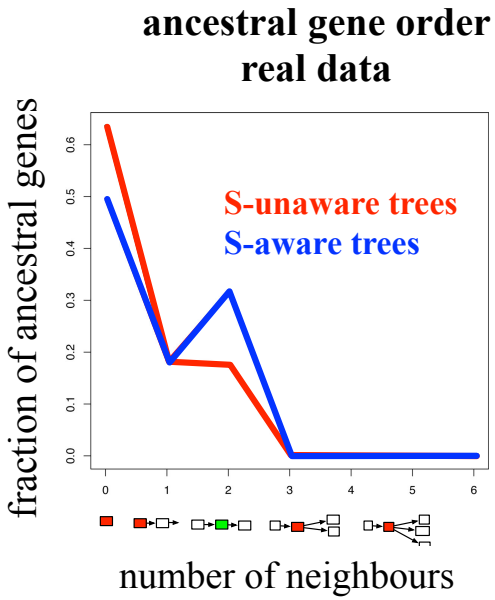


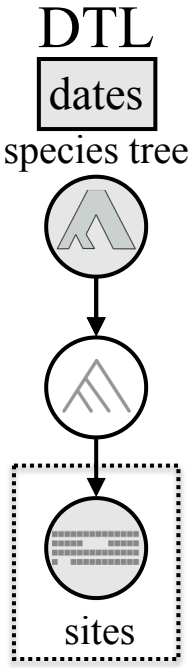




Real data and experiments suggest S-aware methods are important

More accurate gene trees, ancestral sequences (simulations & experiment) and chromosomes (synteny):





implemented in ALE:
http://github.com/ssolo/ALE

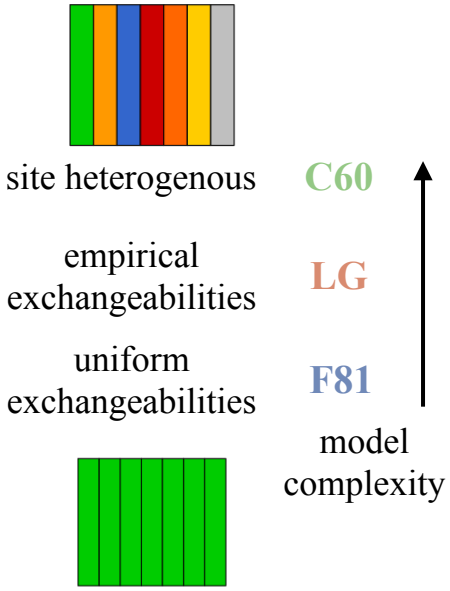
Groussin, Hobbs, **Szöllősi**, Gribaldo, Arcus & Gouy ***Mol. Biol. Evol.*** (2015)
Toward More Accurate Ancestral Protein Genotype–Phenotype Reconstructions with the Use of Species Tree-Aware Gene Trees

Szöllősi, Tannier, Lartillot & Daubin ***Systematic Biology*** (2013)
Lateral Gene Transfer from the Dead

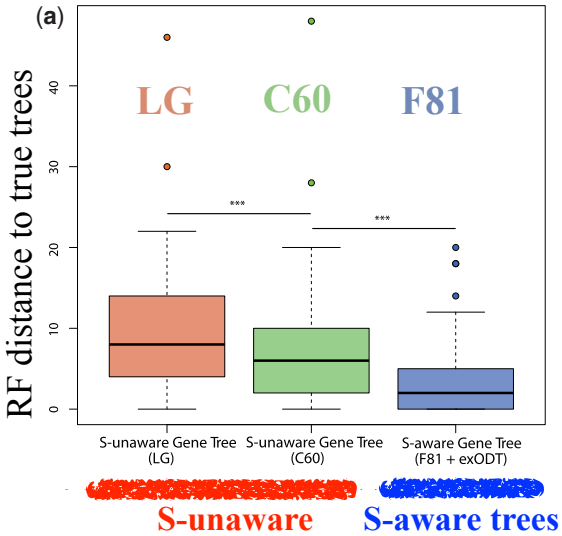
Szöllősi, Rosikiewicz, Boussau, Tannier & Daubin ***Systematic Biology*** (2013)
Efficient exploration of the space of reconciled gene trees

S-aware method are better at reconstructing gene trees..

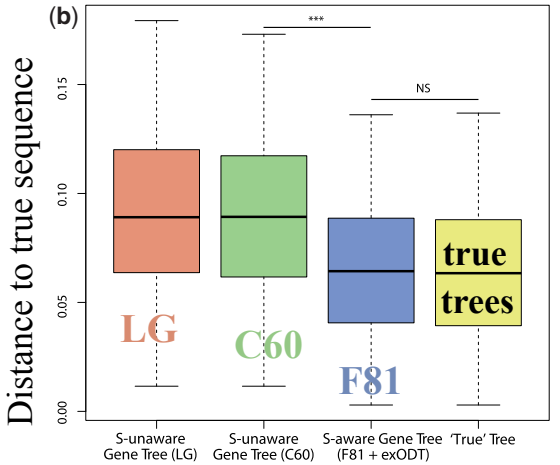
S-aware gene trees and ancestral sequences reconstructed along them
are significantly more accurate according to simulations



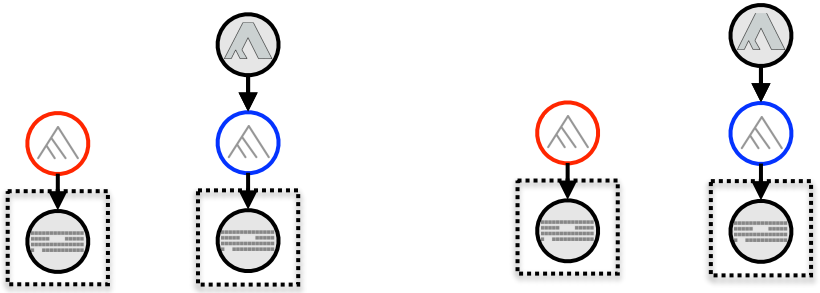
gene tree accuracy
simulation

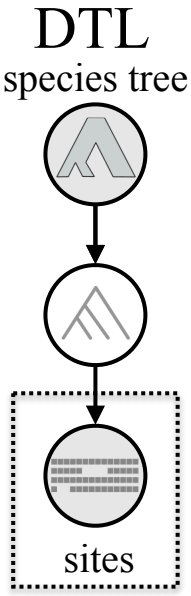


ancestral sequence accuracy
simulation



ancestral sequences





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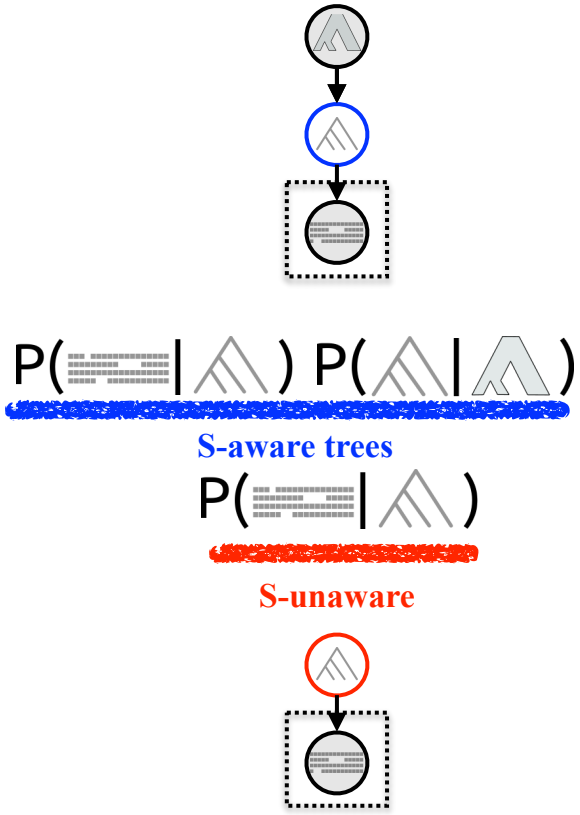
Toward More Accurate Ancestral Protein Genotype–Phenotype Reconstructions with the Use of Species Tree-Aware Gene Trees

S-aware method are better at reconstructing gene trees..

Ancestral sequences reconstructed along S-aware gene trees produce
a biochemically more realistic and thermodynamically more stable ancestral protein.



in vitro biochemical essay on reconstructed ancestral sequences

Enzyme	$K_M^{(TPM)}$ (mM)	T_{opt} ($^\circ C$)	$\Delta G^{\ddagger}_{N-U}$ ($kJmol^{-1}$)
BPSYC	0.2	47	94.9
BSUB	0.7	53	95.9
BCVX	1.1	69	100.7
S-aware Tree + LG	**1.5**	**85**	**114.4**
S-aware Tree + EX_EHO	**1.6**	**85**	**110.9**
S-unaware Tree + EX_EHO	**6.8**	**78**	**91.4**

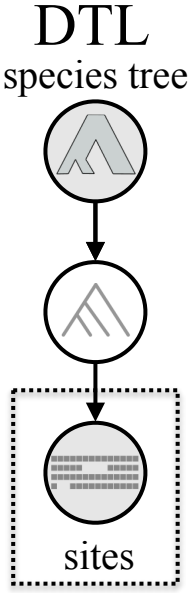
resurrected LeuB of Firmicutes LCA

Table 1: **Biophysical parameters for the ancestral LeuB enzyme of the Firmicutes ancestor.** Values obtained in this study for the ancestor of Firmicutes (bold characters) were inferred using either the LeuB sequence tree or the LeuB reconciled tree and either with the site-homogeneous LG model or with the site-heterogeneous EX_EHO model. Data for contemporary (first three lines) are shown for comparison)

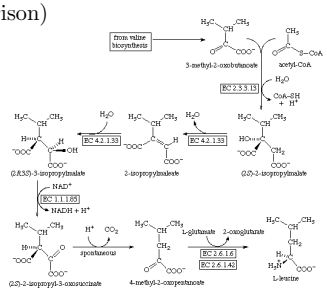
input

output

input



Leucine Biosynthesis:



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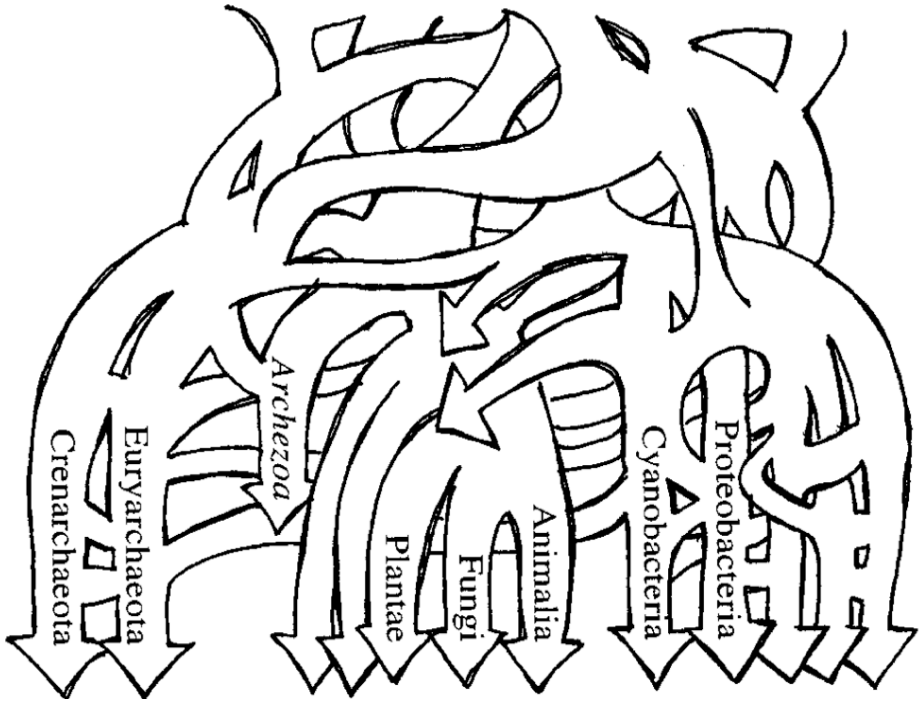
Toward More Accurate Ancestral Protein Genotype–Phenotype Reconstructions with the Use of Species Tree-Aware Gene Trees

just how much HGT is there?

LUCA

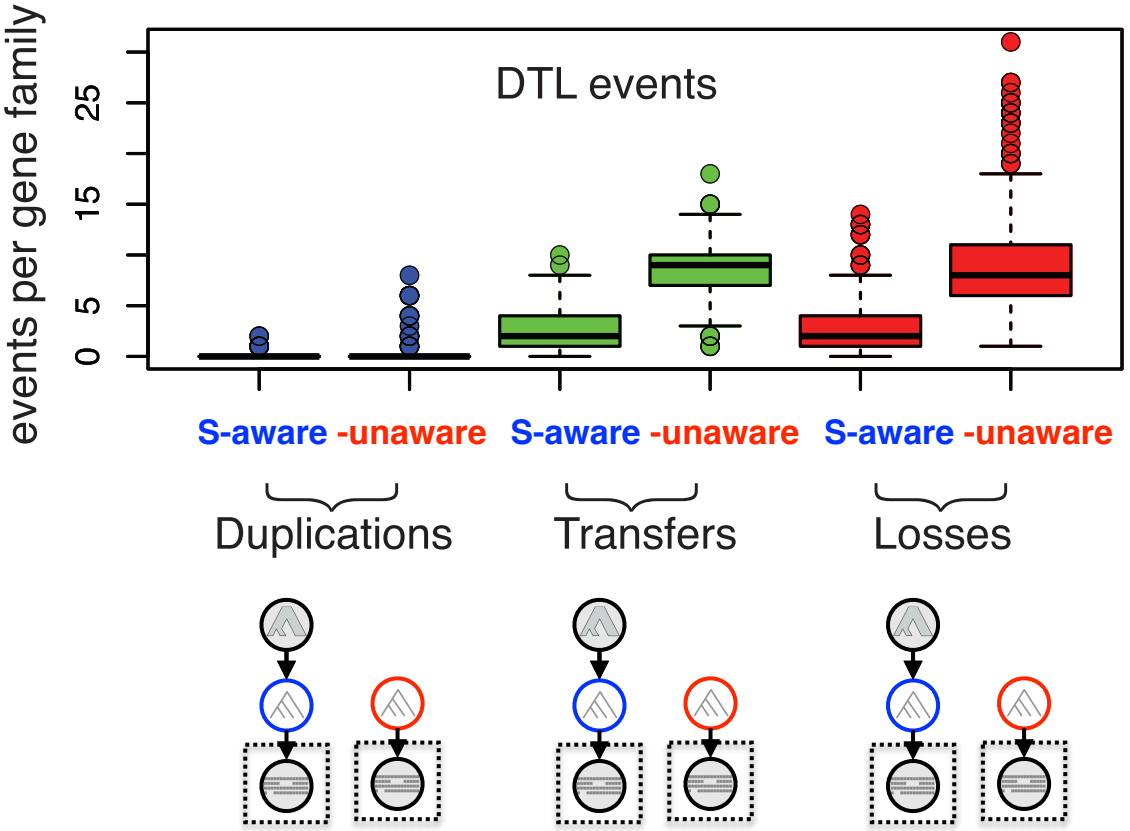


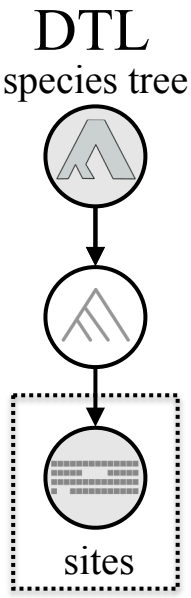
Doolittle 1999

just how much HGT is there?

Two out of three transfers inferred based S-unaware gene trees **are the result phylogenetic errors.**

Two out of three losses inferred based S-unaware gene trees are the result phylogenetic errors.

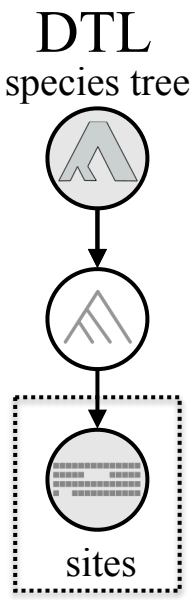




Szöllősi, Rosikiewicz, Boussau, Tannier & Daubin ***Systematic Biology*** (2013)
Efficient exploration of the space of reconciled gene trees

just how much HGT is there?

what about ancestral gene content?



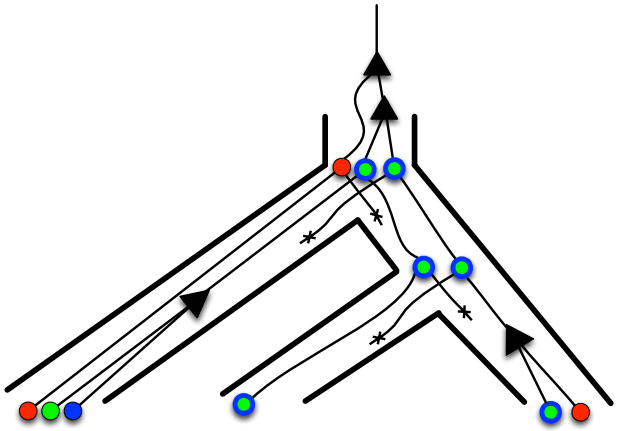
Szöllősi, Rosikiewicz, Boussau, Tannier & Daubin ***Systematic Biology*** (2013)
Efficient exploration of the space of reconciled gene trees

just how much HGT is there?

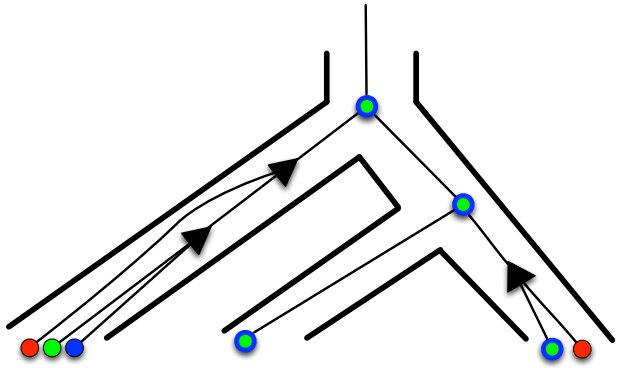
what about ancestral gene content?

Spurious (**false positives**) Ds lead to an **overestimation** of ancestral genome contents, missing Ds (**false negatives**) lead to an **underestimation**.

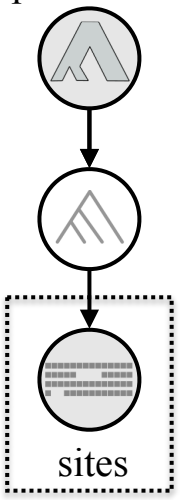
gene tree with errors

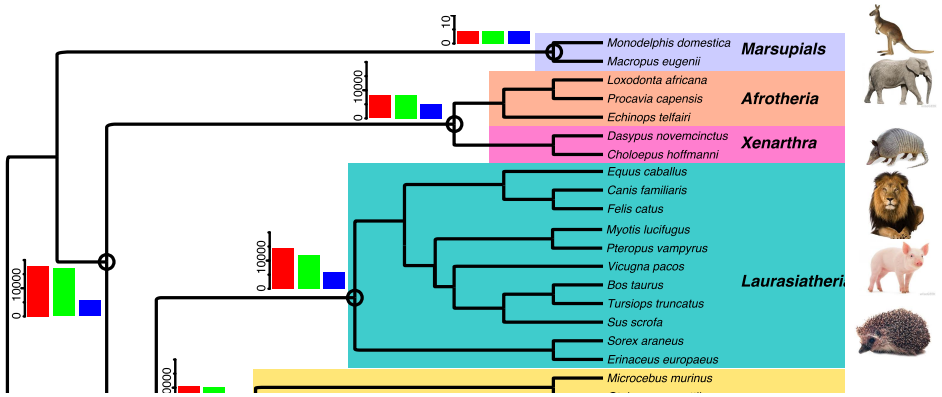


correct gene tree



DTL
species tree

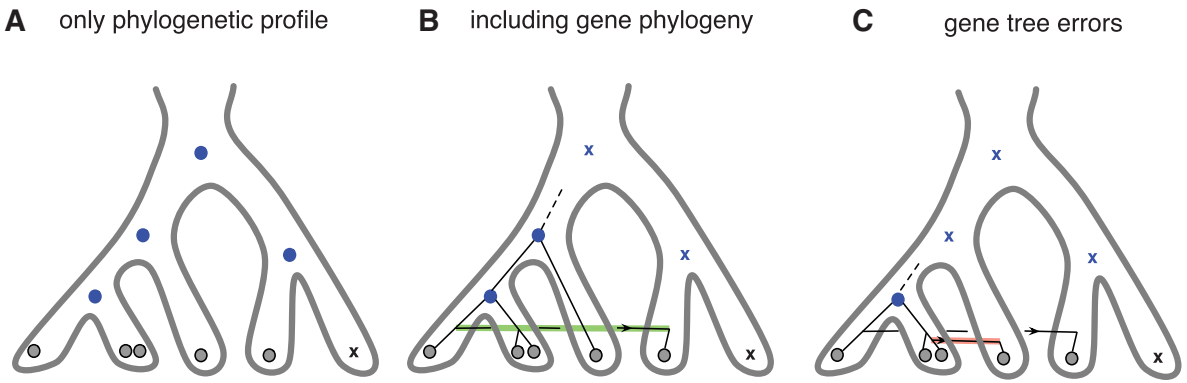




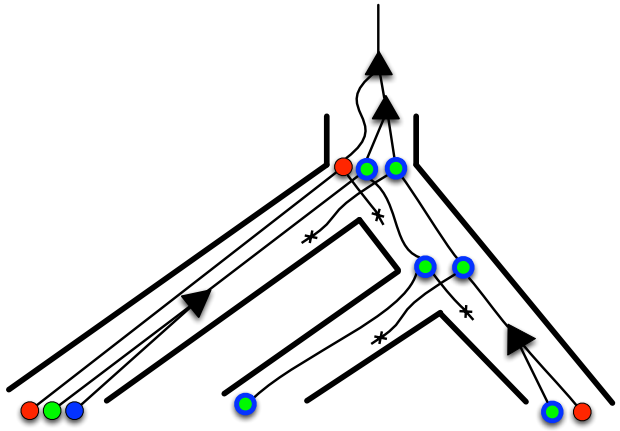
just how much HGT is there?

what about ancestral gene content?

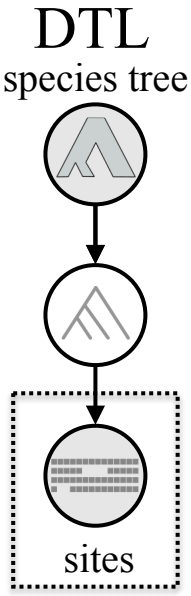
Spurious (**false positives**) Ts lead to an **underestimation** of ancestral genome contents, missing Ts (**false negatives**) lead to an **overestimation** at deep nodes.



Ignoring transfer, i.e. **considering only DL also leads to an overestimate**.

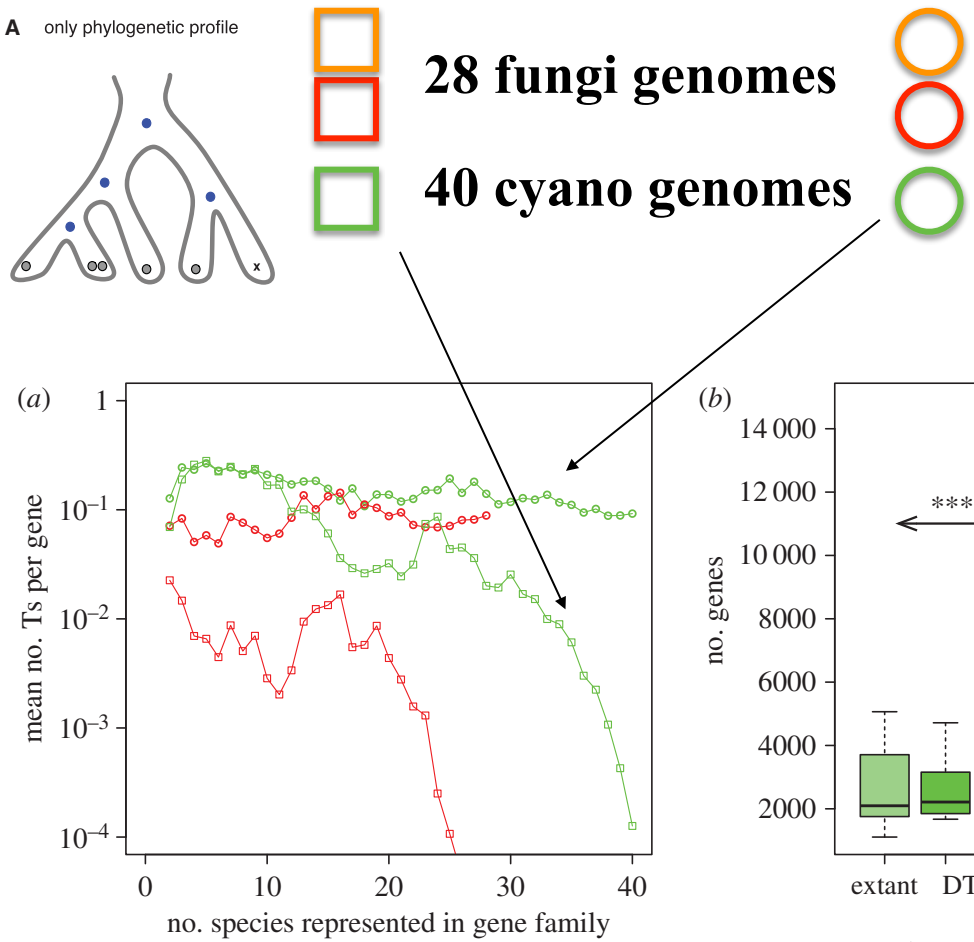


gene tree with “unmodelled” transfers

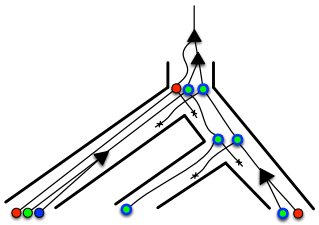


just how much HGT is there?

Is HGT frequent only in prokaryotes?



"un-modelled" transfers

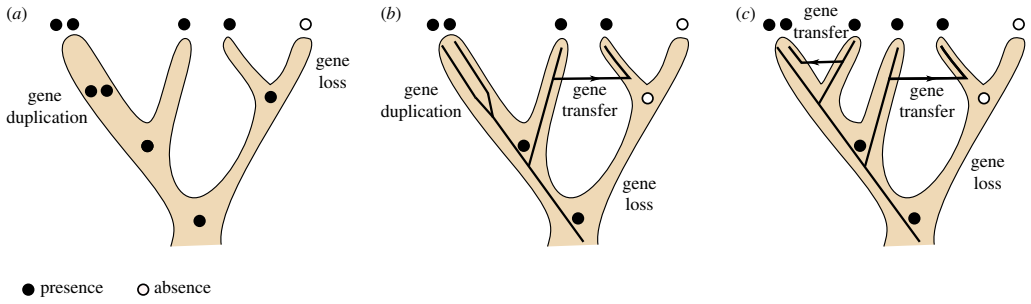


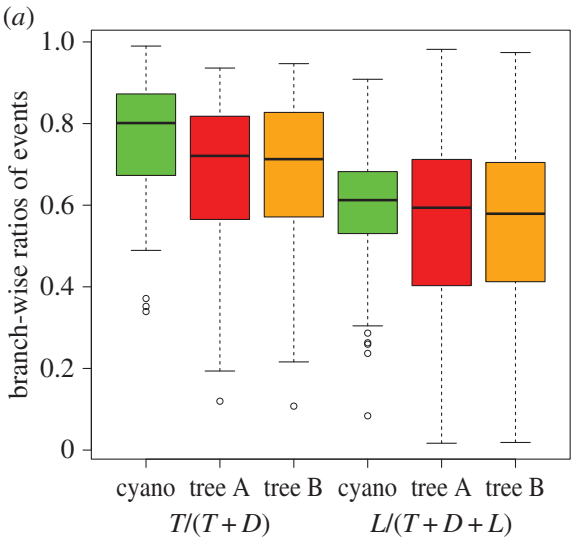
Ignoring transfer, i.e. considering only DL leads to an overestimate..

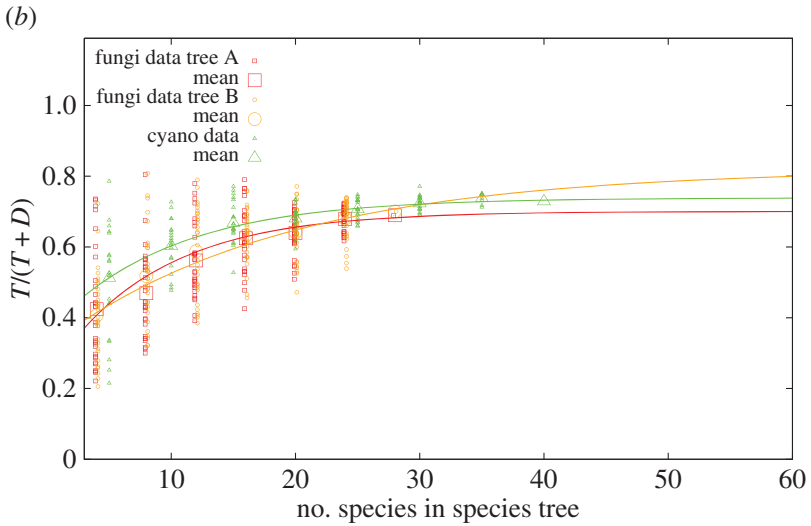
Szöllősi, Davin, Tannier, Daubin & Boussau *Phil.Trans.Roy.Soc.B* (2015)
Genome-scale phylogenetic analysis finds extensive gene transfer among fungi.

just how much HGT is there?

There is extensive gene transfer among fungi





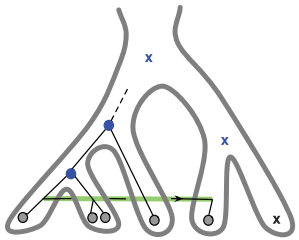


Szöllősi, Davin, Tannier, Daubin & Boussau *Phil.Trans.Roy.Soc.B* (2015)
Genome-scale phylogenetic analysis finds extensive gene transfer among fungi.

just how much HGT is there?

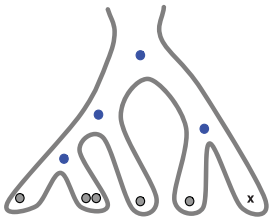
There is extensive gene transfer among fungi

B including gene phylogeny



28 fungi genomes

A only phylogenetic profile



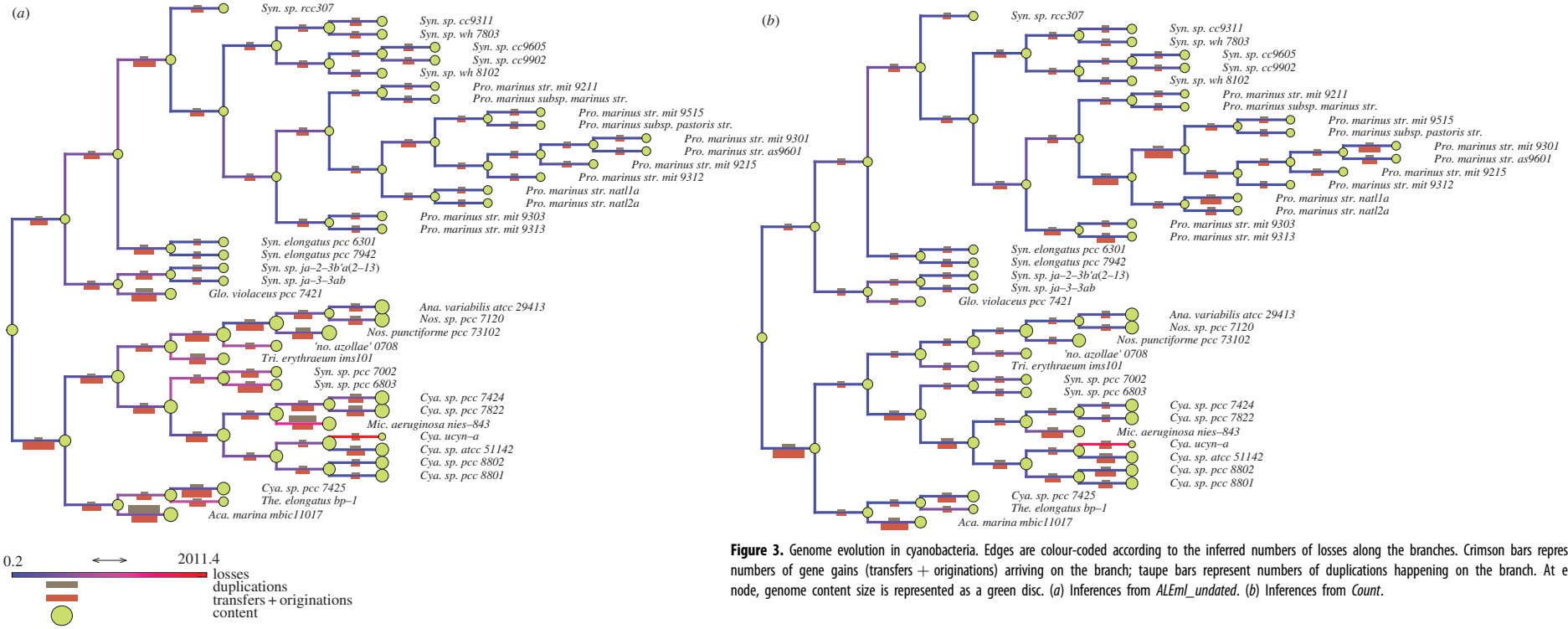


Figure 3. Genome evolution in cyanobacteria. Edges are colour-coded according to the inferred numbers of losses along the branches. Crimson bars represent numbers of gene gains (transfers + originations) arriving on the branch; taupe bars represent numbers of duplications happening on the branch. At each node, genome content size is represented as a green disc. (*a*) Inferences from *ALEml_undated*. (*b*) Inferences from *Count*.

Szöllősi, Davin, Tannier, Daubin & Boussau *Phil.Trans.Roy.Soc.B* (2015)
Genome-scale phylogenetic analysis finds extensive gene transfer among fungi.

Stronger transfer highways in fungi

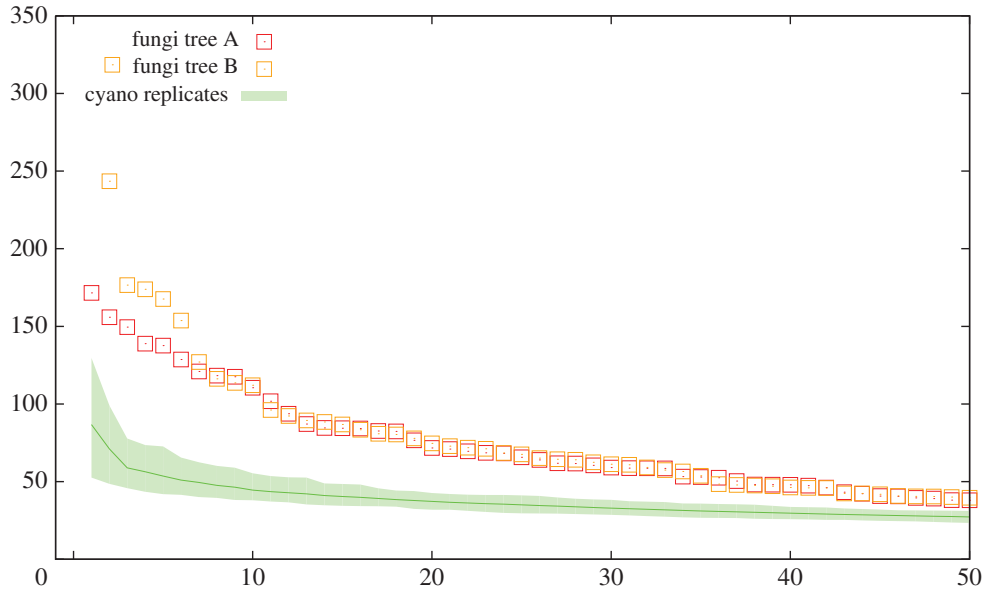


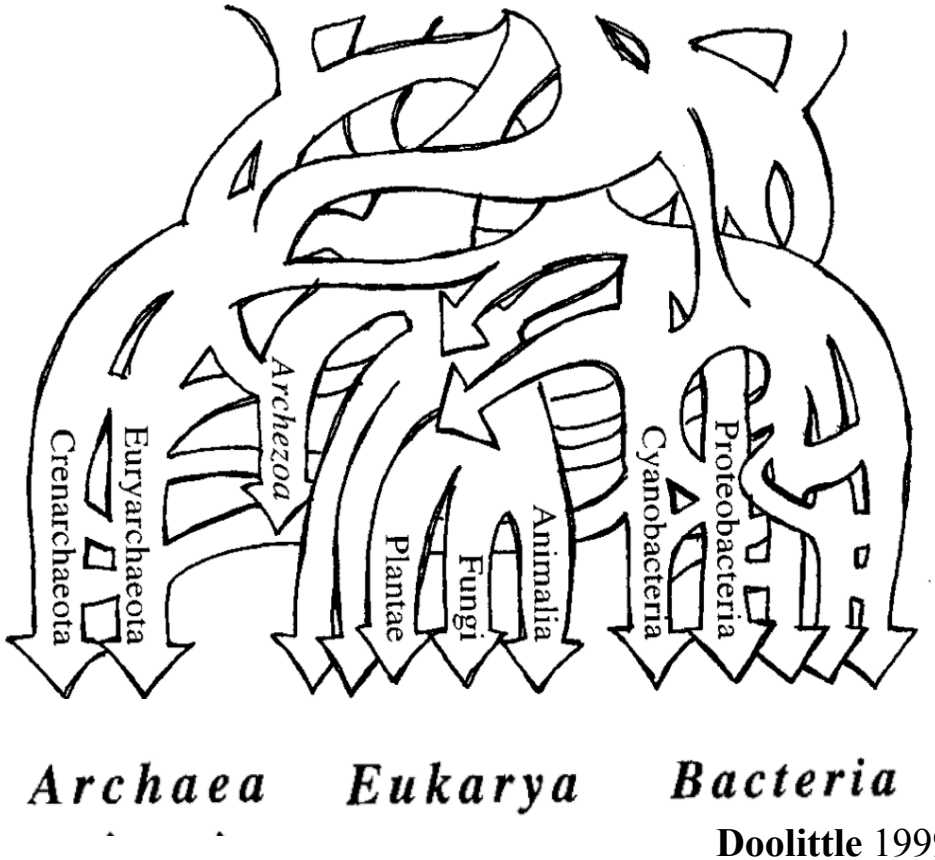
Figure 6. Stronger highways in fungi. Data points, red for tree A and orange for tree B, correspond to numbers of transfers between pairs of branches ('highways of transfers') in either fungi phylogeny plotted in decreasing order. The continuous line (green online) shows the mean number of transfers between pairs of branches among 25 replicates where a random set of 28 cyanobacterial genomes were chosen as in figure 5*b*. The shaded area shows the 95% CI. Fungi are in red and cyanobacteria in green throughout.

Szöllősi, Davin, Tannier, Daubin & Boussau *Phil.Trans.Roy.Soc.B* (2015)
Genome-scale phylogenetic analysis finds extensive gene transfer among fungi.

Horizontal gene transfer as noise

Gene transfers result in apparently contradicting gene phylogenies, fungi can seem closely related to aphids. A potentially high rate of transfer esp. early in the evolution of life, suggests that the vertical signal may be drowned in noise.

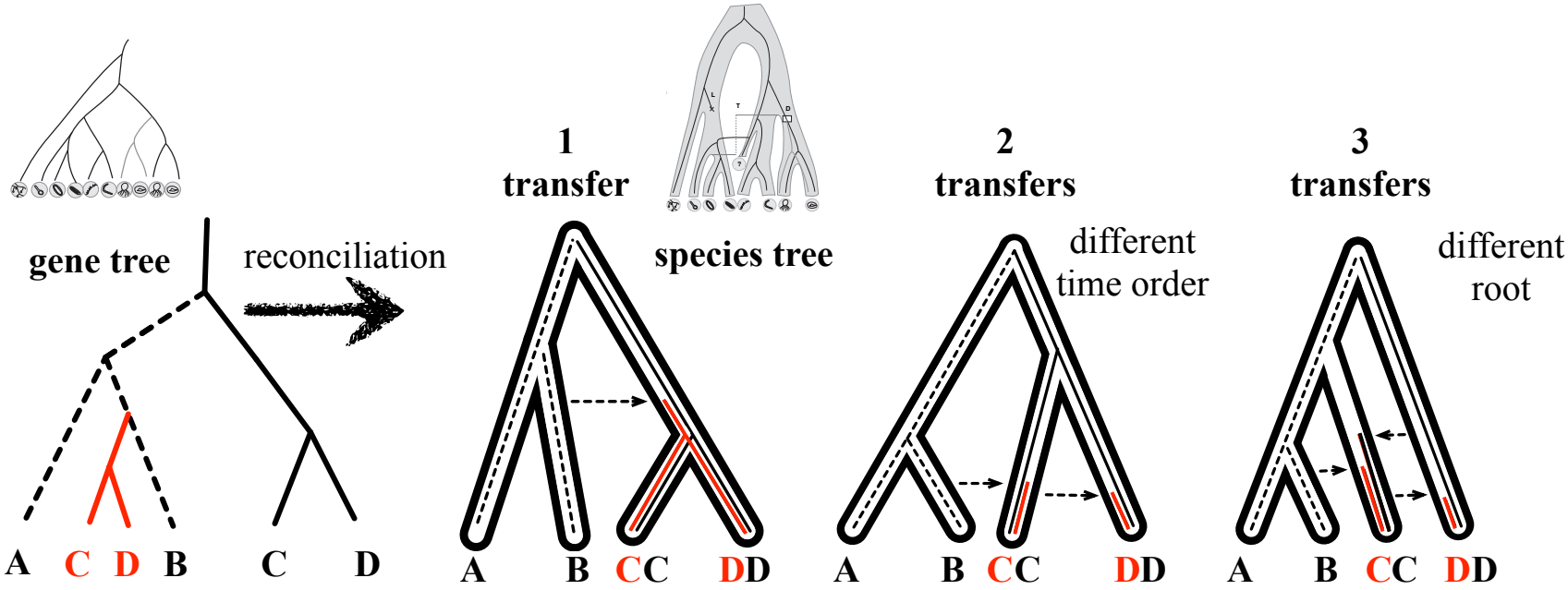
LUCA



Doolittle 1999

Horizontal gene transfer as information

Transfer events, encoded in the topologies of gene trees can be thought of as "*molecular fossils*" that record the order of speciation events.



Vincent Daubin

LBBE

Szöllősi, Boussau, Abby, Tannier & Daubin ***PNAS*** (2012)
Phylogenetic modeling of lateral gene transfer reconstructs the pattern and relative timing of speciations

Gene trees and species trees can be jointly reconstructed

Estimating genes and species history can be achieved through a hierarchical structure, on top of which a species tree is inferred from gene trees through models of gene family evolution, themselves inferred from sequence alignments through models of sequence evolution.

parallel computation scheme

$$\mathcal{L}(\{G_j\}, S, \text{rates}|\{A_{ij}\}) :$$

server:
calculate

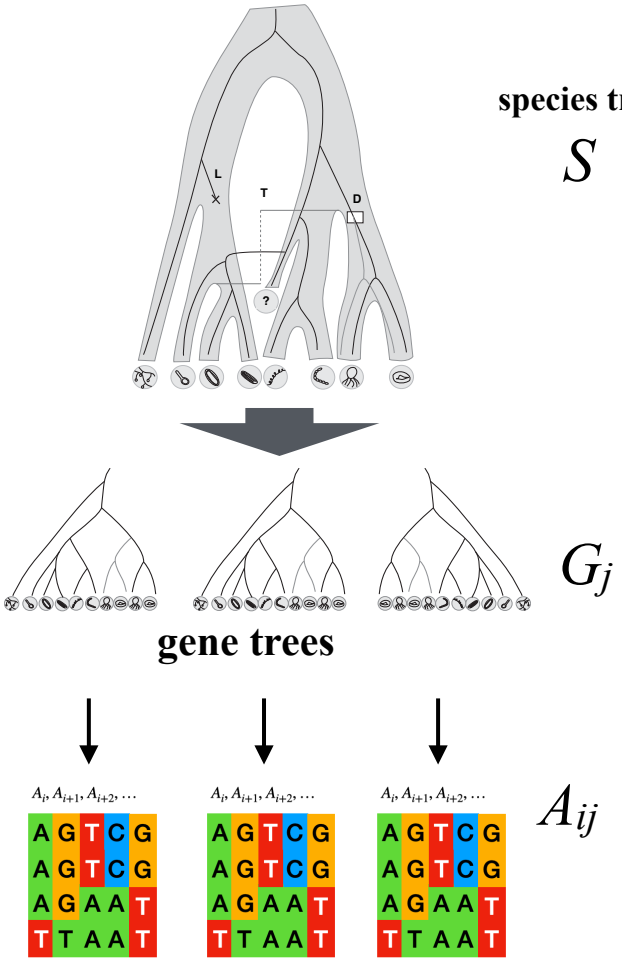
$$\prod_j$$

optimise S
and estimate rates

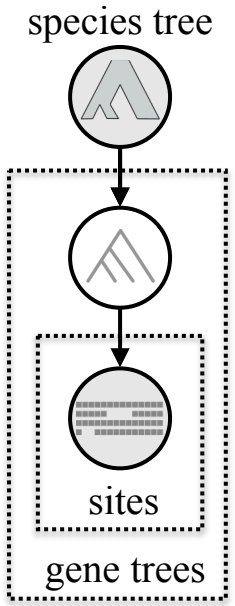
clients:
calculate

$$\prod_i p(A_{ij}|G_j) \times \; p(G_j|S, \text{rates})$$

optimise (or integrate over) G_j



Daubin & Boussau 2011

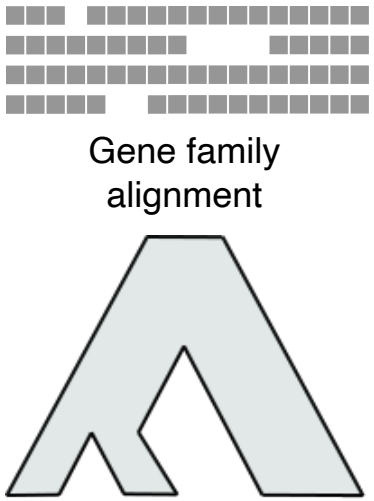


Boussau, **Szöllősi**, Duret, Gouy, Tannier & Daubin *Genome Res.* (2013)
Genome-scale coestimation of species and gene trees

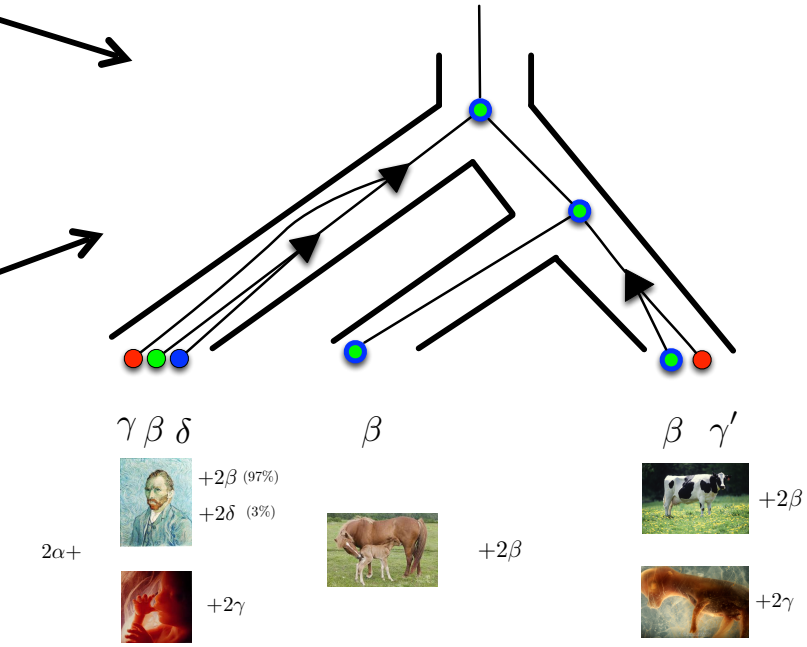
The solution is to model how gene trees are generated along the species tree

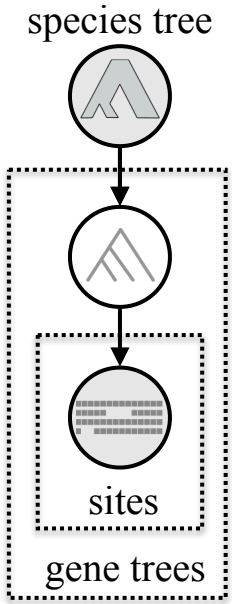
Given the **species tree, which gene tree** produced my **sequences**? ..
and in **what evolutionary context?**

Joint likelihood: $P(\text{gene trees} \mid \text{species tree})\ P(\text{species tree})$

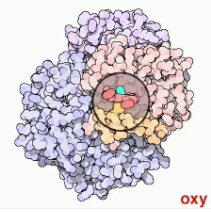


Most likely species tree-aware gene tree





hemoglobin



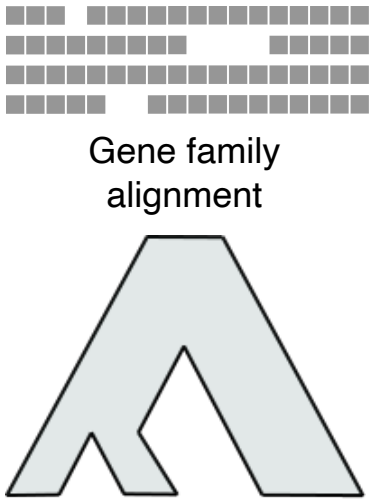
SZÖLLŐSI

gergely.szollosi@oist.jp

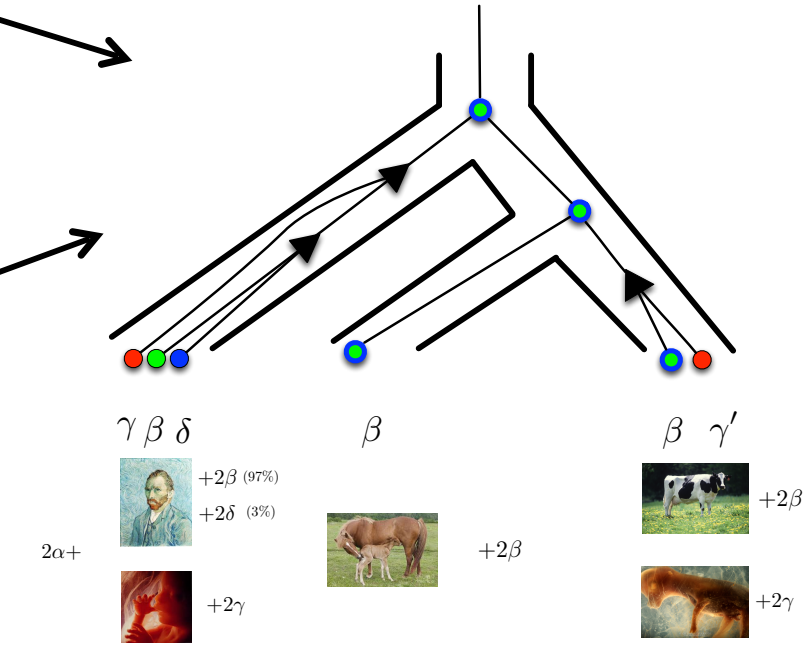
The solution is to model how gene trees are generated along the species tree

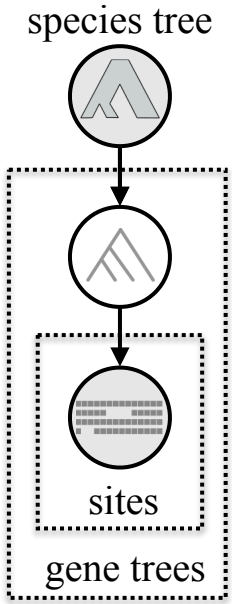
Given the **species tree, which gene tree** produced my **sequences**? ..
and in **what evolutionary context?**

Joint likelihood: $P(\text{gene trees} \mid \text{species tree})\ P(\text{species tree})$

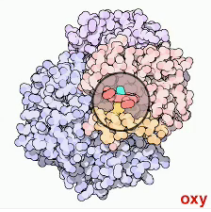


Most likely species tree-aware gene tree





hemoglobin



SZÖLLŐSI

gergely.szollosi@oist.jp

Amalgamated Likelihood Estimation

Efficiently exploring the space of reconciled gene trees

Based on a sample of trees conditional clade probabilities can be used to efficiently sum over gene tree uncertainty and sample **species tree-aware** gene trees along with there reconciliations.

Given the **species tree, which gene tree** produced my **sequences**? .. and in **what evolutionary context?**

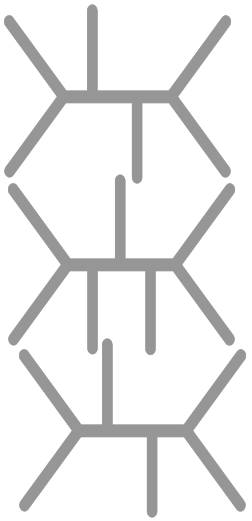
Sequence likelihood:

$P(\text{sequences} \mid \text{species tree})$

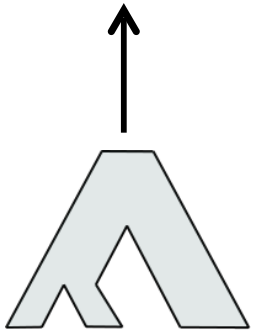
Joint likelihood:

$\sum_{\text{species tree}} P(\text{sequences} \mid \text{species tree})\, P(\text{species tree} \mid \text{species tree})$

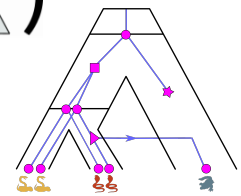
Gene family alignment

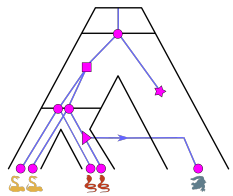


Gene tree distribution



Rooted species tree





Reconciled **species tree-aware** gene trees

Szöllősi, Tannier, Lartillot & Daubin ***Systematic Biology*** (2013)
Lateral Gene Transfer from the Dead

Szöllősi, Rosikiewicz, Boussau, Tannier & Daubin ***Systematic Biology*** (2013)
Efficient exploration of the space of reconciled gene trees

ALE

http://github.com/ssolo/ALE

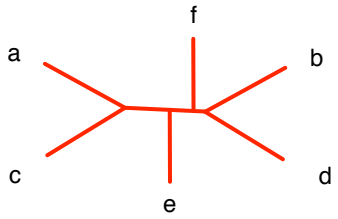
Efficiently exploring the space of reconciled gene trees

Based on a sample of trees conditional clade probabilities can be used to estimate posterior probability of any gene tree that can be amalgamated. This is usually a very large number of trees (e.g. for 10^4 samples 10^{12} trees, but up to 10^{40}).

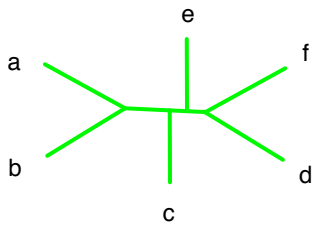
Felsenstein 1981

$P(\text{gene tree} \mid \text{species tree})$ **Gene tree sample**

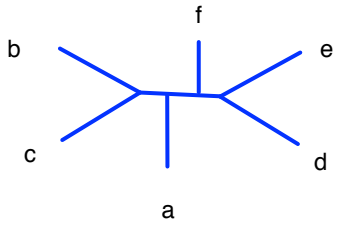
$\approx 2/10$ 2X



$\approx 3/10$ 3X

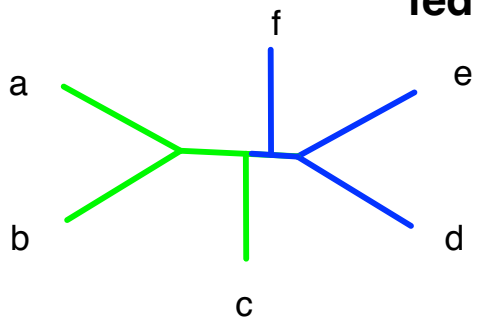


$\approx 5/10$ 5X



$P(\text{gene tree} \mid \text{species tree}) \approx 3/8 \times 5/10$

$\frac{\textbf{ab-c}}{\textbf{abc}} = 3/8$ $\frac{\textbf{ed-f}}{\textbf{fed}} = 5/10$



more precisely:

$P(\text{species tree} \mid \text{gene tree}) \propto P(\text{gene tree} \mid \text{species tree}) P(\text{species tree})$

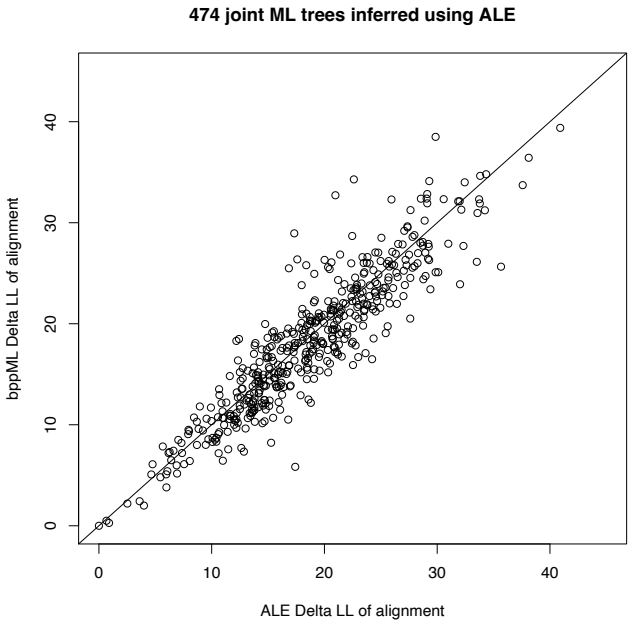
posterior — likelihood — prior (uniform)

Efficiently exploring the space of reconciled gene trees

Based on a sample of trees conditional clade probabilities can be used to estimate posterior probability of any gene tree that can be amalgamated. This is usually a very large number of trees (e.g. for 10^4 samples 10^{12} trees, but up to 10^{40}).

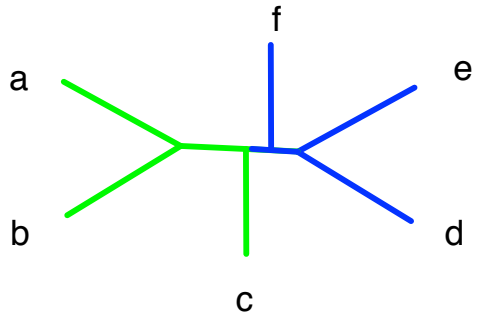
$P(\quad | \quad)$

explicit ML LL



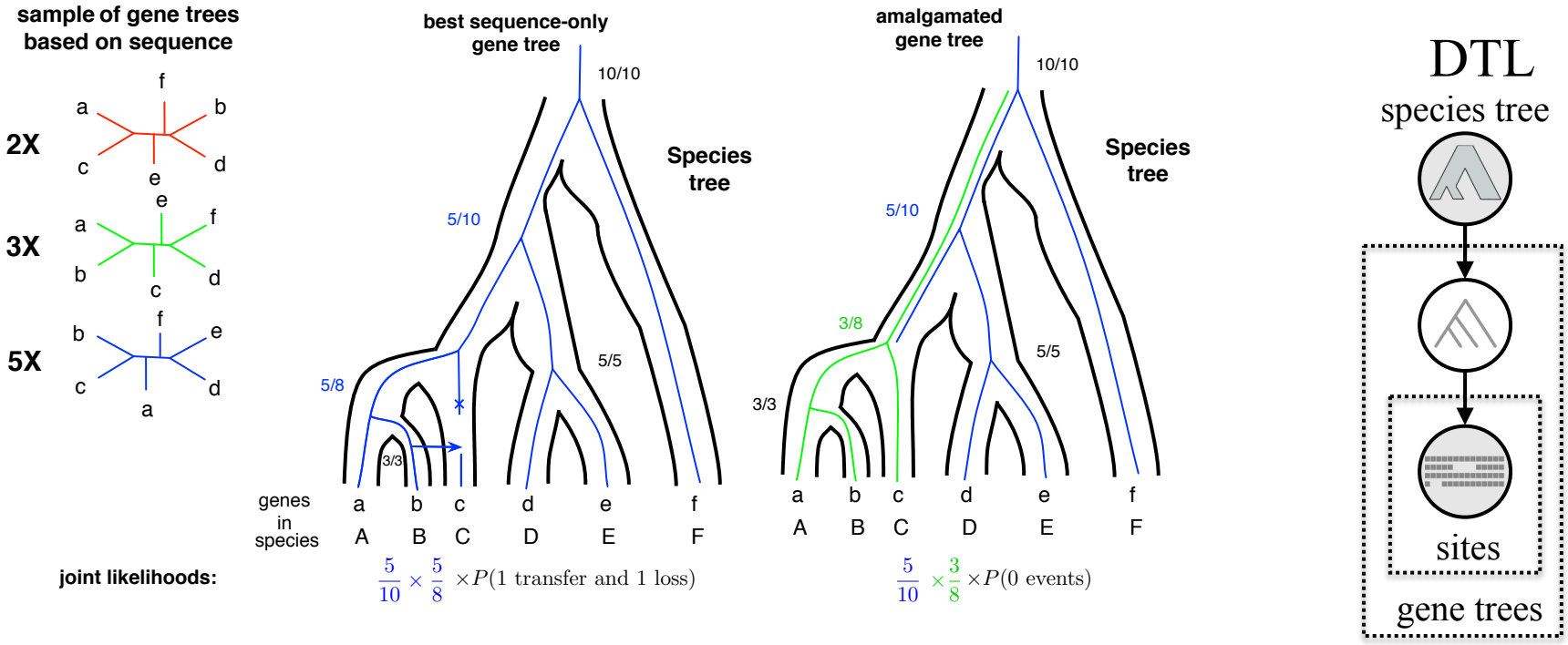
ALE LL

$\approx$ 3/8 × 5/10



Efficiently exploring the space of reconciled gene trees

Based on a sample of trees conditional clade probabilities can be used to estimate posterior probability of any gene tree that can be amalgamated. This is usually a very large number of trees (e.g. for 10^4 samples 10^{12} trees, but up to 10^{40}). *The dynamic programming used in gene tree-species tree reconciliation can be extended to approximate the joint likelihood efficiently for a very large set of gene trees.*



implemented in ALE:

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Szöllősi, Tannier, Lartillot & Daubin *Systematic Biology* (2013)
Lateral Gene Transfer from the Dead

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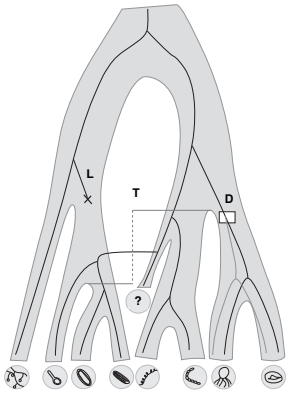
Efficient exploration of the space of reconciled gene trees

Szöllősi, Tannier, Daubin & Boussau *Systematic Biology* (2015)
The inference of gene trees with species trees

Using phylogenetic incongruence to reconstruct a dated ToL

Estimating genes and species history can be achieved through a hierarchical structure, on top of which a species tree is inferred from gene trees through models of gene family evolution, themselves inferred from sequence alignments through models of sequence evolution.

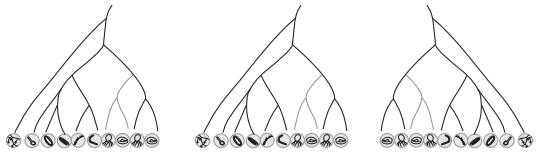
Rooted dated species tree



S

Daubin & Boussau 2011

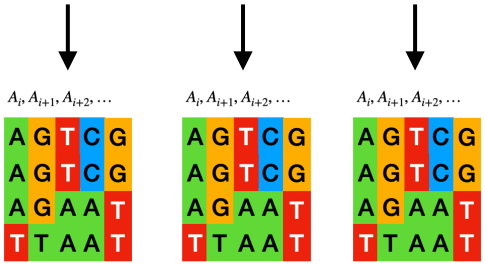
Fossils & HGT



$\int_{G_j} G_j$

gene trees

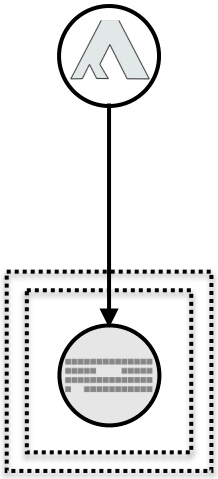
Alignment of homologous genes from complete genomes



A_{ij}

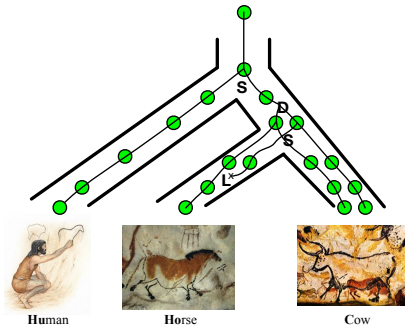
alignments

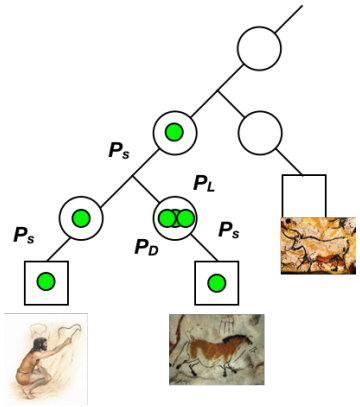
DTL
species tree

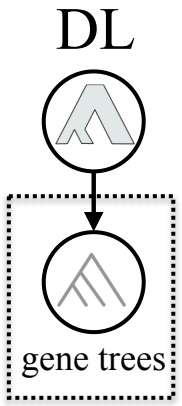


.. but gene trees are generated along the species tree

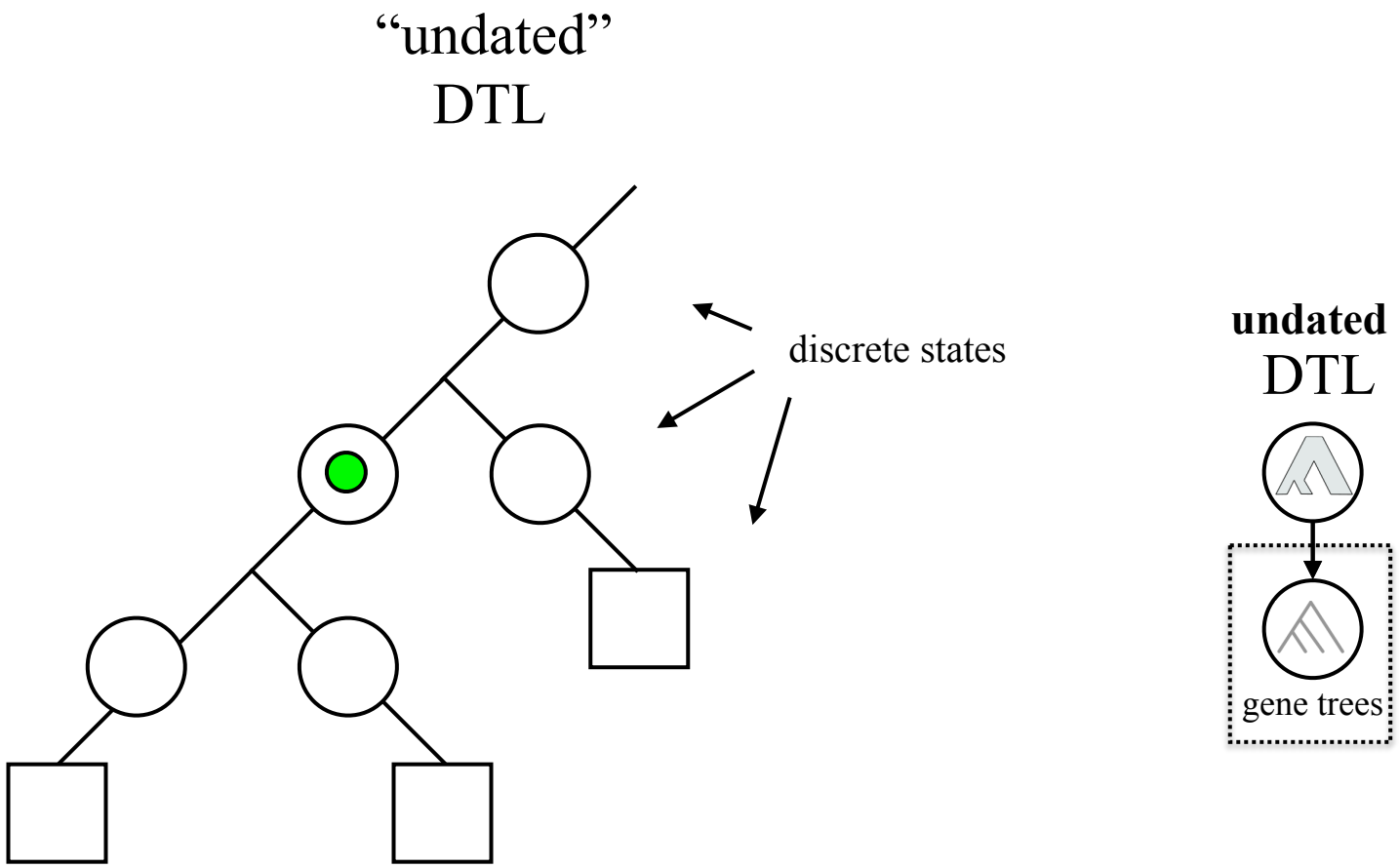
If we model the process generating gene trees along the species tree we can hope to infer better gene trees and species trees. To calculate the likelihood of a ***gene tree*** we sum over all possible ***gene birth and death events*** along a given ***species tree.***



	calculation complexity	**parameters (ML or Bayes)**
	DL ~10 × log(#species) × #genes DTL ~ 10 × #species² × #genes	DL D&L rates branch lengths, root DTL D,T&L rates dated tree
	DL log(#species) × #genes “undated” DTL #species × log(#species) × #genes	DL D&L rates, root “undated” DTL D,T&L rates, root



faster *models of gene family evolution with DT&L*



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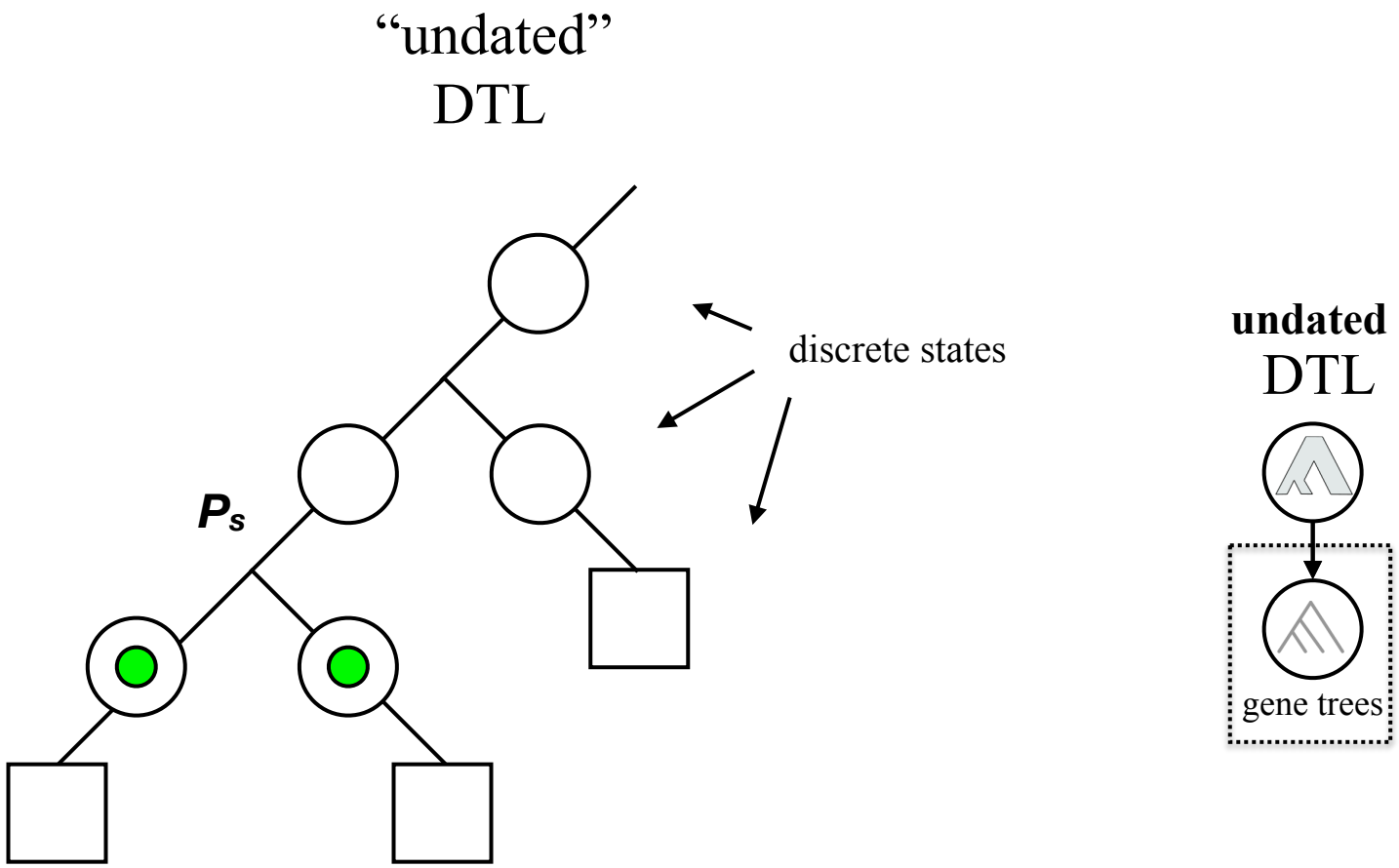
faster *models of gene family evolution with DT&L*



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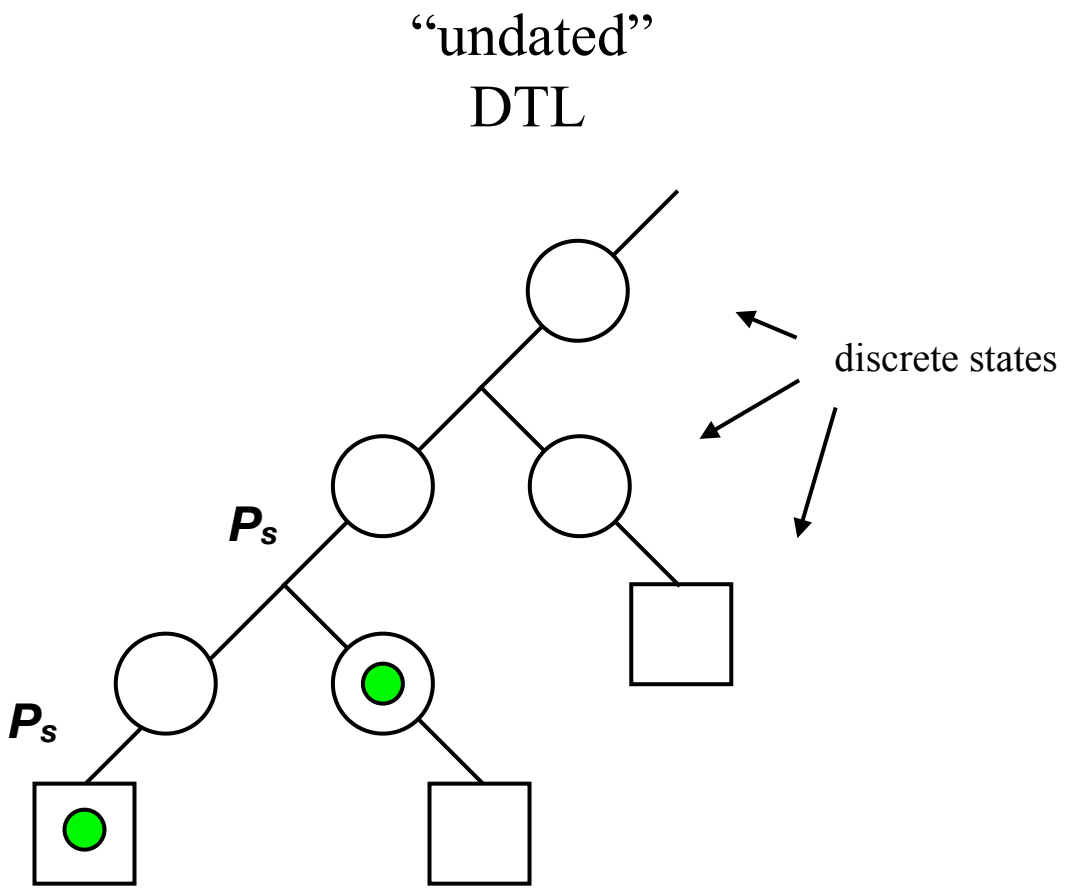

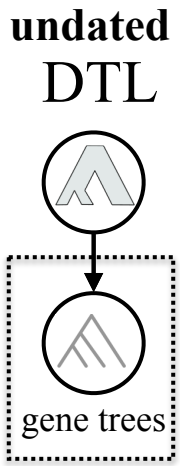

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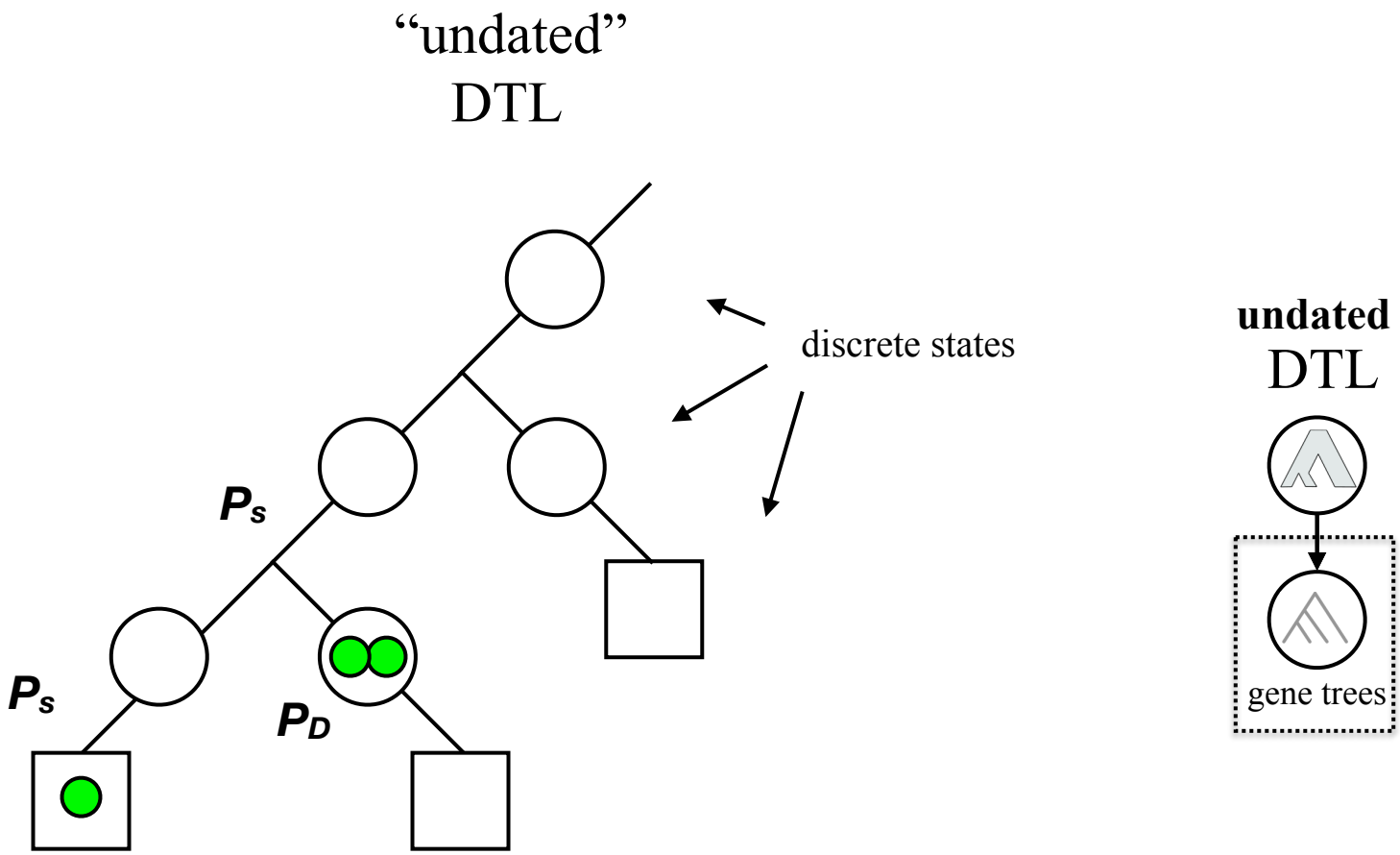

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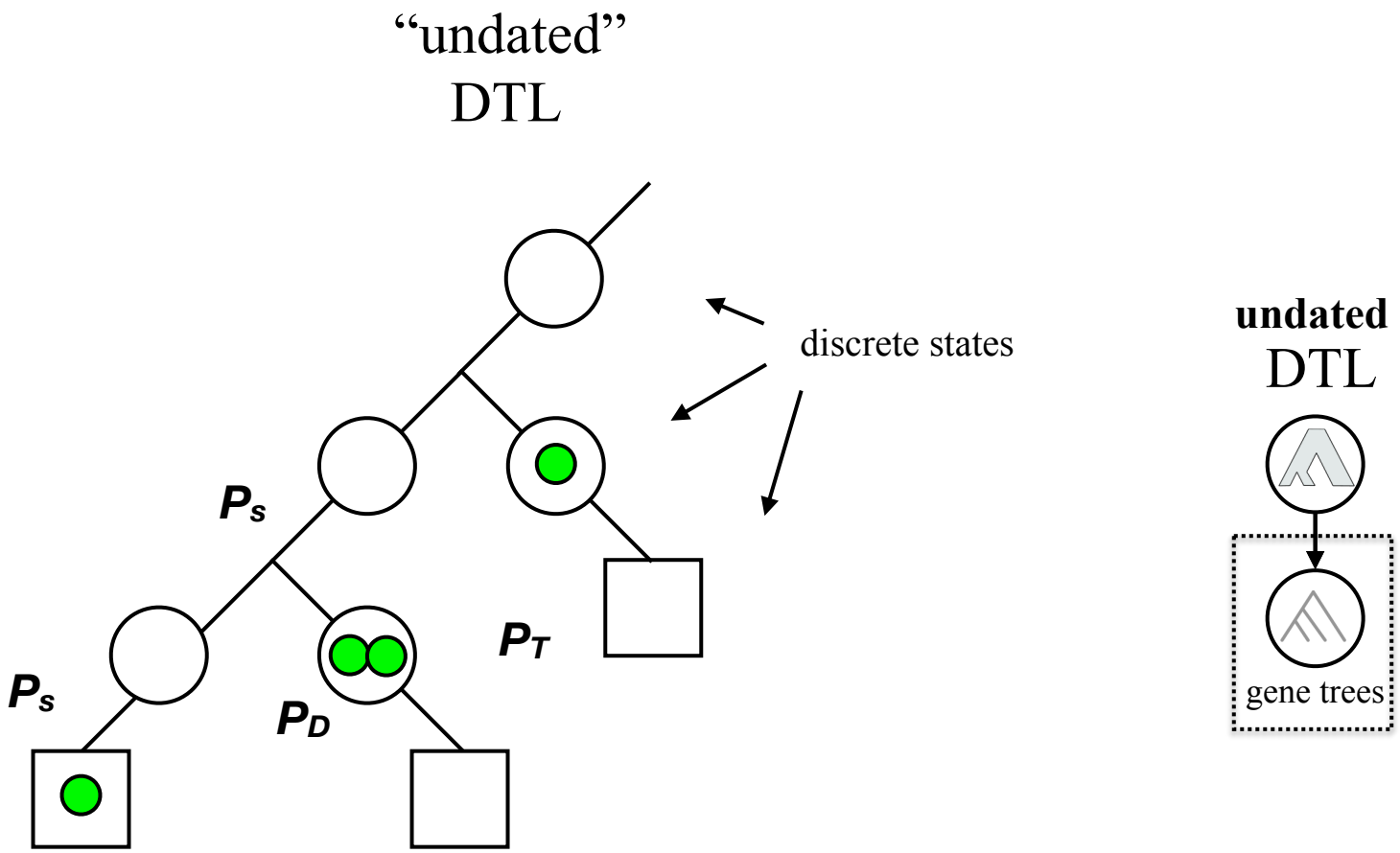

implemented in ALE:

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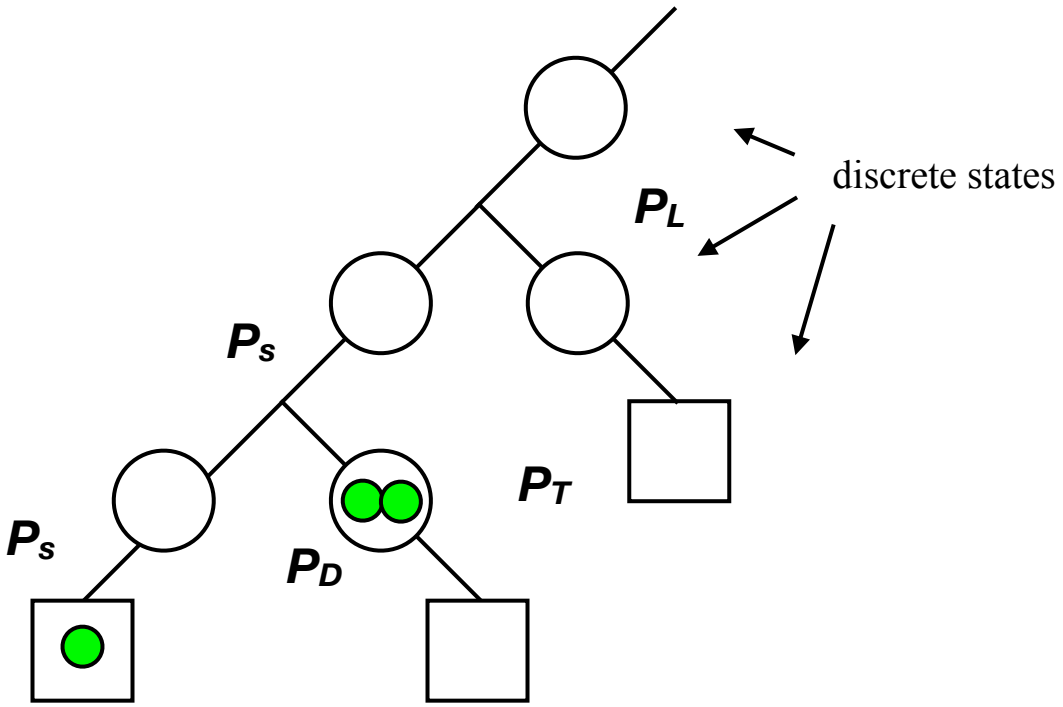
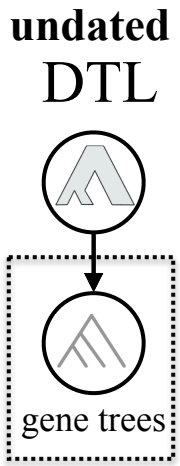
faster *models of gene family evolution with DT&L*

$P_S + P_D + P_T + P_L = 1$



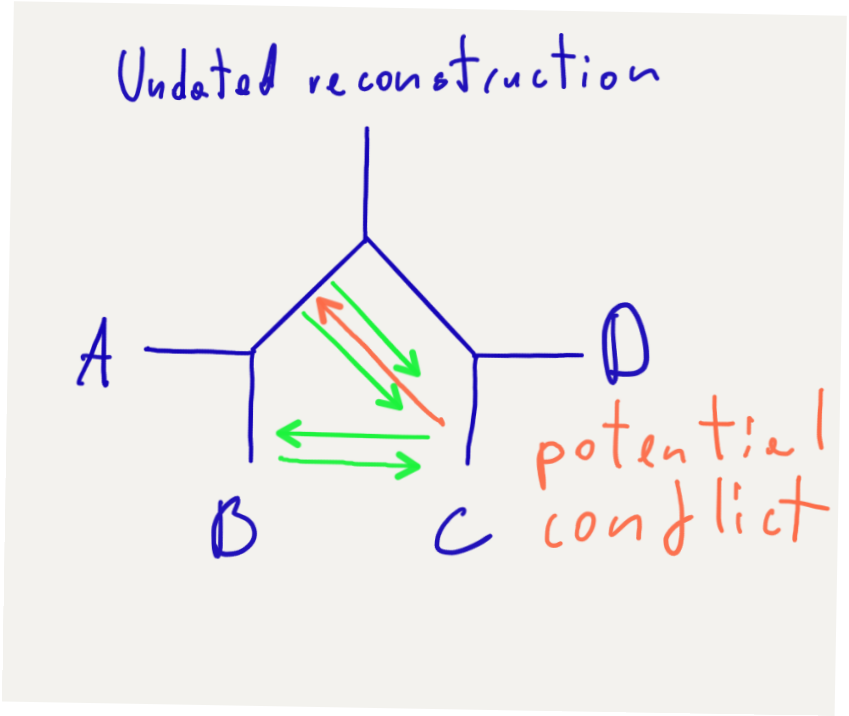


implemented in ALE:

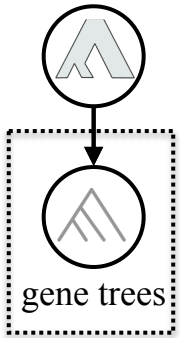
http://github.com/ssolo/ALE

faster *models of gene family evolution with DT&L*

“undated”
DTL



undated
DTL



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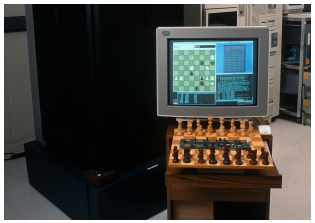
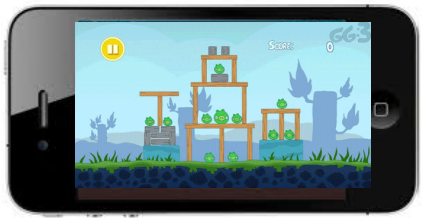


“undated” DTL



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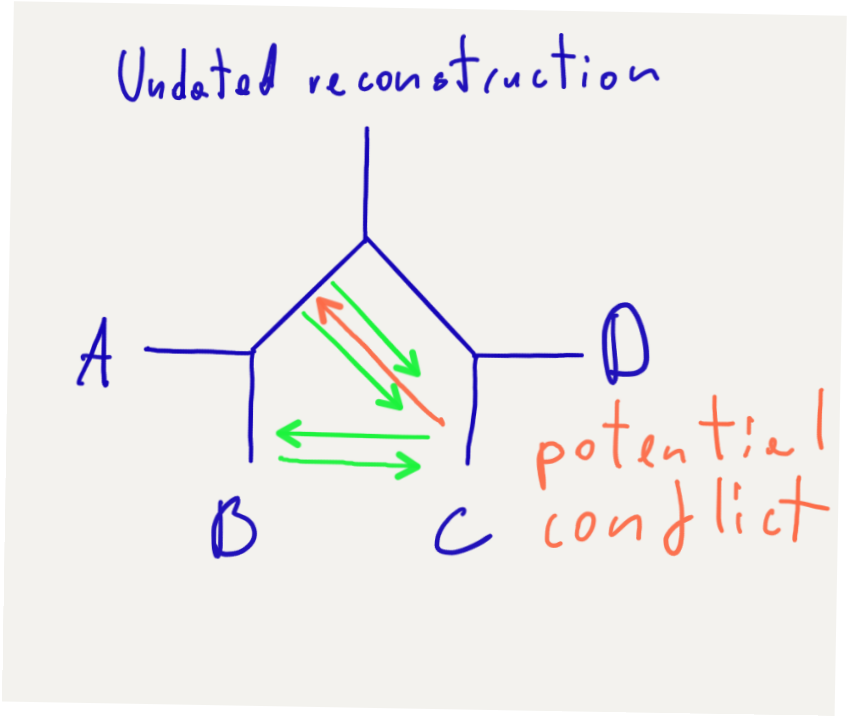
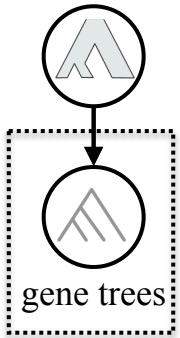


undated
DTL



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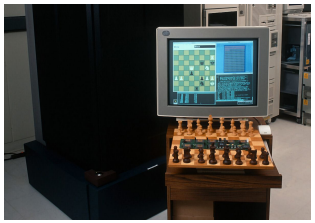

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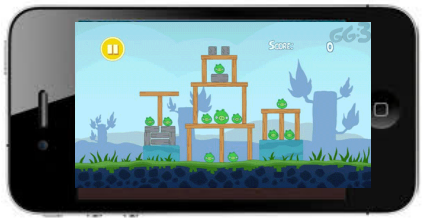


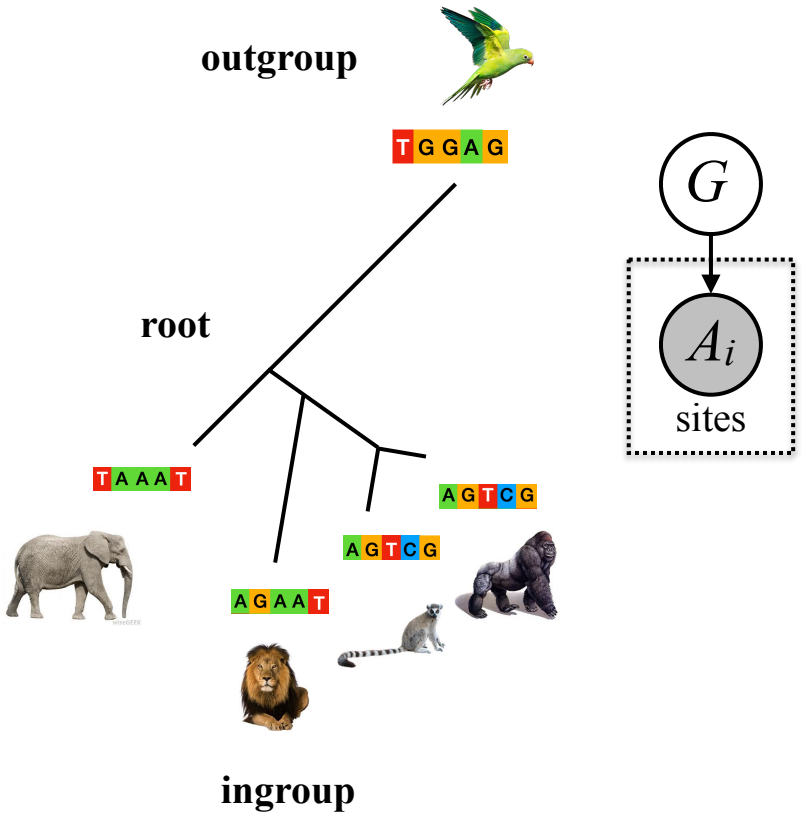
implemented in ALE:

http://github.com/ssolo/ALE

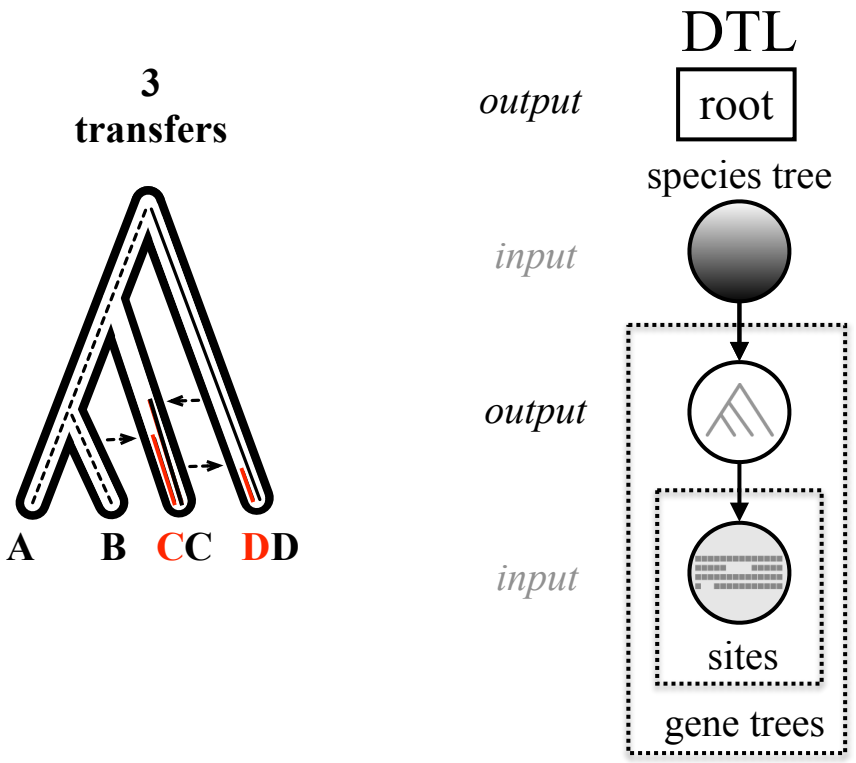
GENECLOCKS

RECONSTRUCTING A DATED TREE OF LIFE USING PHYLOGENETIC INCONGRUENCE

OUTGROUP ROOTING



OUTGROUP-FREE ROOTING



outgroup-free rooting

Transfers can root the archaeal tree of life

Using ALE on gene families from 60 genomes allowed us to **root the Archaeal tree without an out-group** while at the same time reconstructing ancestral gene contents **using the history of 1% as a scaffold.**

62 genomes / **31,236 gene families**

PNAS

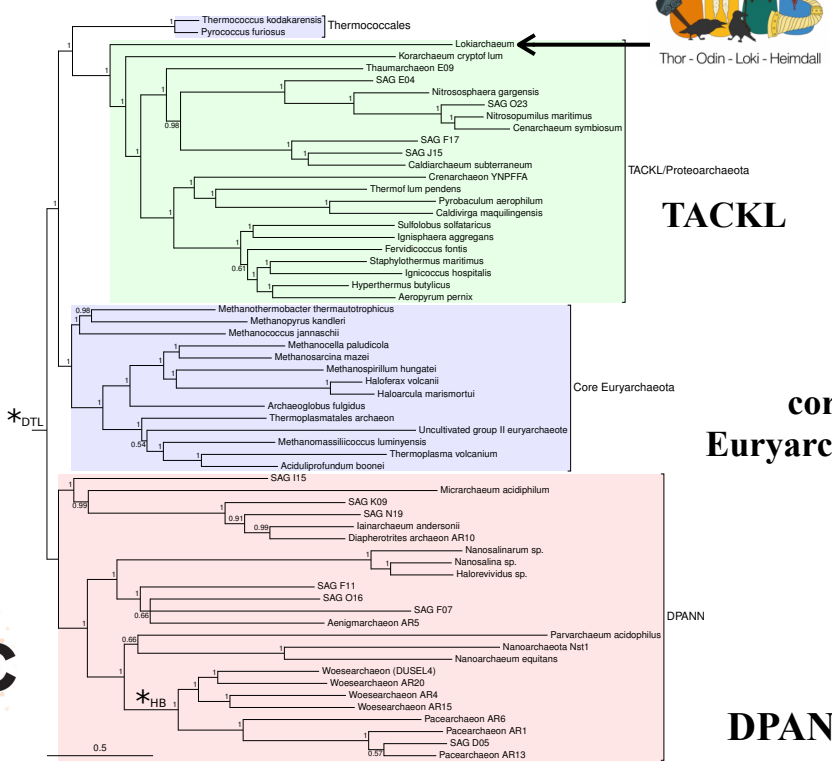
Integrative modeling of gene and genome evolution roots the archaeal tree of life

Tom A. Williams[a,b,1], Gergely J. Szöllősi[c,2], Anja Spang[d,2], Peter G. Foster[e], Sarah E. Heaps[b,f], Bastien Boussau[g], Thijs J. G. Ettema[d], and T. Martin Embley[b]

[a]School of Earth Sciences, University of Bristol, Bristol BS8 1TQ, United Kingdom; [b]Institute for Cell and Molecular Biosciences, Newcastle University, Newcastle upon Tyne NE2 4HH, United Kingdom; [c]MTA-ELTE Lendület Evolutionary Genomics Research Group, 1117 Budapest, Hungary; [d]Department of Cell and Molecular Biology, Science for Life Laboratory, Uppsala University, SE-75123 Uppsala, Sweden; [e]Department of Life Sciences, Natural History Museum, London SW7 5BD, United Kingdom; [f]School of Mathematics & Statistics, Newcastle University, Newcastle upon Tyne NE1 7RU, United Kingdom; and [g]Univ Lyon, Université Lyon 1, CNRS, Laboratoire de Biométrie et Biologie Evolutive UMR5558, F-69622 Villeurbanne, France

Edited by W. Ford Doolittle, Dalhousie University, Halifax, Canada, and approved April 24, 2017 (received for review November 7, 2016)

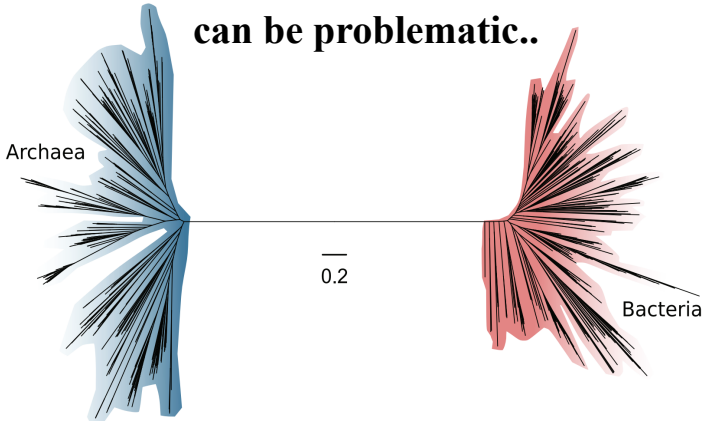
U.Bristol

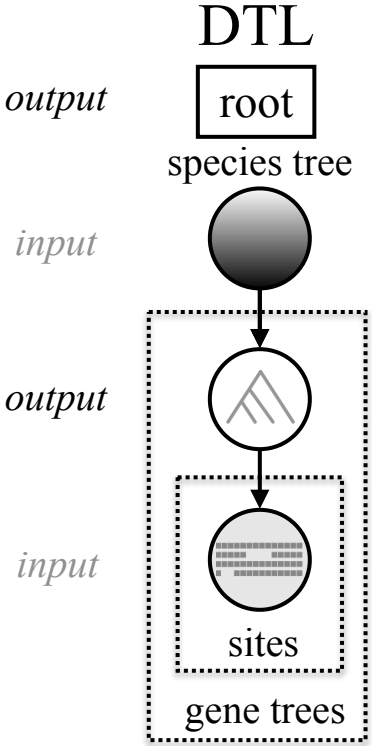


TACKL

core Euryarchaeota

DPANN





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outgroup-free rooting

Resolving LACA

Using ALE on gene families from 60 genomes allowed us to **root the Archaeal tree without an out-group** while at the same time reconstructing ancestral gene contents **using the history of 1% as a scaffold.**

62 genomes / **31,236 gene families**

Integrative modeling of gene and genome evolution roots the archaeal tree of life

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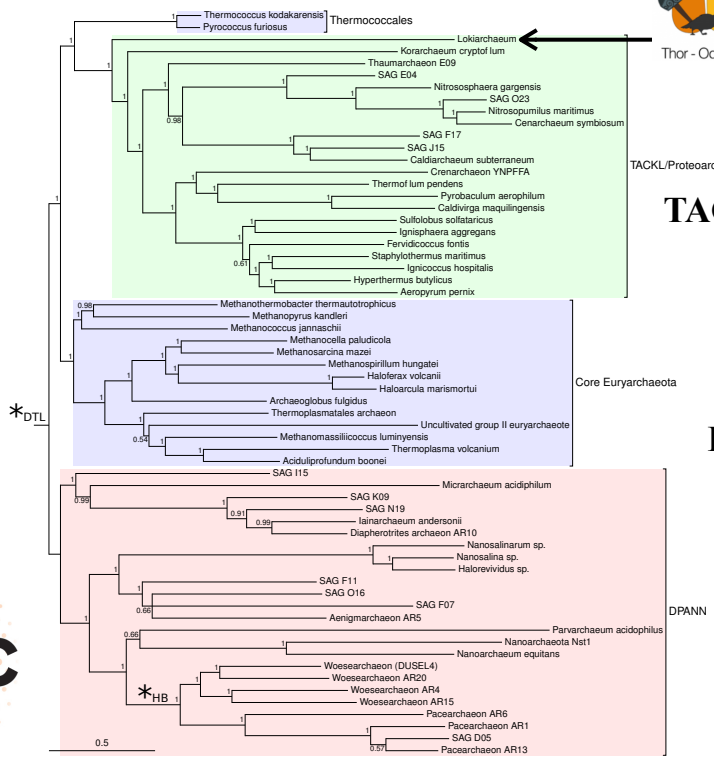
NIOZ

Thor - Odin - Loki - Heimdall

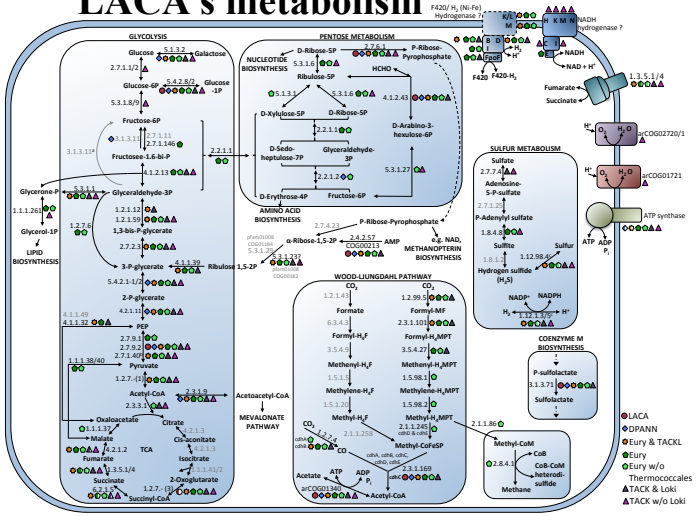


TACKL

core Euryarchaeota

DPANN

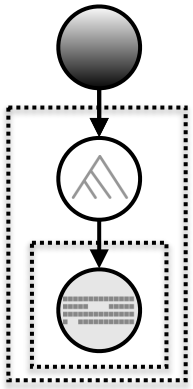
LACA's metabolism



An **anaerobe** that could fix **CO_2** to **acetyl-CoA** and generate **acetate** and **ATP** from it.

DTL

ancestral gene contents



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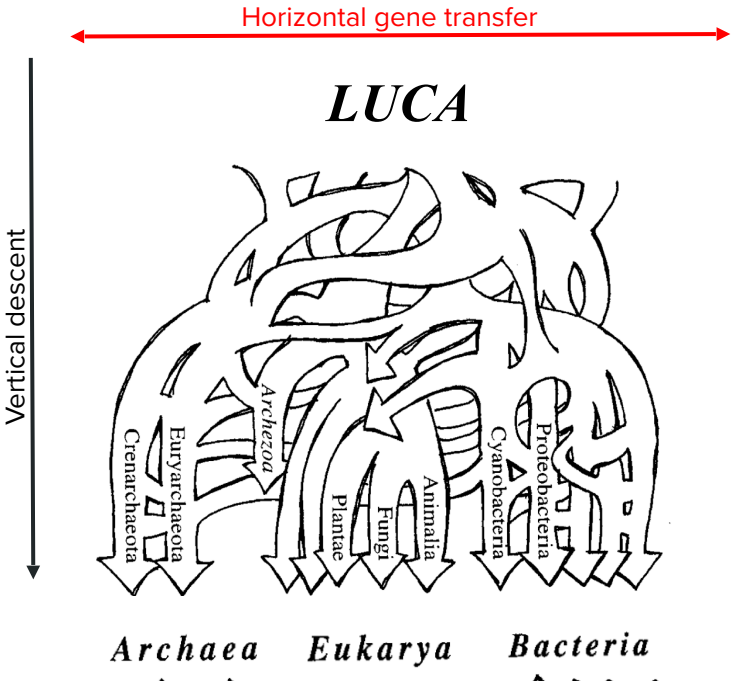
outgroup-free rooting

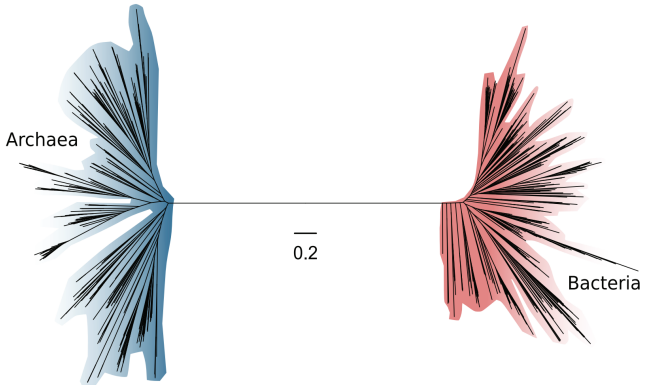
Early bacterial evolution is a playground full of open fundamental questions

- Among the most genetically and metabolically diverse group of cellular lifeforms
- Shaped evolution of the planet
- Enormous “new” diversity
- Interesting open questions about their early evolution

1. Is there a tree? Where’s the root?
2. What was the last bacterial common ancestor like?
3. How did the rise of oxygen (re)shape bacterial evolution?

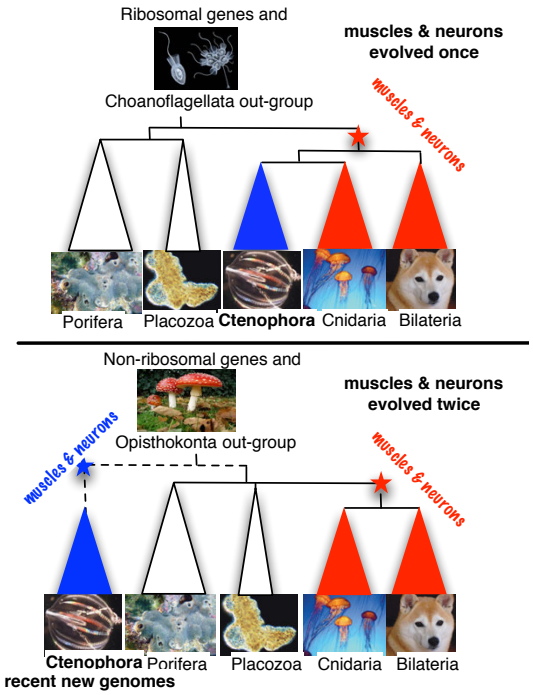


Hug et al. (2016); Doolittle (1999)

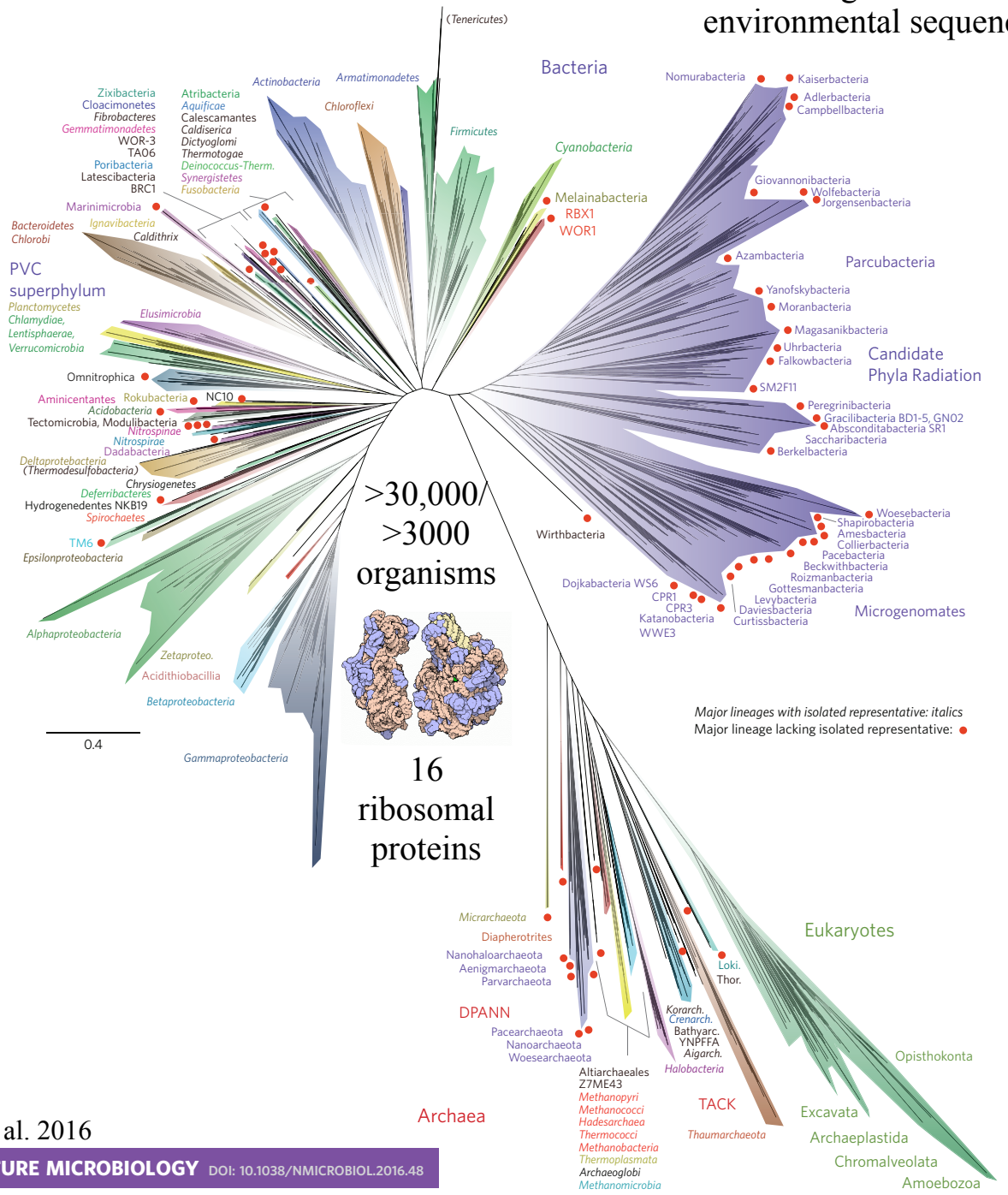


New genomes, old questions

Distant out-groups can distort the root of the in group

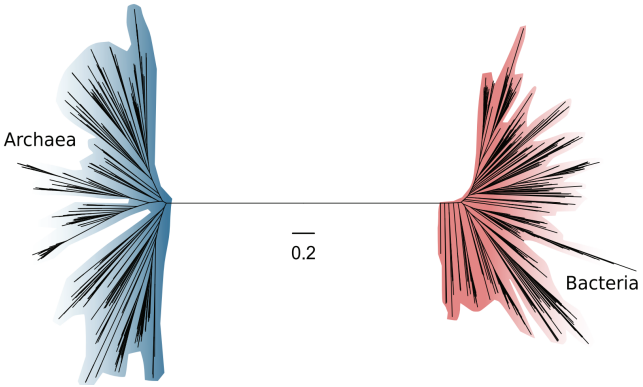


>1000 new genomes from environmental sequences

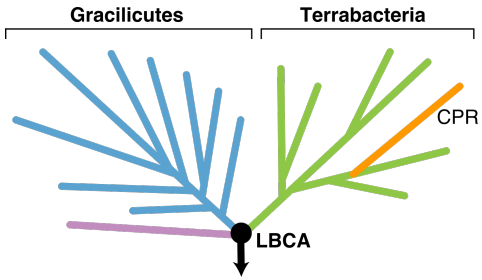


Hug et al. 2016
NATURE MICROBIOLOGY DOI: 10.1038/NMICROBIOL.2016.48

New genomes, old questions

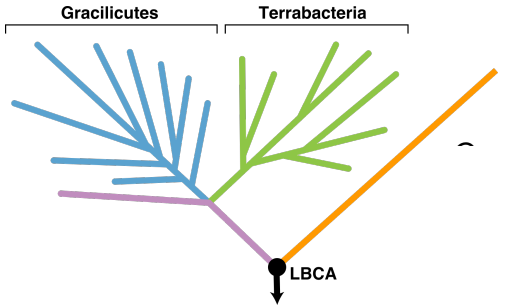


CPR nested within Bacteria



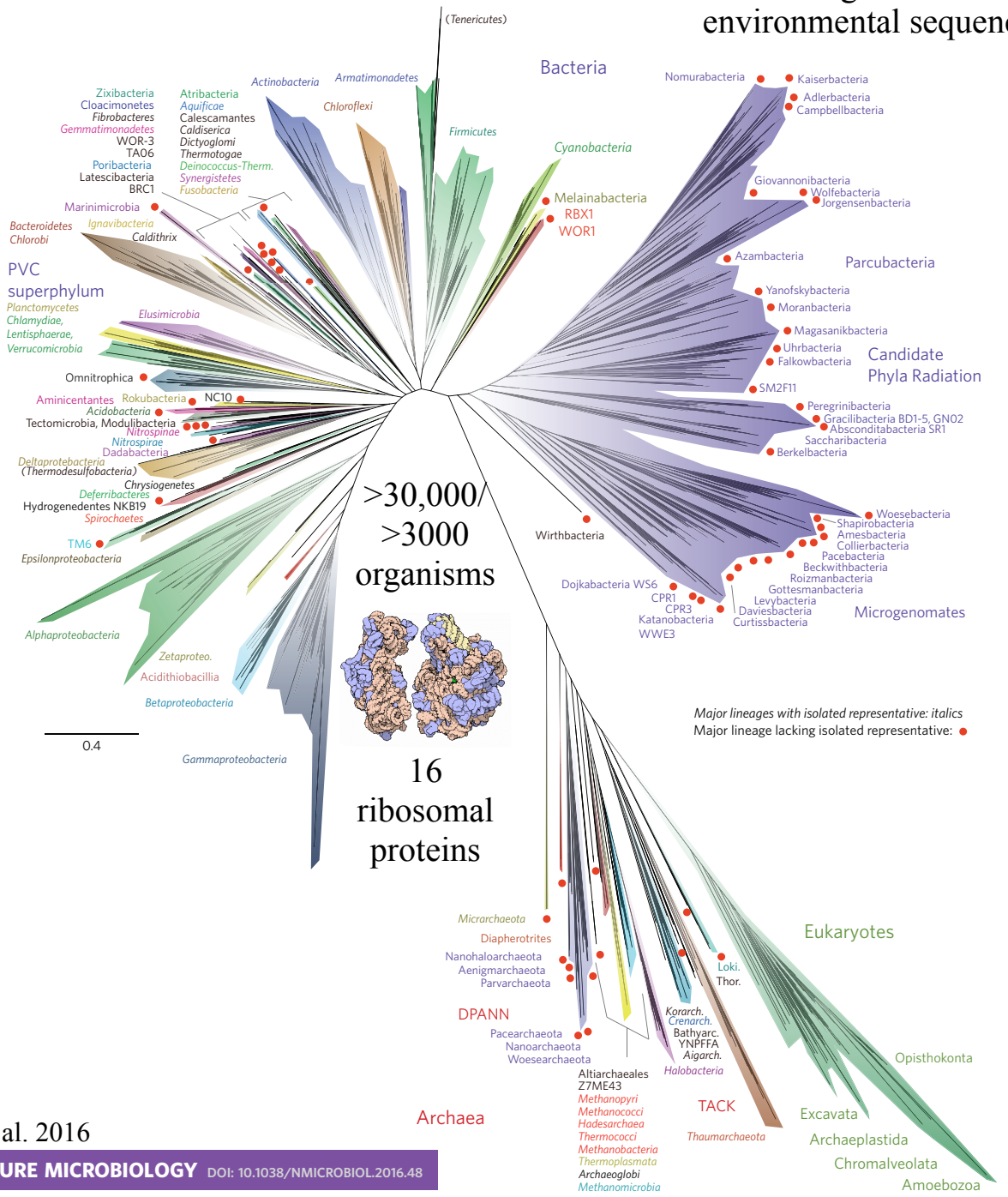
- More complex, free-living ancestor
- Diderm (double-membraned) ancestor?

CPR basal



- Small-genomed, host-associated ancestor?
- Monoderm (single-membraned ancestor?)

>1000 new genomes from environmental sequences



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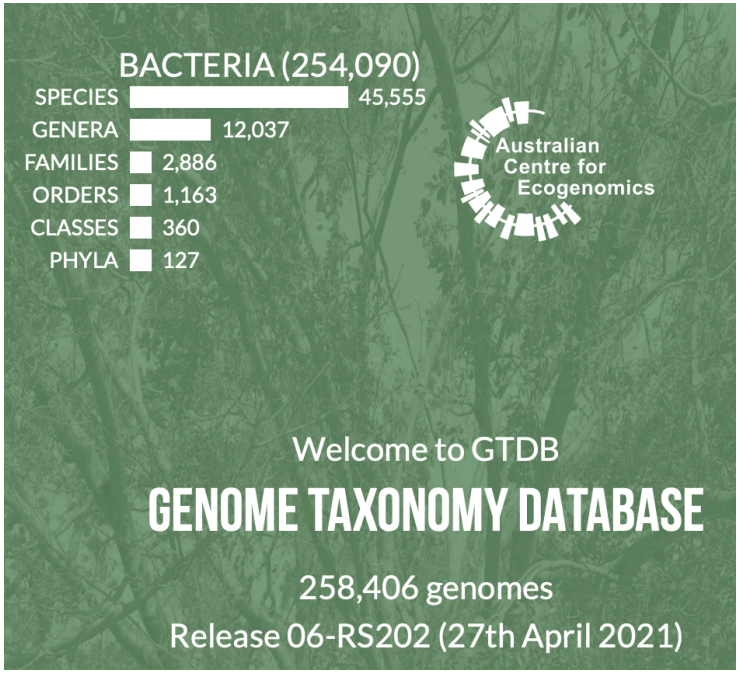
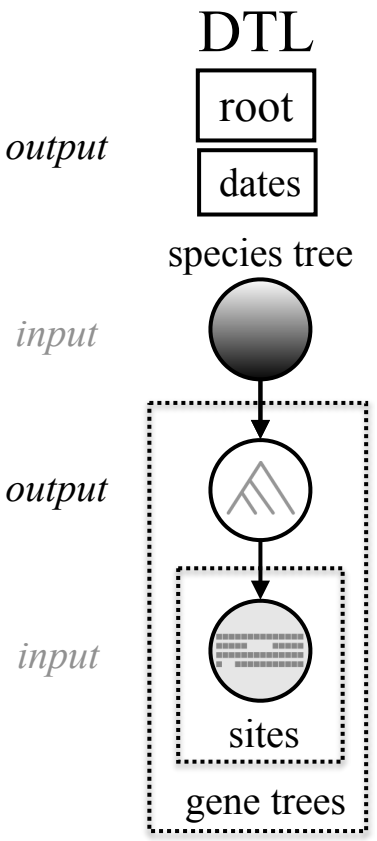
Fewer genomes, but better models, more signal?

What we need is a good sample..



..to access alternative rooting signal.

2 x 265 genomes / 11,272 gene families
62 marker genes



Coleman *et al.*, *Science* **372**, eabe0511 (2021) 7 May 2021

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ssolo@elte.hu

outgroup-free rooting

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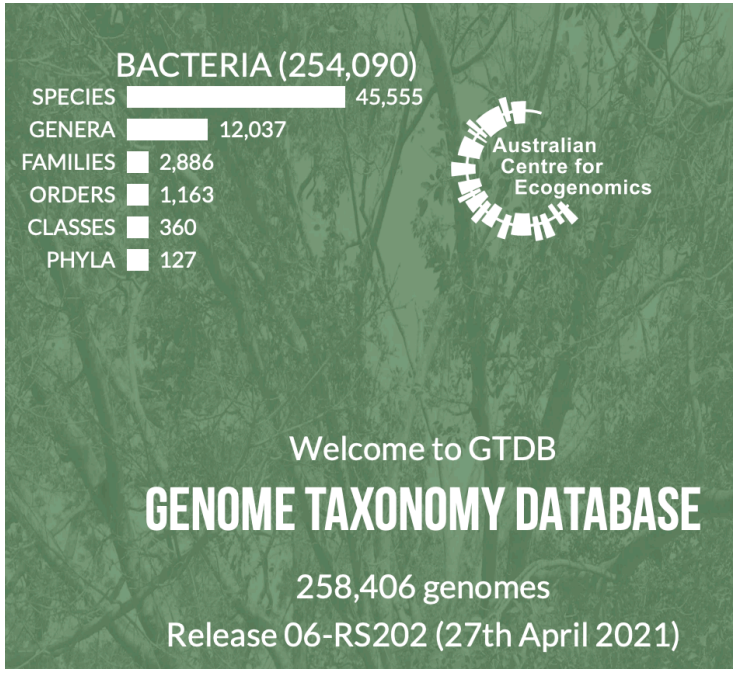

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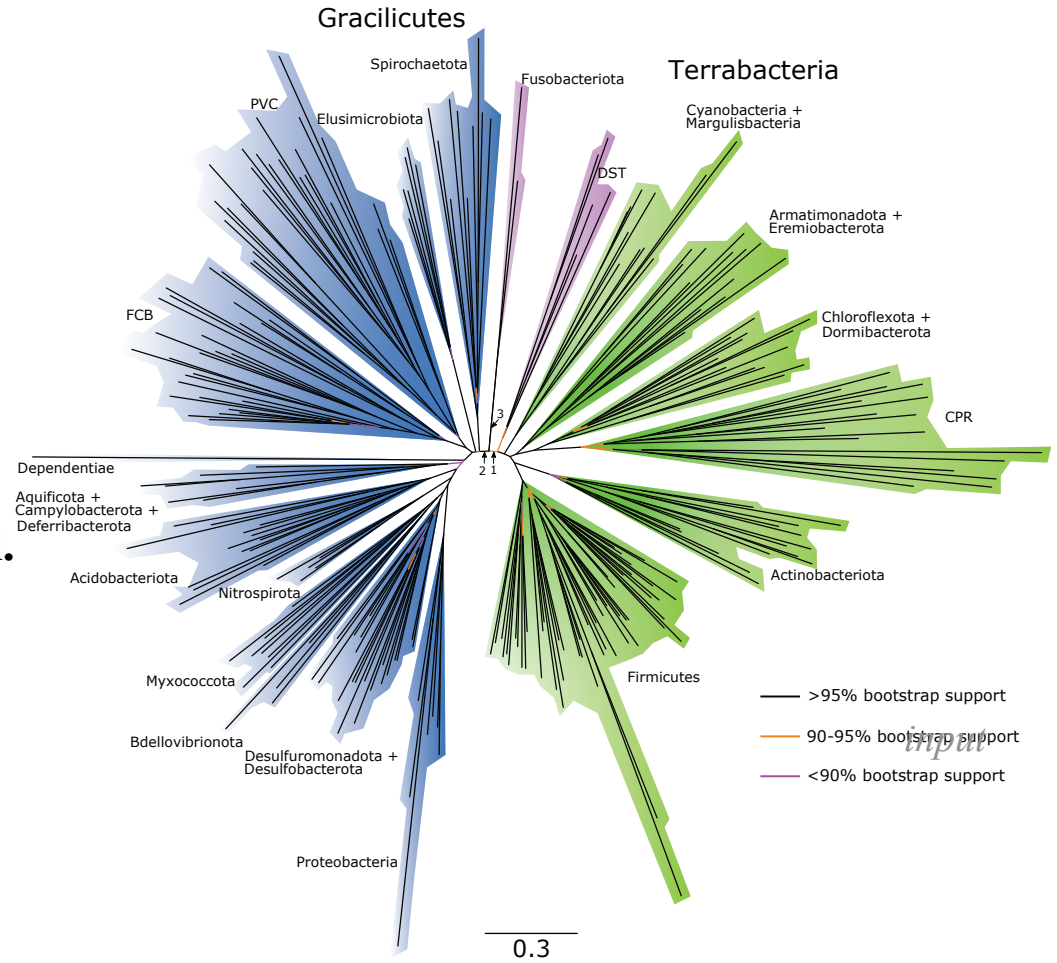
265 genomes / 11,272 gene families
62 marker genes
using the history of 1% as a scaffold



Coleman *et al.*, *Science* **372**, eabe0511 (2021) 7 May 2021

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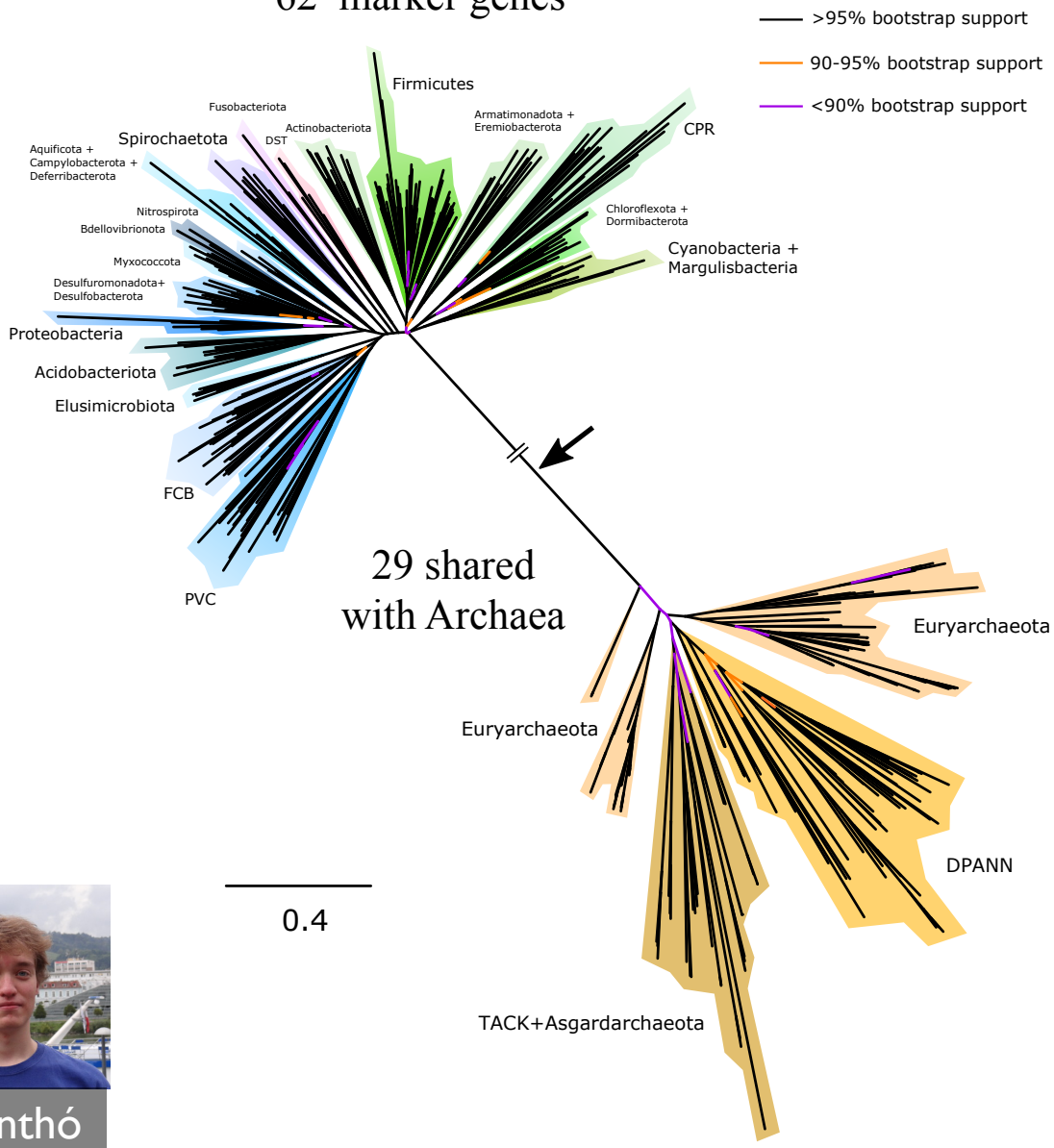
outgroup-free rooting

Using the history of 1% as a scaffold

Can an archaeal outgroup resolve the root?

62 marker genes



Coleman *et al.*, *Science* **372**, eabe0511 (2021) 7 May 2021

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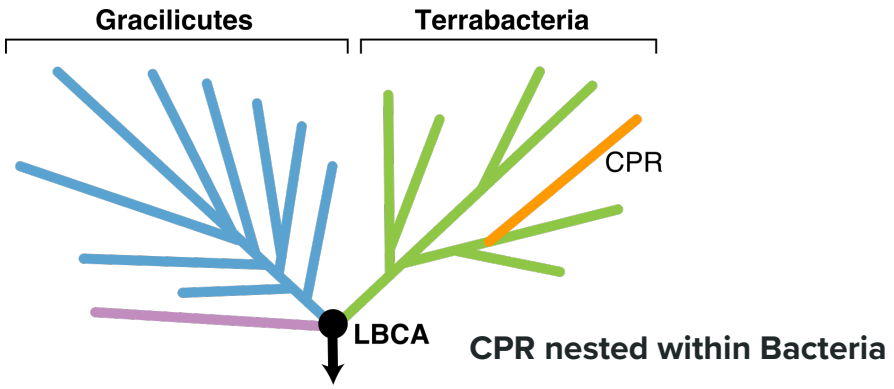
outgroup-free rooting

Using the history of 1% as a scaffold

The archaeal outgroup *cannot* resolve the root

Root hypothesis	log-likelihood difference to ML	*p*-value	Study
Observed outgroup root (Fig. S1)	0	0.58	This study (ML tree)
Between Firmicutes and Actinobacteriota	-3.3	0.50	(*26*)
Deinococcota, Synergistota and Thermotogota basal*	-3.7	0.52	
Planctomycetota basal	-4.9	0.49	(*8*)
Chloroflexota basal	-6.2	0.52	(*9*)
CPR basal	-16.7	0.37	(*11*, *16*)
DPANN basal within archaeal outgroup	-19.4	0.37	(*1*, *20*)
Fusobacteriota basal	-24.2	0.33	
Between Gracilicutes and Terrabacteria	-24.5	0.33	This study (ALE root, see below)

Table S2: Support for published hypotheses using outgroup rooting. *Our unrooted topology was incompatible with some published hypotheses, including a clade of Thermotogales and Aquificales at the root (*6*, *7*).



- More complex, free-living ancestor
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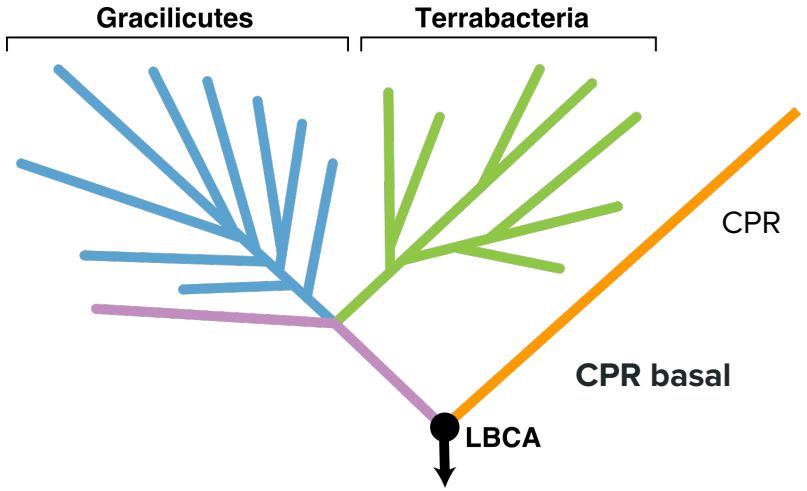

- Small-genomed, host-associated ancestor?
- Monoderm (single-membraned ancestor?)

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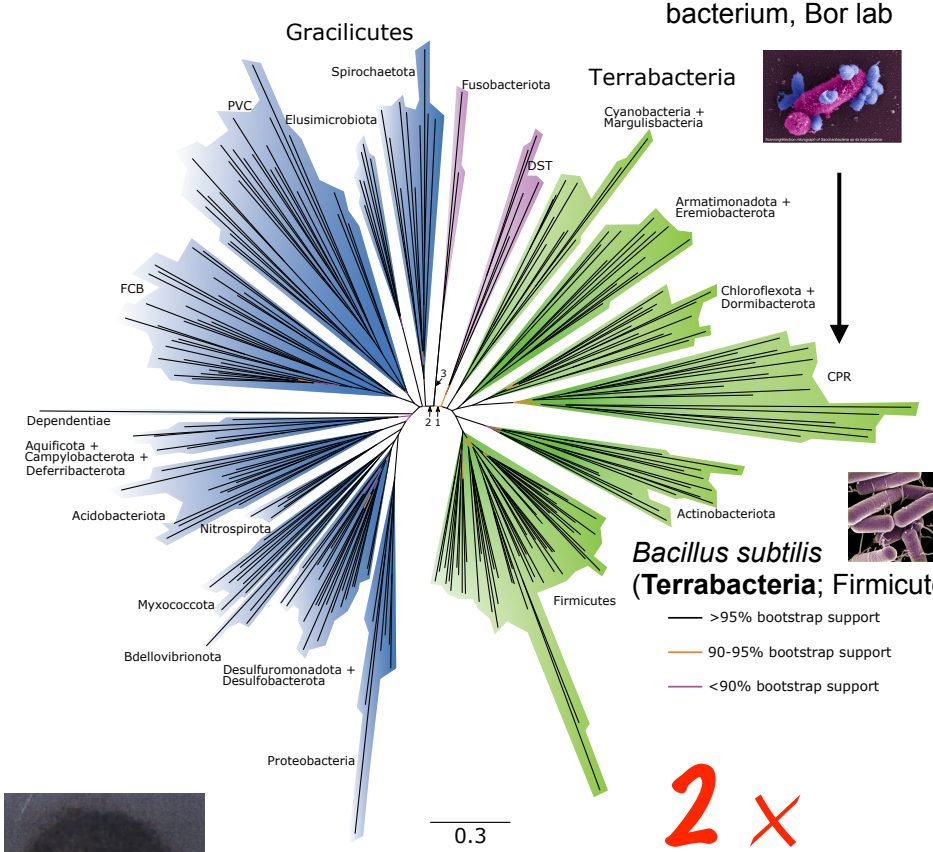
outgroup-free rooting

Transfers can root the bacterial tree of life

The root falls between two major clades of Bacteria, the Gracilicutes and the Terrabacteria, on one of three statistically equivalent adjacent branches



TM7 (**CPR**) on host bacterium, Bor lab

Bacillus subtilis (**Terrabacteria**; Firmicutes)

>95% bootstrap support

90-95% bootstrap support

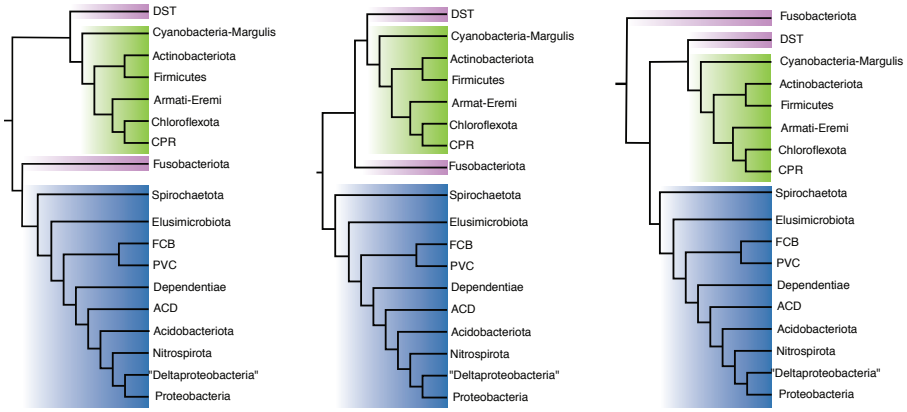
<90% bootstrap support

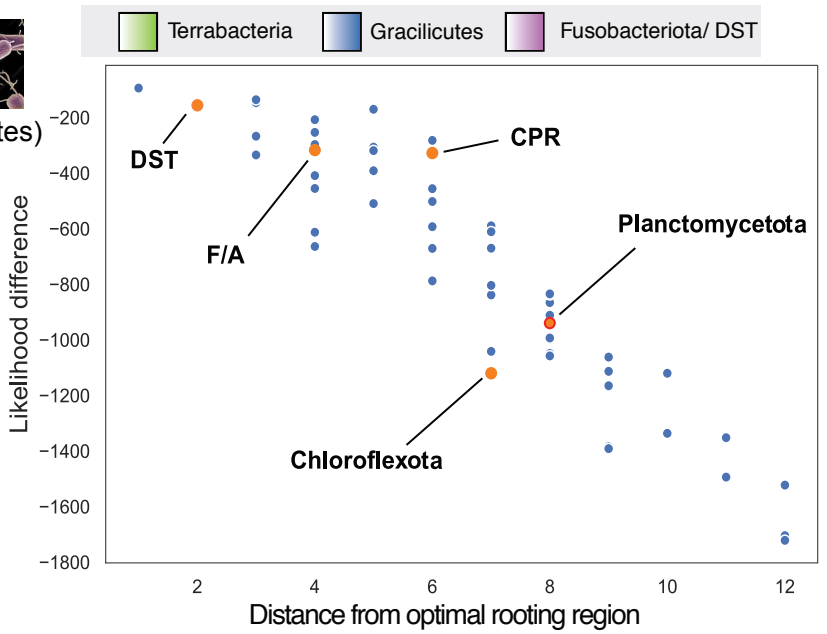
2 ×

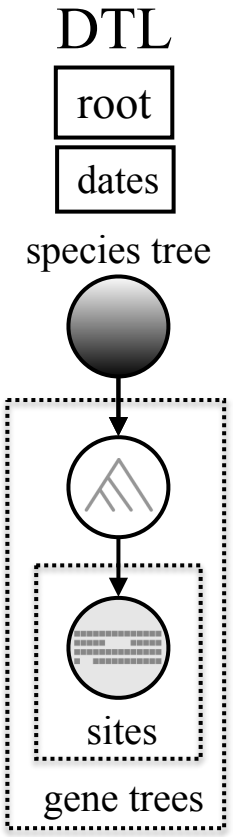
265 genomes
11,272 gene families
62 marker genes

E. coli (**Gracilicutes**; Gamma-proteobacteria)

Adrian Davin





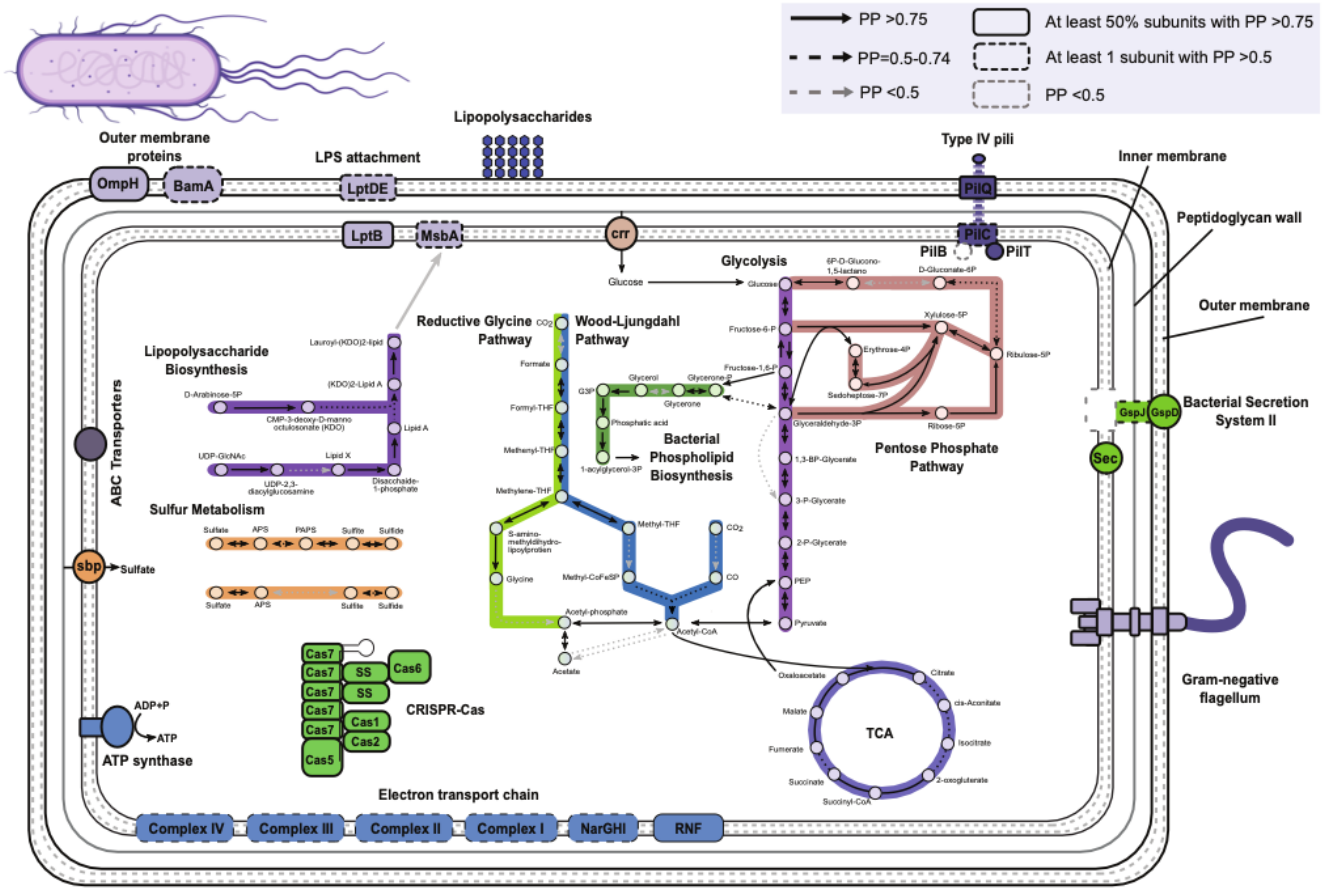


outgroup-free rooting

Resolving LBCA

2 x

265 genomes / 11,272 gene families
62 marker genes



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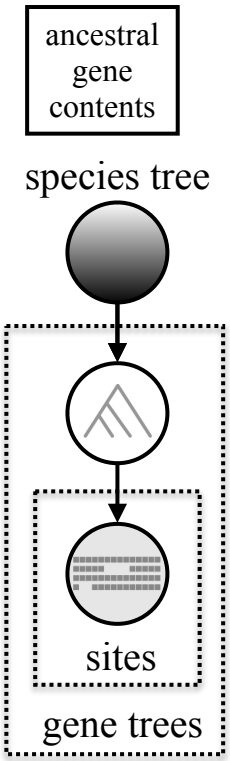
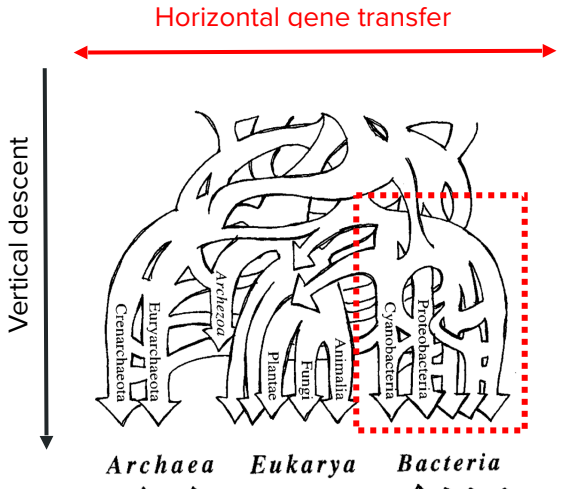


Tara Mahend -rarajah

- Map genes to the root of the inferred tree using reconciliations.
- Genome size ~1.6-2.7Mb.
- Anaerobic acetogen.
- Rod-shaped; flagella and chemotaxis; CRISPR-Cas; **double-membraned**.

just how much HGT is there?

Is there a tree of bacteria?



2 x

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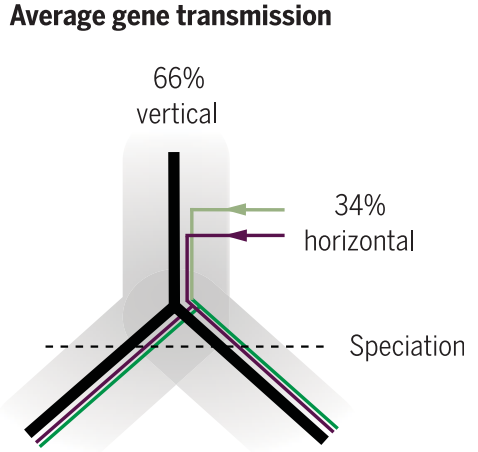
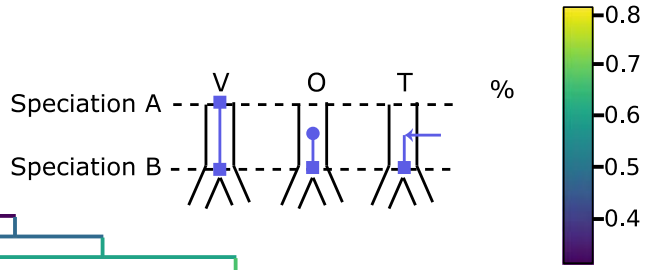
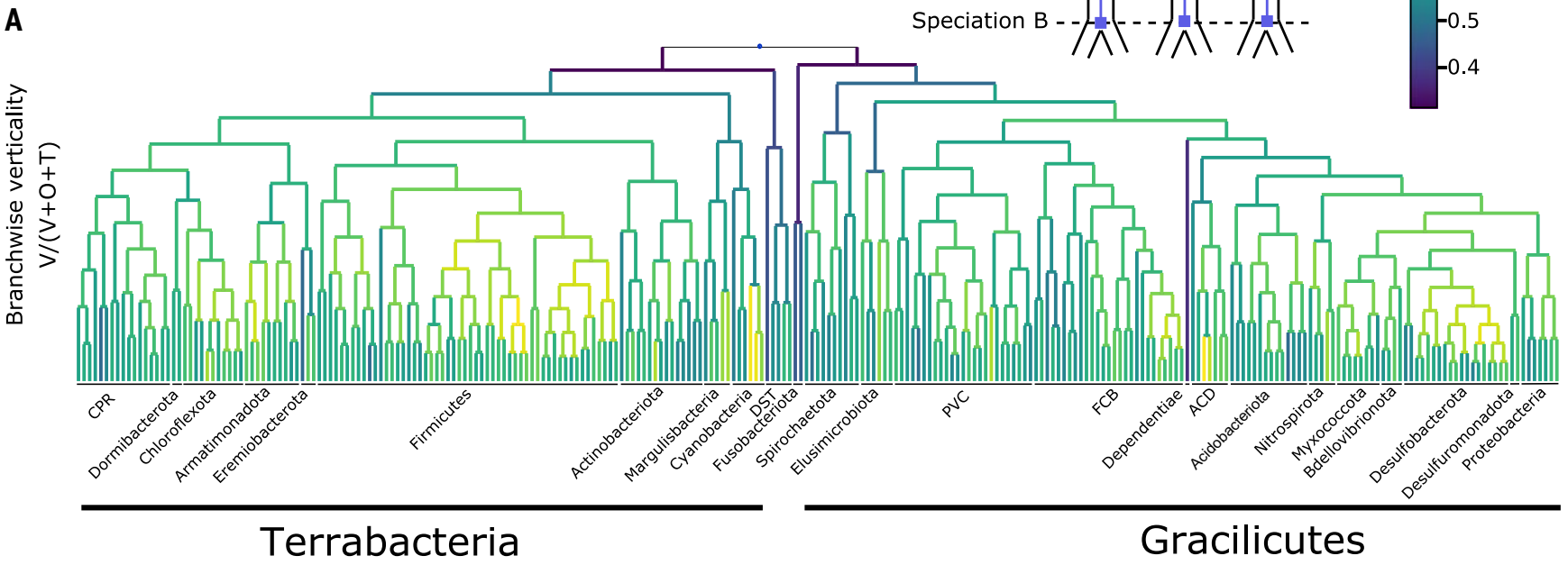
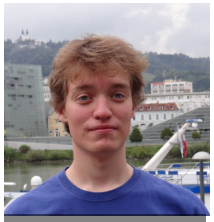


% Vertical Evolution







Szánthó Lénárd

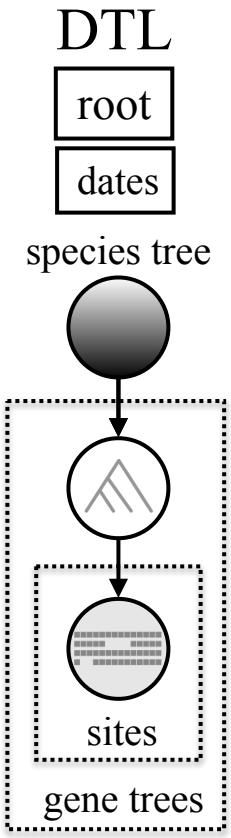
Adrian Davin

Applying species tree-aware inference

GENECLOCKS

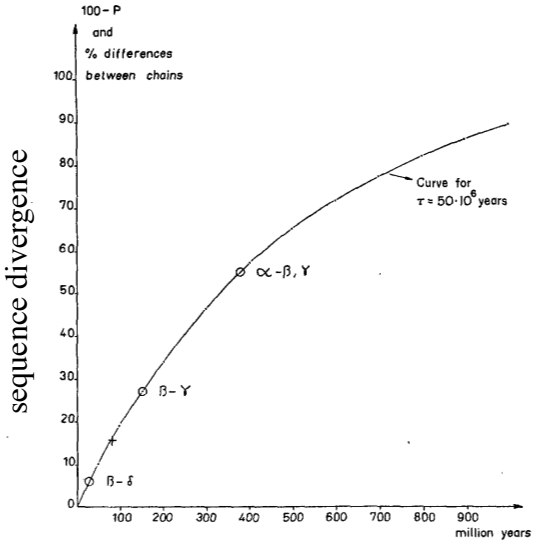
RECONSTRUCTING A DATED TREE OF LIFE USING PHYLOGENETIC INCONGRUENCE

WHERE IS THE DATED TREE?



Molecular Clocks

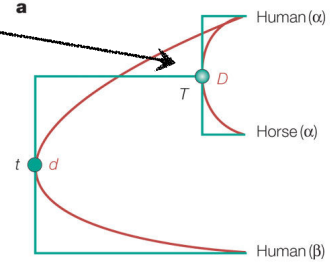
The molecular clock hypothesis reflects the observation that the **differences between homologous** amino acid **sequences** from different mammals **are roughly proportional to their time of divergence.**



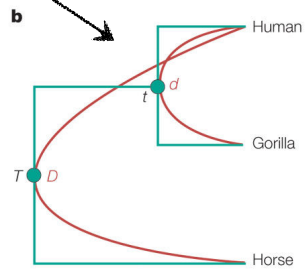
divergence time according to fossils

Zukerkandl and Pauling 1965

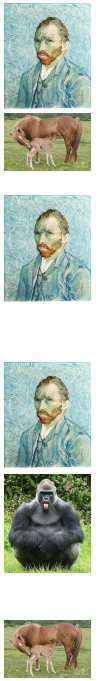
~130 million years
18 aa substitutions

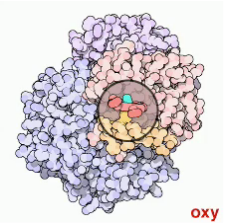


1 & 2 substitutions
~11 million years



Nature Reviews | Genetics





$2\alpha + 2\beta$

Molecular Clocks

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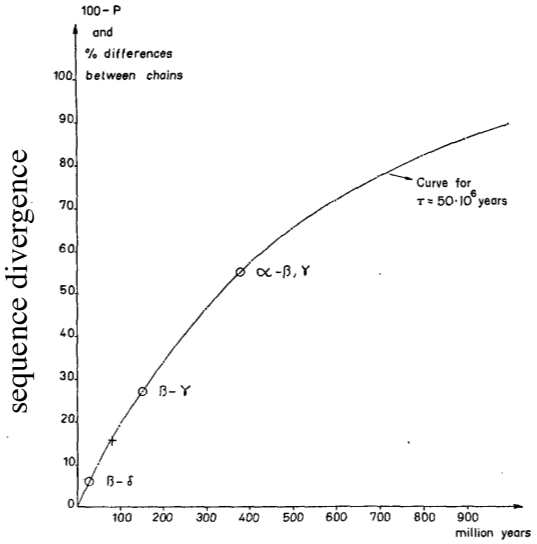

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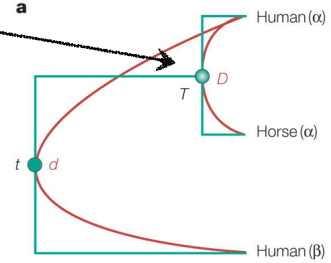

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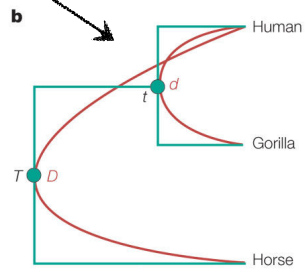
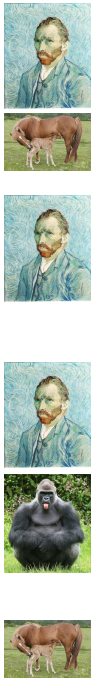
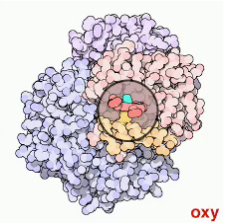


Nature Reviews | Genetics





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Molecular Clocks

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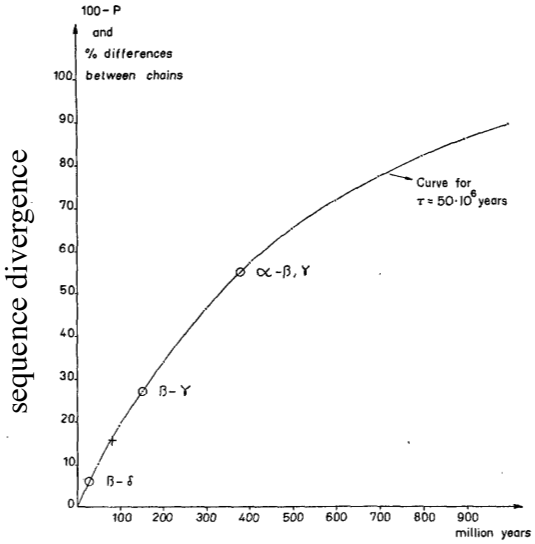
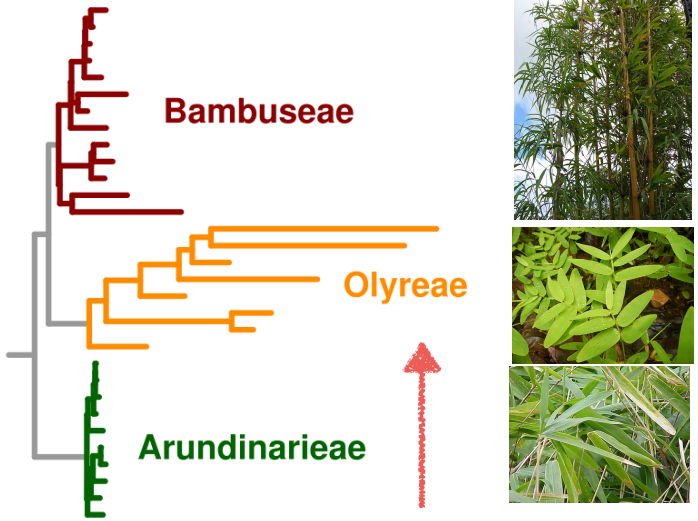


divergence time according to fossils

Zukerkandl and Pauling 1965

evolutionary rates vary
molecular clocks are local

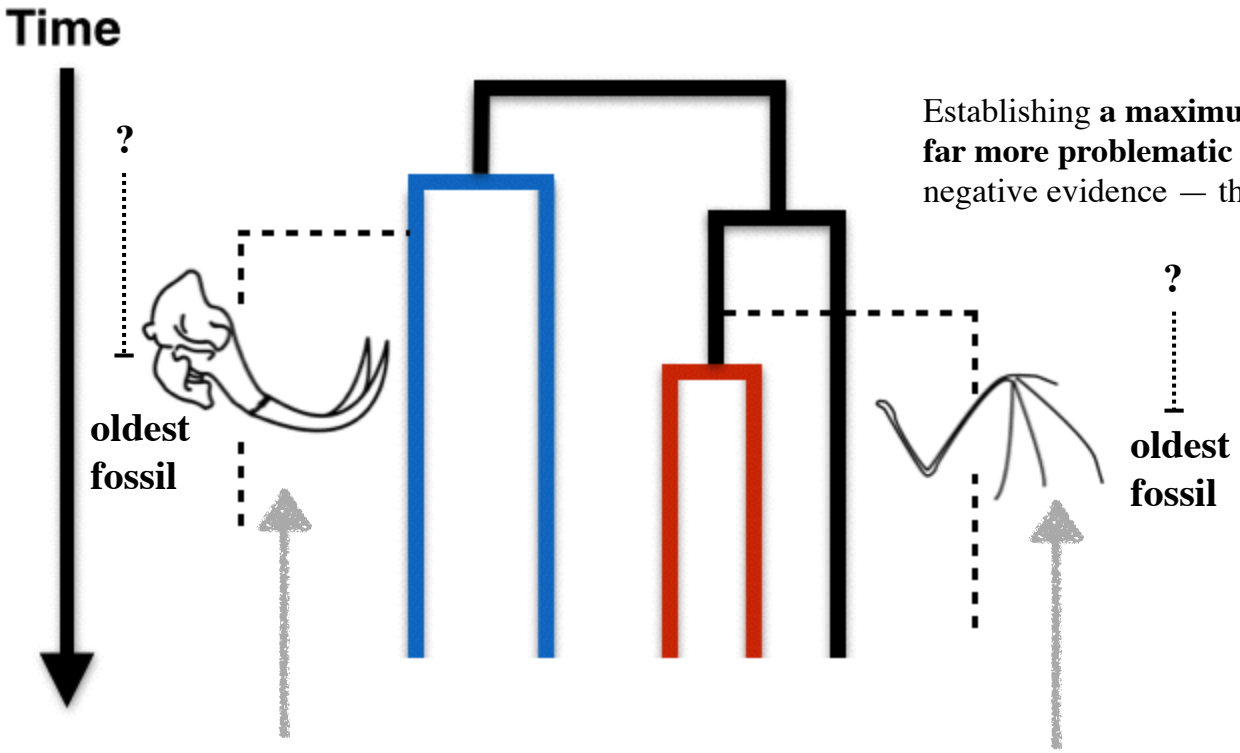


faster local clock

Wysocki et al. 2014 & Wikipedia

Rocks

The geological record is the only source of information concerning absolute time



Establishing **a maximum constraint is far more problematic** — it relies on negative evidence — the absence of fossil.

The fossil record is **directly informative on the minimum ages** of clades based on the age of their oldest fossil representative

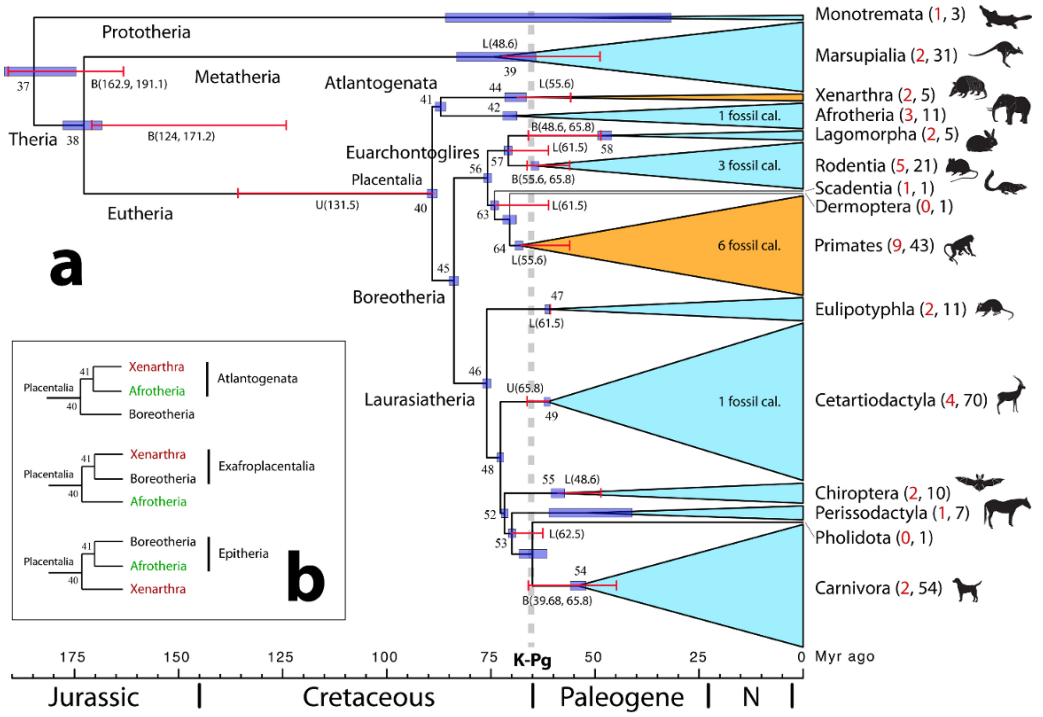
ssolo@elte.hu

Rocks & Clocks

Inadequate modelling of the global violation of the molecular clock historically lead to great controversies..

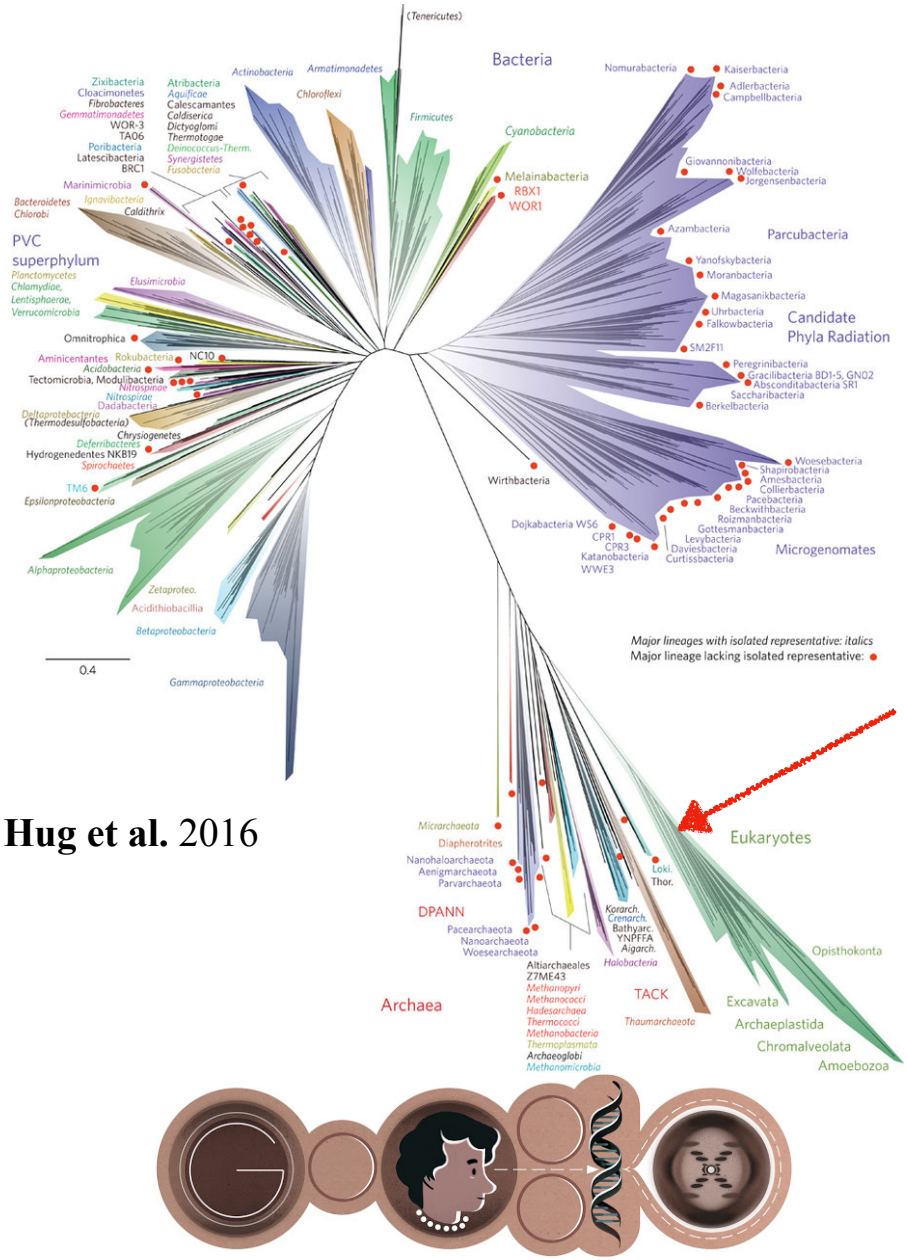
Donoghue and Yang 2015

… today, Bayesian RMC methods have resolved most, but not all controversies, using **sequence based local molecular clocks anchored by multiple fossil calibrations.**



dos Reis et al. 2012

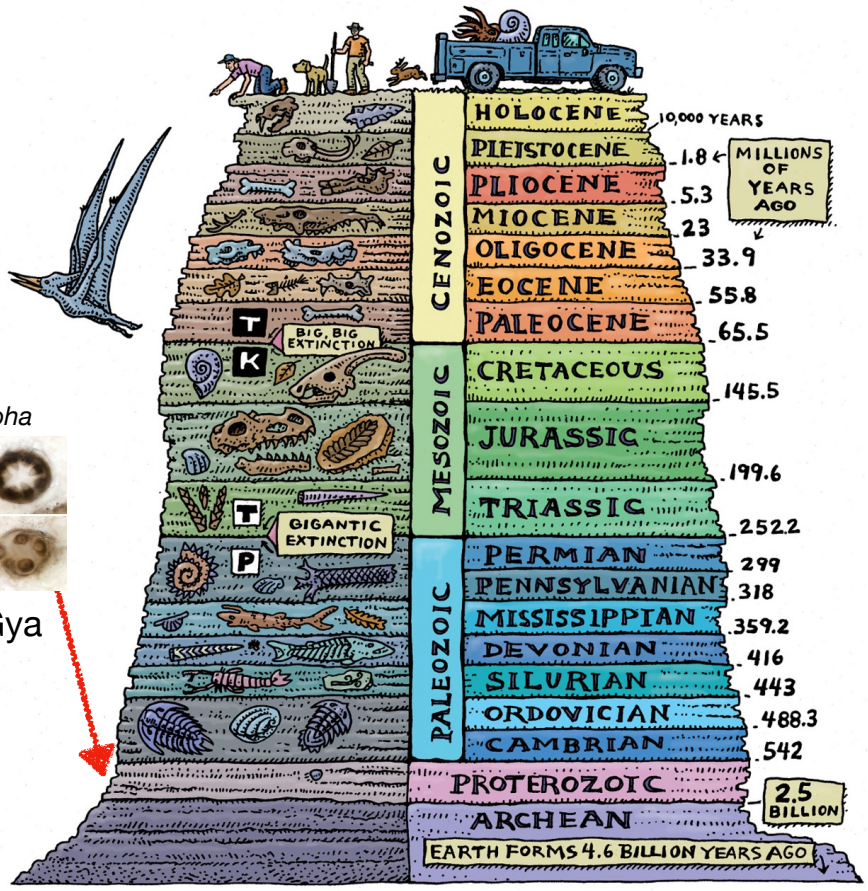
Rocks & Clocks

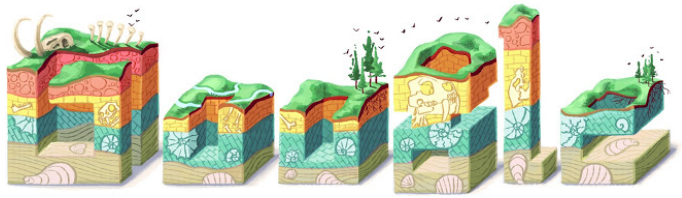


Hug et al. 2016

Bangiomorpha

~ 1-1.5 Gya

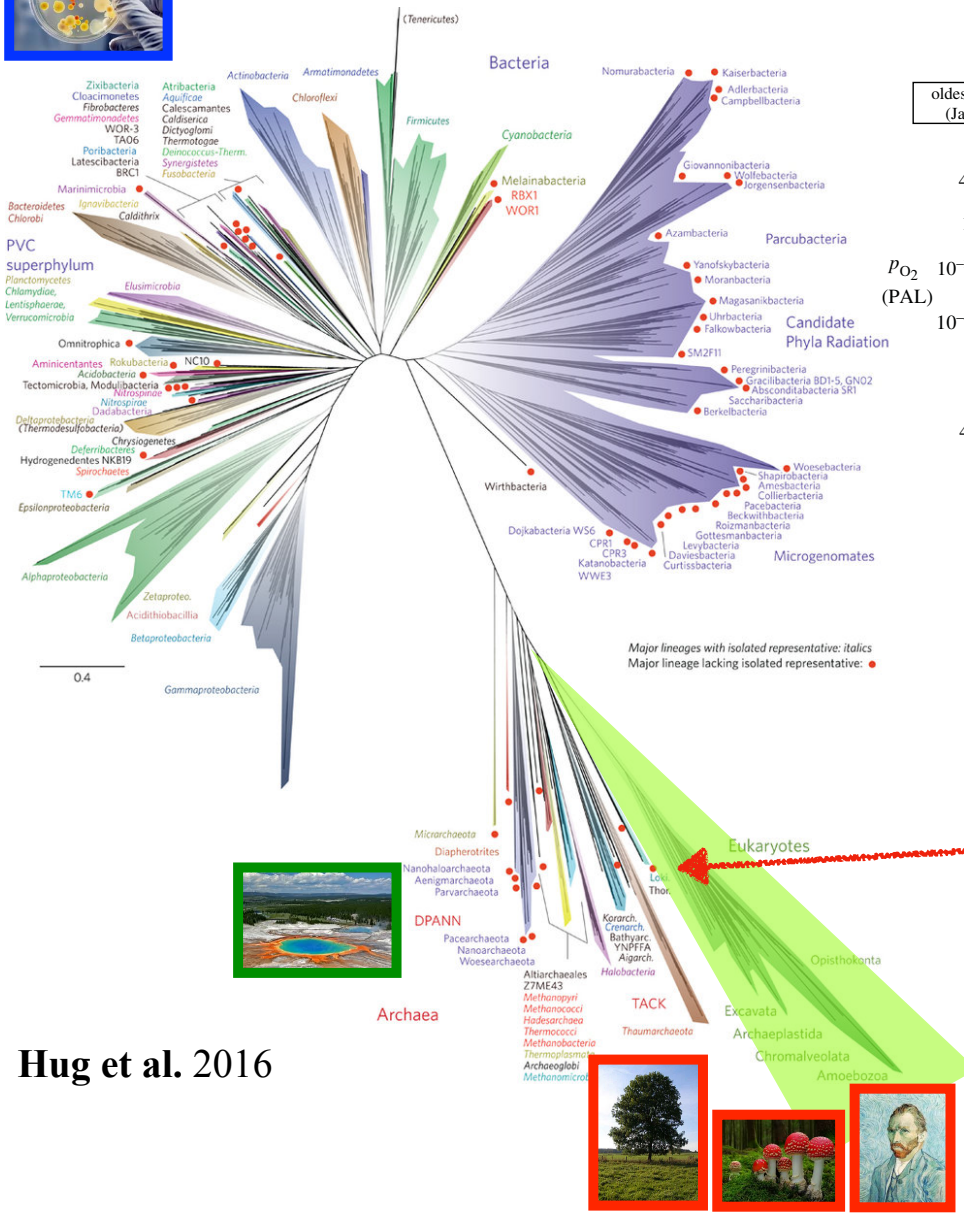




ssolo@elte.hu

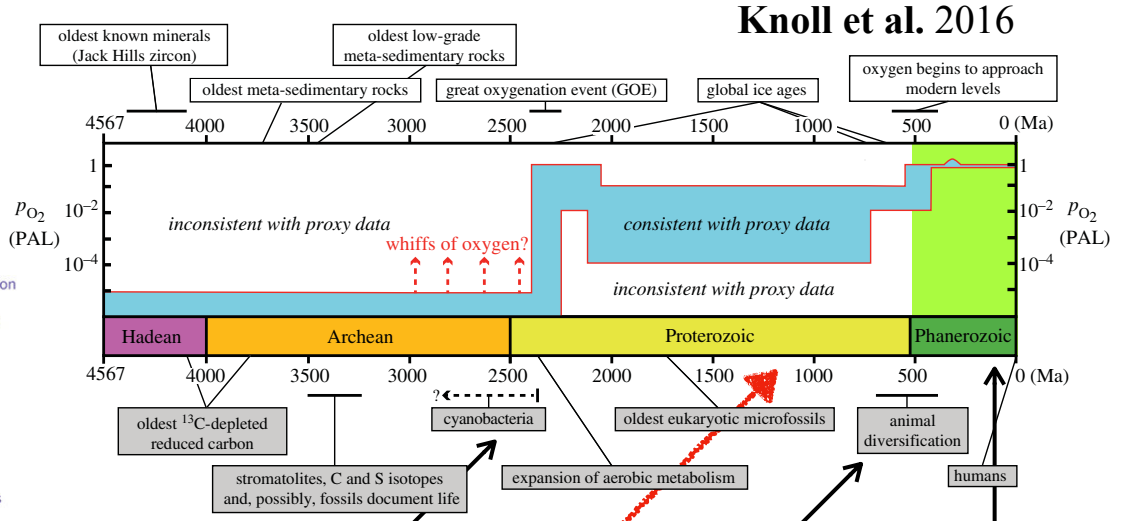
Rocks & Clocks

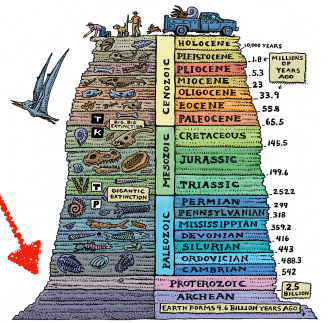
For majority of life and most it's history we lack sufficient fossils to anchor local clocks.



Hug et al. 2016

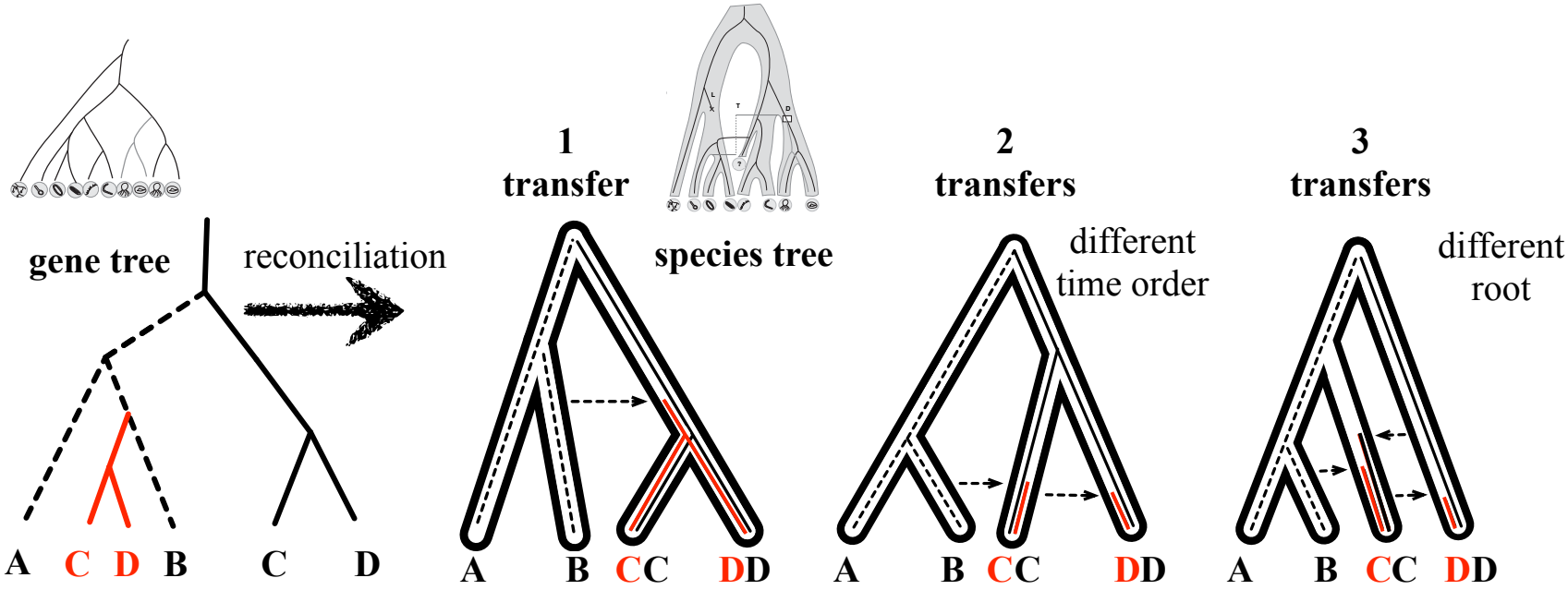
Knoll et al. 2016





Horizontal gene transfer as information

Transfer events, encoded in the topologies of gene trees can be thought of as "*molecular fossils*" that record the order of speciation events.



Vincent Daubin

LBBE

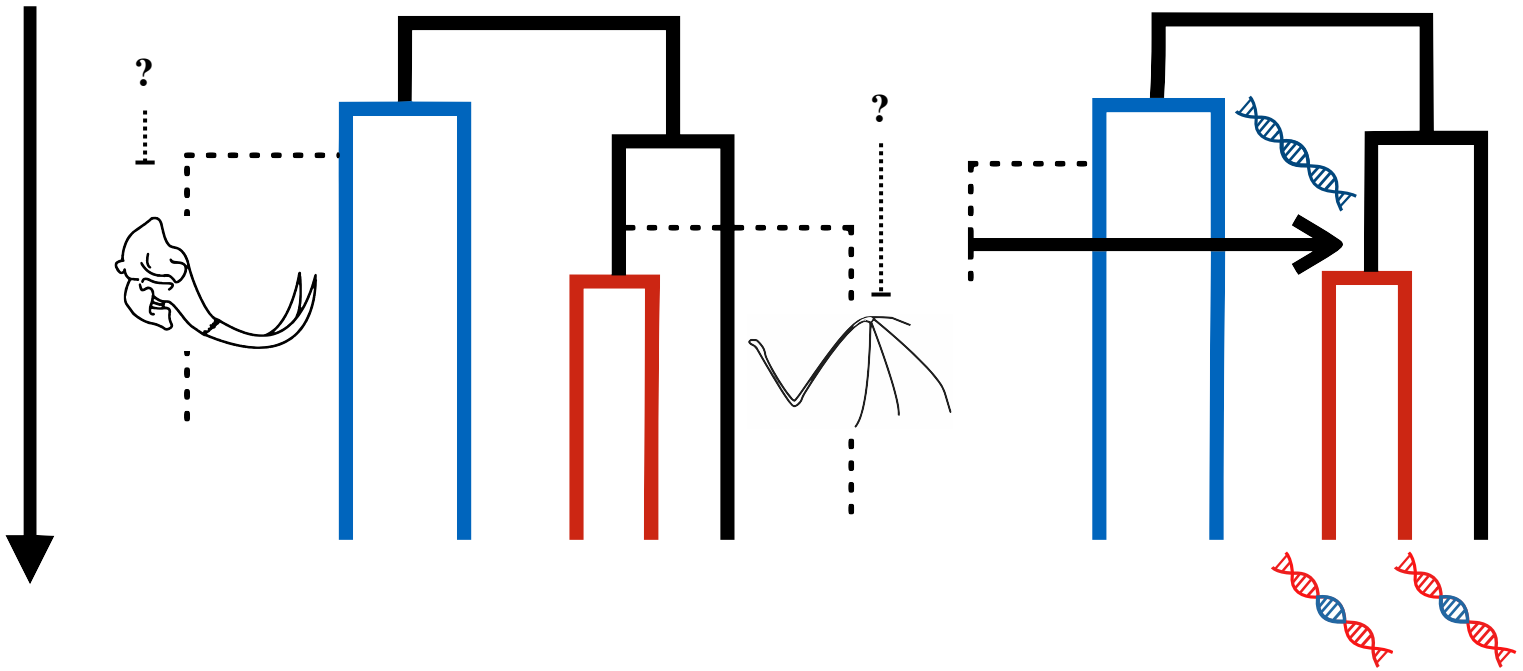
Szöllősi, Boussau, Abby, Tannier & Daubin ***PNAS*** (2012)
Phylogenetic modeling of lateral gene transfer reconstructs the pattern and relative timing of speciations

ssolo@elte.hu

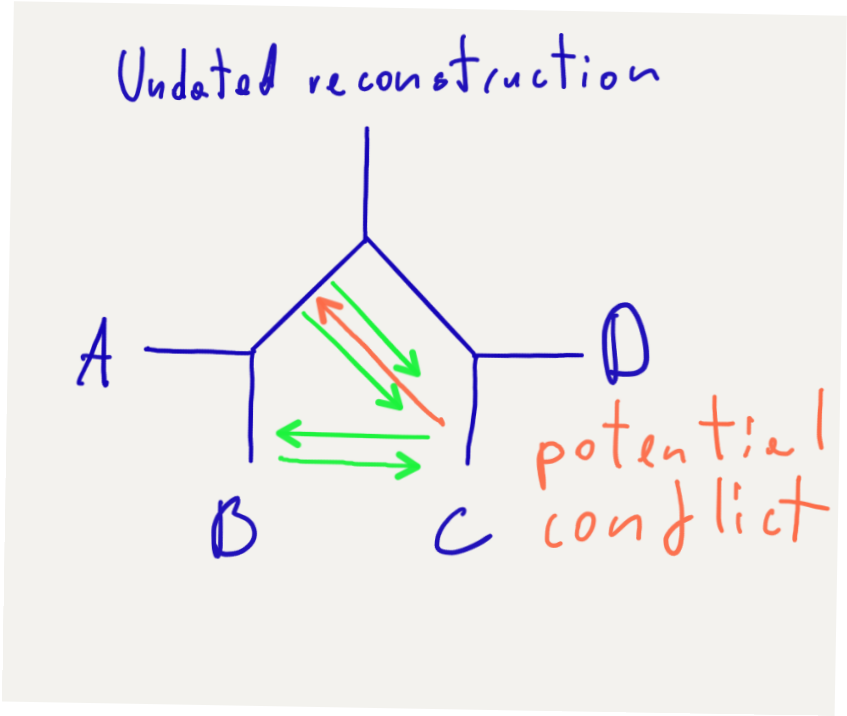
… and genes from other species!

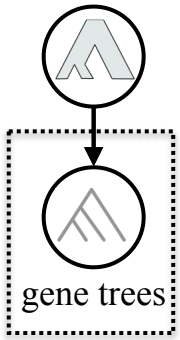
Fossils provide **direct evidence on minimum age**, but only **indirect evidence on maximum and relative ages**.

Transfers are not informative on absolute age, but do provide **direct evidence on relative ages**.

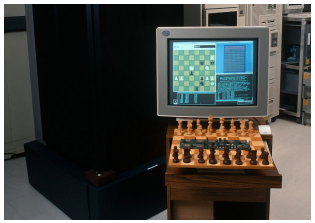


"undated" DTL





DTL



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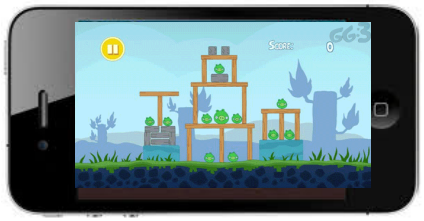
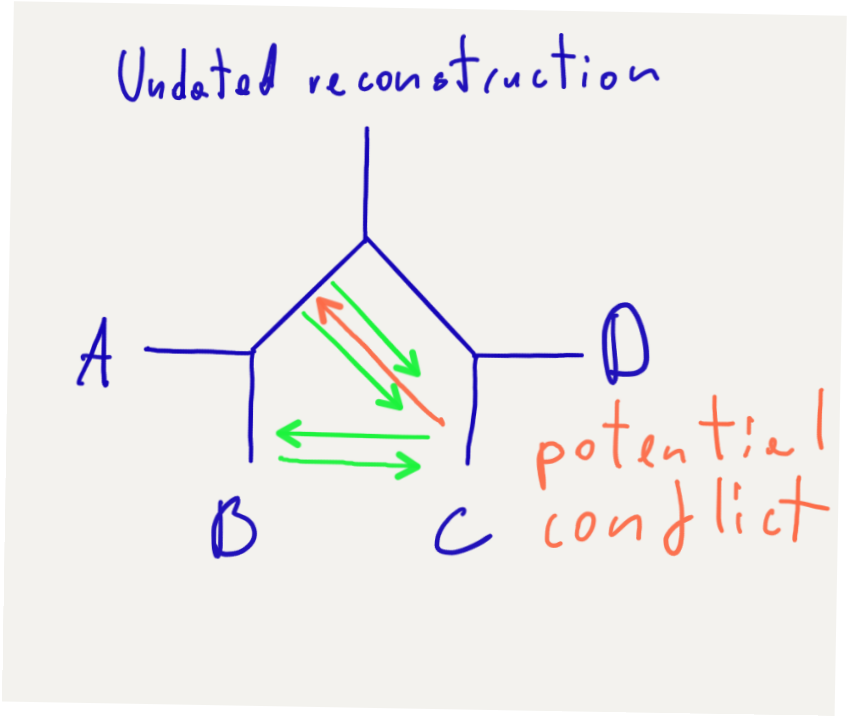
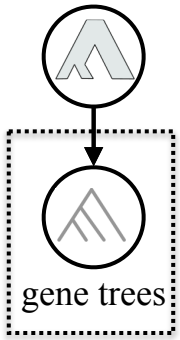


implemented in ALE:

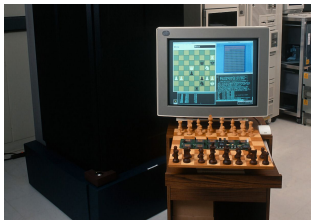
http://github.com/ssolo/ALE

"undated" DTL





DTL



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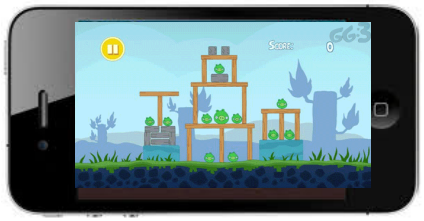
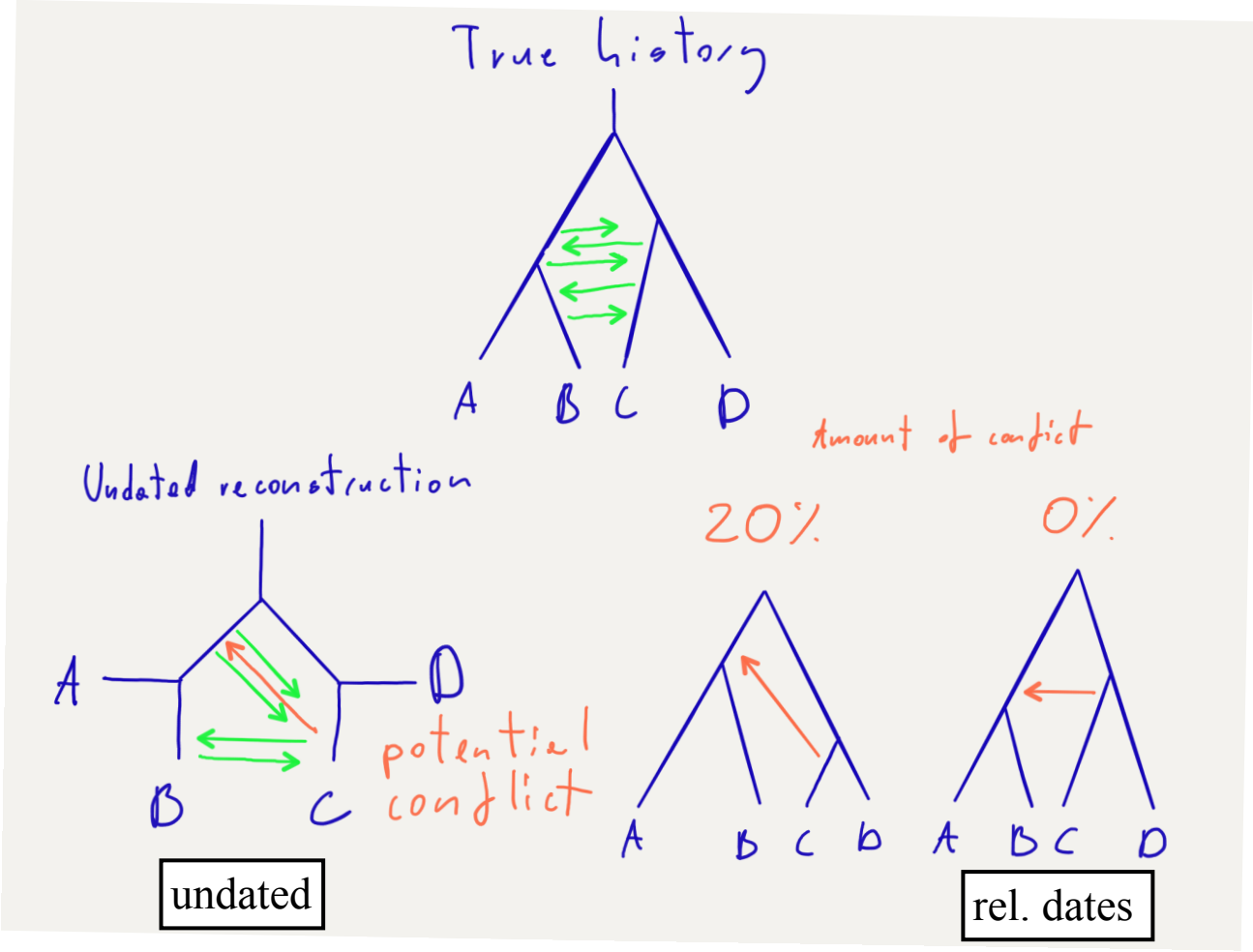


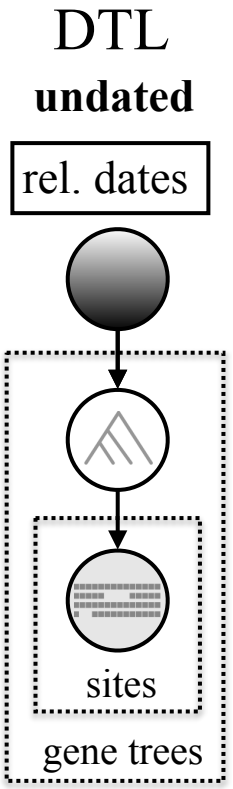
implemented in ALE:

http://github.com/ssolo/ALE

Relative age constrains from transfers

HGT events inferred by an "undated" version of the species tree-aware method ALE were input into the MaxTiC (**max**imal **ti**me **c**onsistency) optimisation method to obtain relative age constrains.

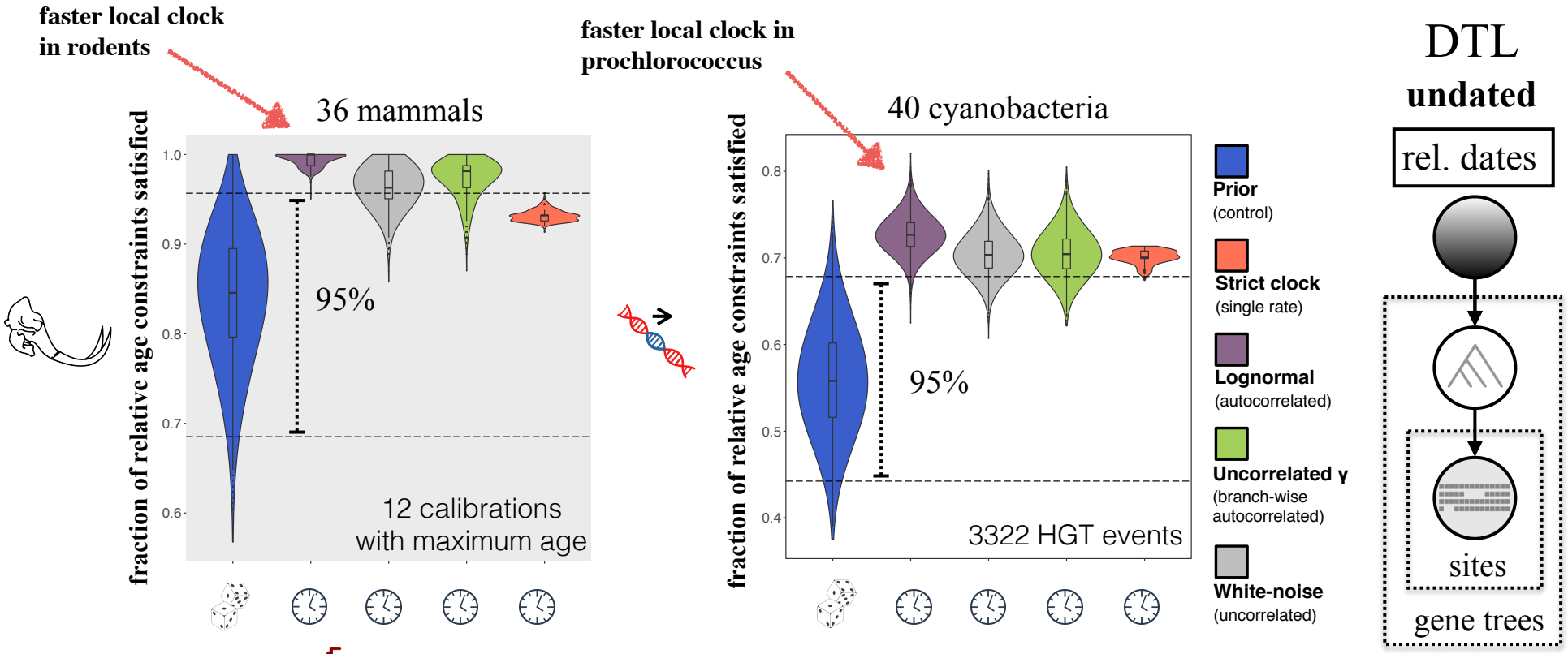


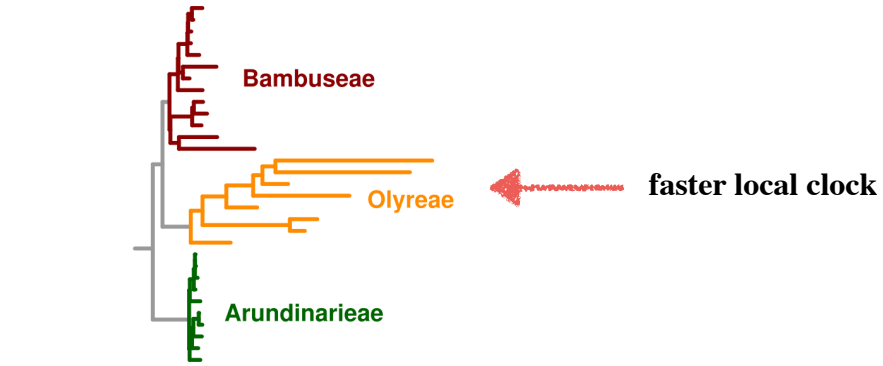


Eric Tannier
LBBE

Rocks, clocks and genes from other species

To directly compare relative age constraints, we measured how different relaxed molecular clock models, without fossil calibrations, are able to predict the relative timing of speciations implied by fossils and by transfers.





Adrian Davin

Davin, Tannier, Williams, Boussau, Daubin & **Szöllősi**, **Nature Ecology and Evolution (2018)**
Gene Transfers Can Dated the Tree of Life

Transfer based relative dates correlate with molecular clocks

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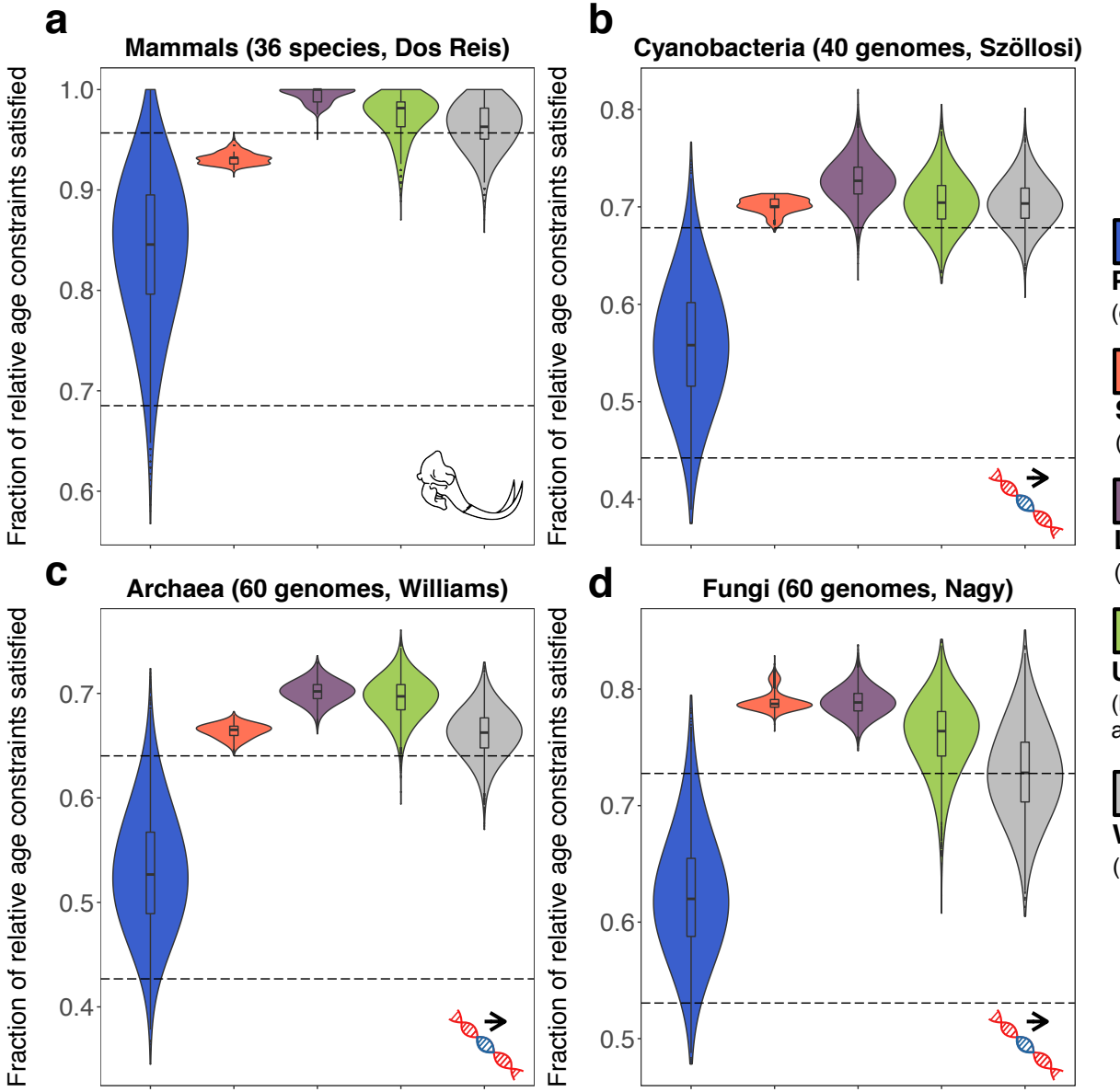
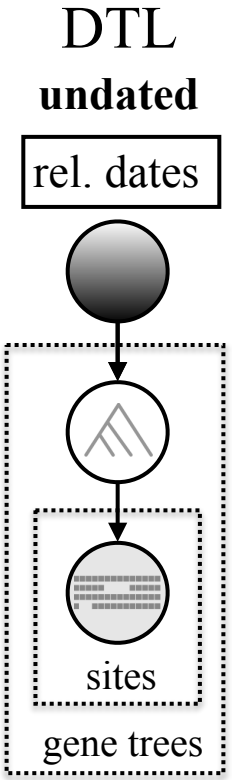


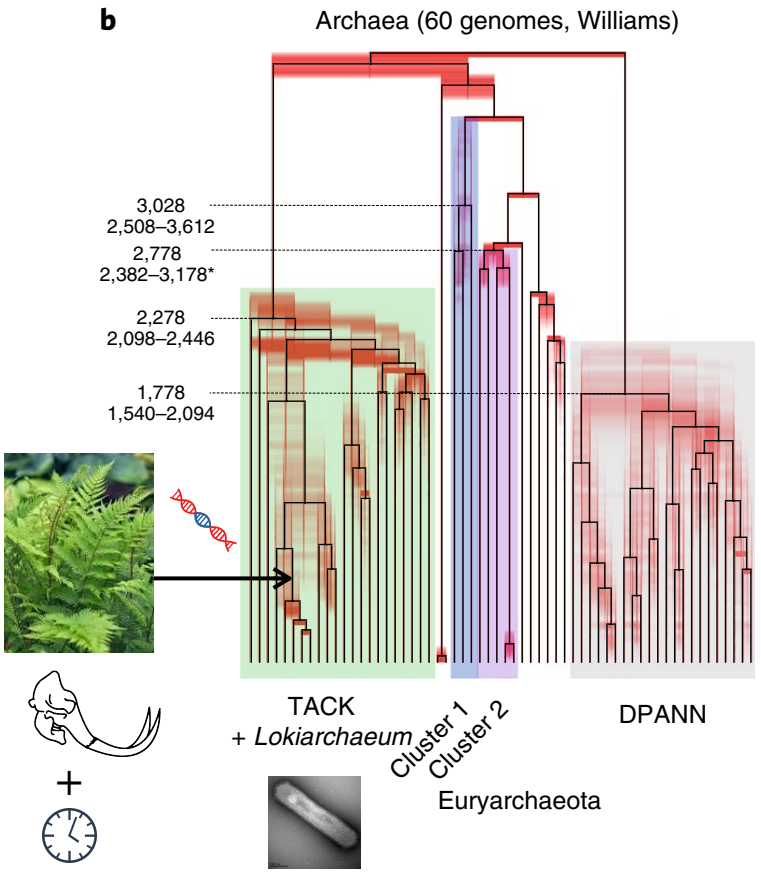


Adrian Davin

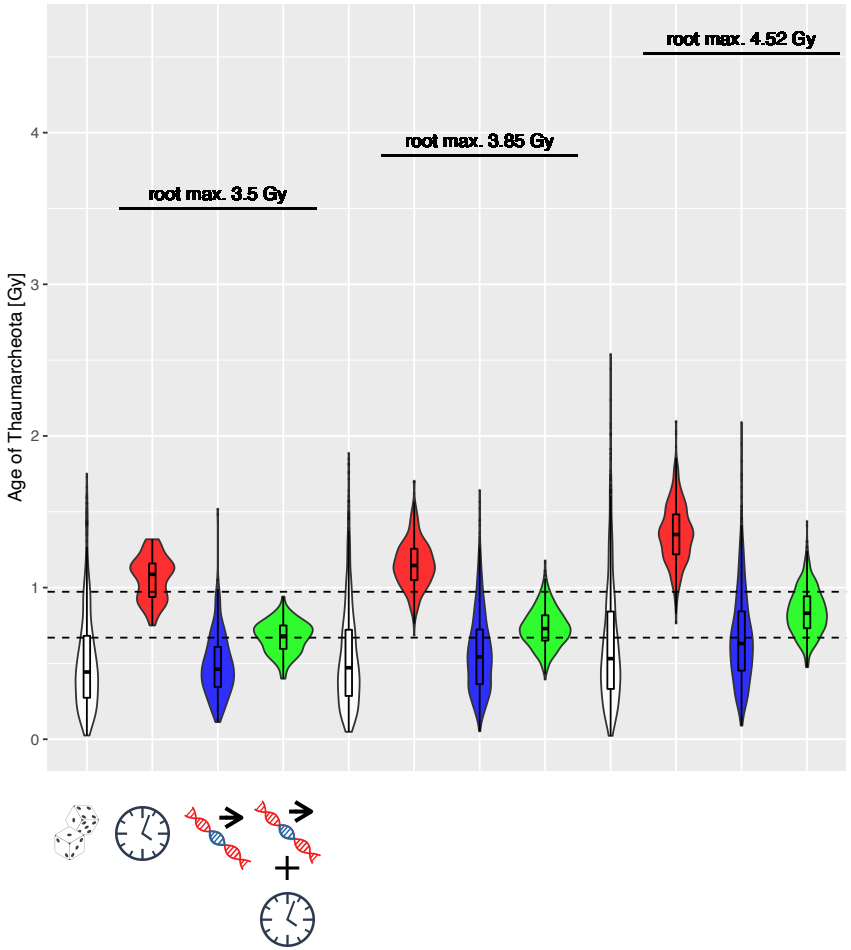
Davin, et al.
Nature Ecology and Evolution (2018)

Do clocks & transfers predict rocks?

Combing **RMCs with relative constraints and fossil calibrations** we can infer dated trees in RevBayes



Thaumarchaeota are the dominant archaea in most soil systems where they constitute up to 5% of all prokaryotes



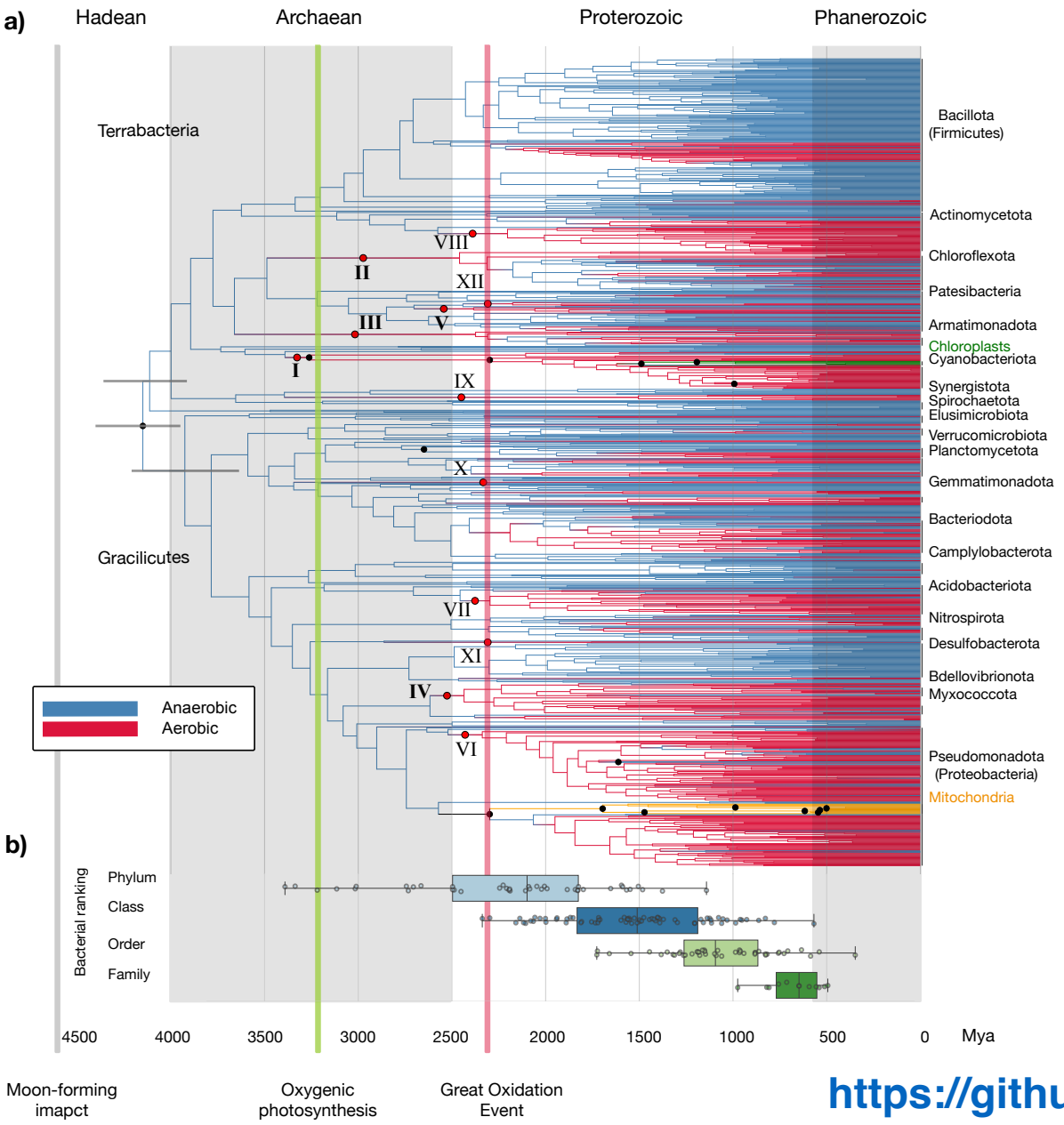
972.4–669.9 My
Morris PNAS 2018

implemented in **MCMCdate**

https://github.com/dschrempf/mcmc-date

Work in progress..

A geological timescale for bacterial evolution and oxygen adaptation



P(A|A)

Condition	log-likelihood	improvement over MFI	AU test *p*-value
Moon-forming impact (MFI)	-4736205	0	1×10^{-14}
MFI + Fossils	-4735968	237	8×10^{-17}
MFI + Fossils + GOE (Concatenate)	-4735871	334	2×10^{-8}
MFI + Fossils + GOE (ExtraTrees)	-4735539	666	9×10^{-6}
MFI + Fossils + GOE (XGBoost)	-4735472	733	1

new “reldate” model

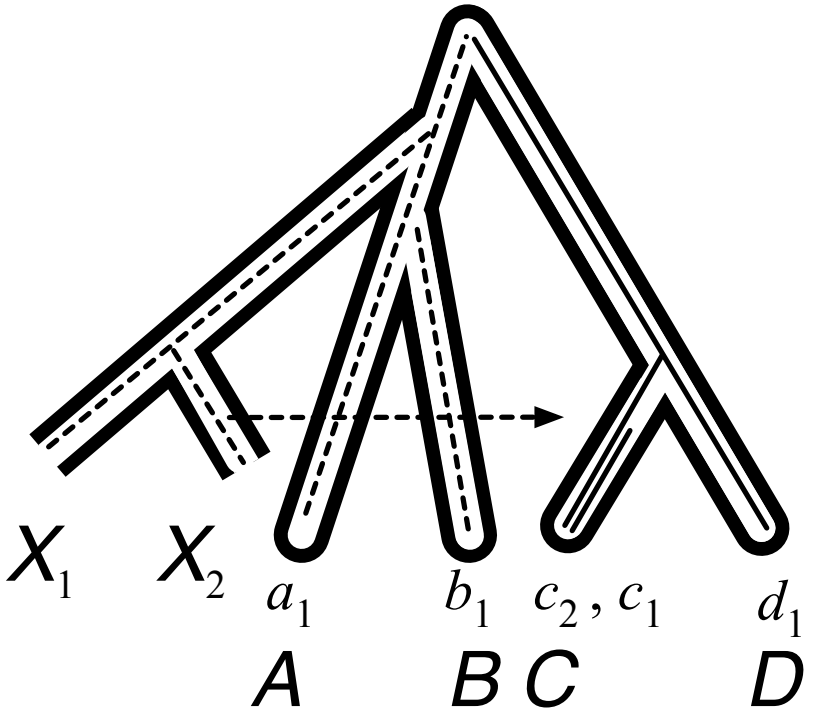
ALE

http://github.com/ssolo/ALE

https://github.com/dschrempf/mcmc-date

Lateral gene transfer from the dead

.. but the species lineage from which a gene was transferred **may have gone extinct** or not have been sampled.



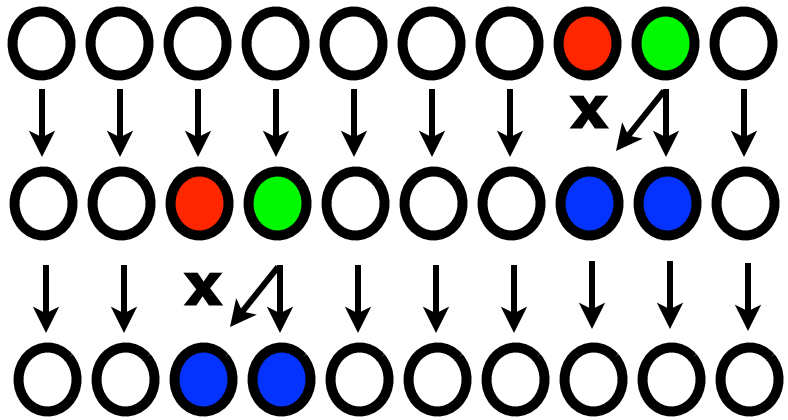
Nicolas Lartillot

Szöllősi, Tannier, Lartillot & Daubin *Systematic Biology* (2013)
Lateral Gene Transfer from the Dead

A minimal model of speciation dynamics

the Moran process

N species

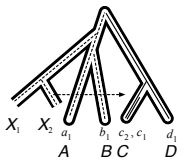


rate per species :

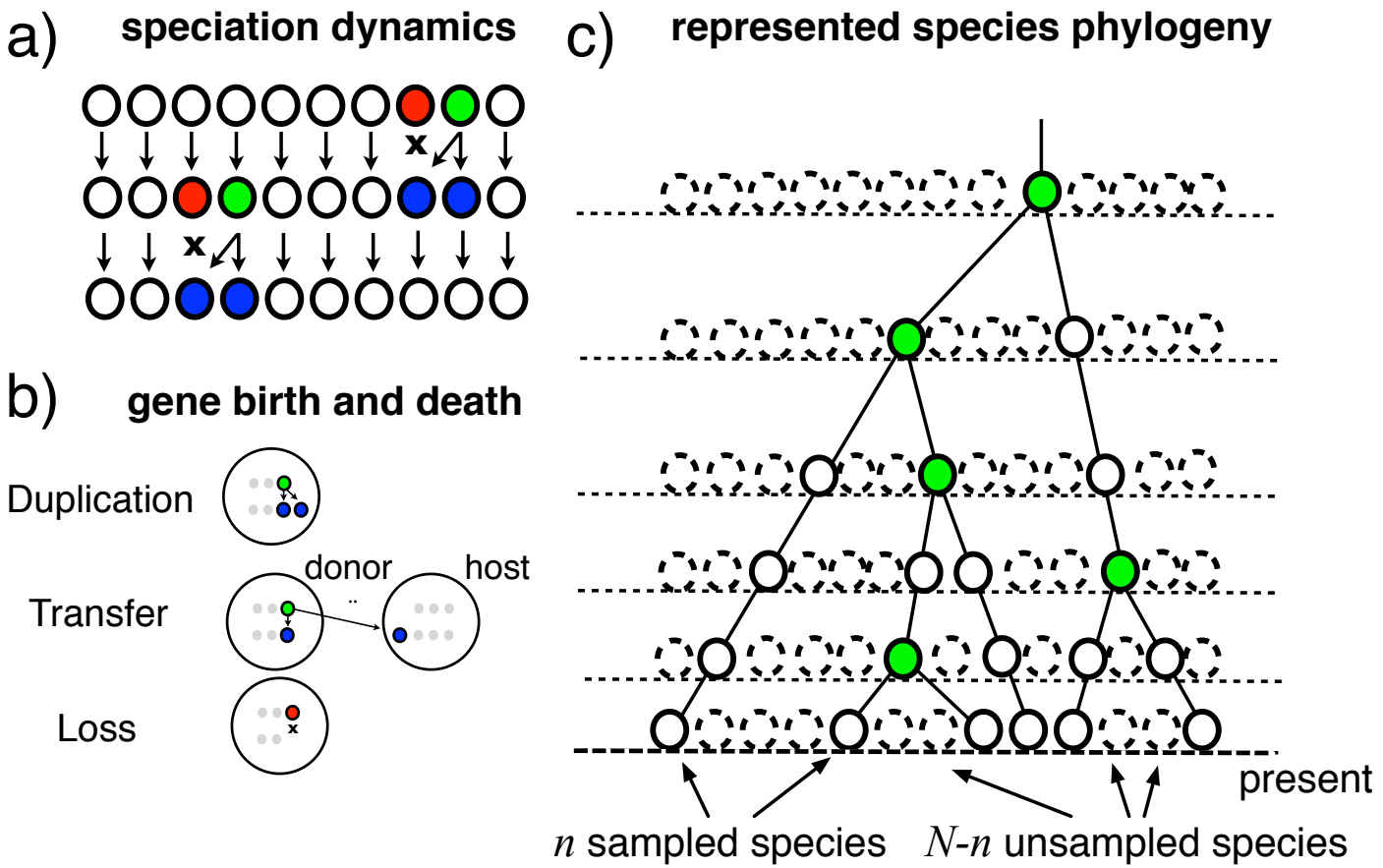
σ

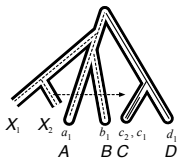
total rate :

$N\sigma$



A minimal model of speciation dynamics





Gene birth-death by **D**uplication, **T**ransfer and **L**oss

Duplication

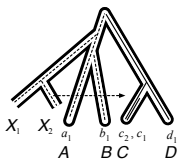
δ duplication rate

τ transfer rate

Transfer

τ/N τ/N

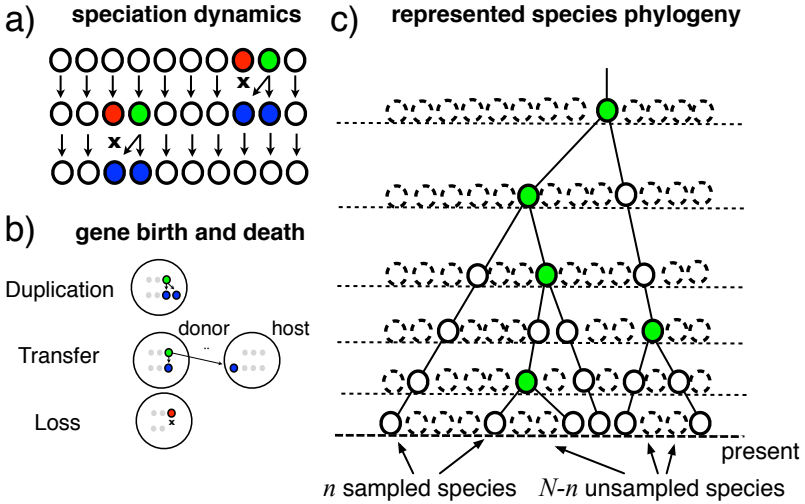
Loss

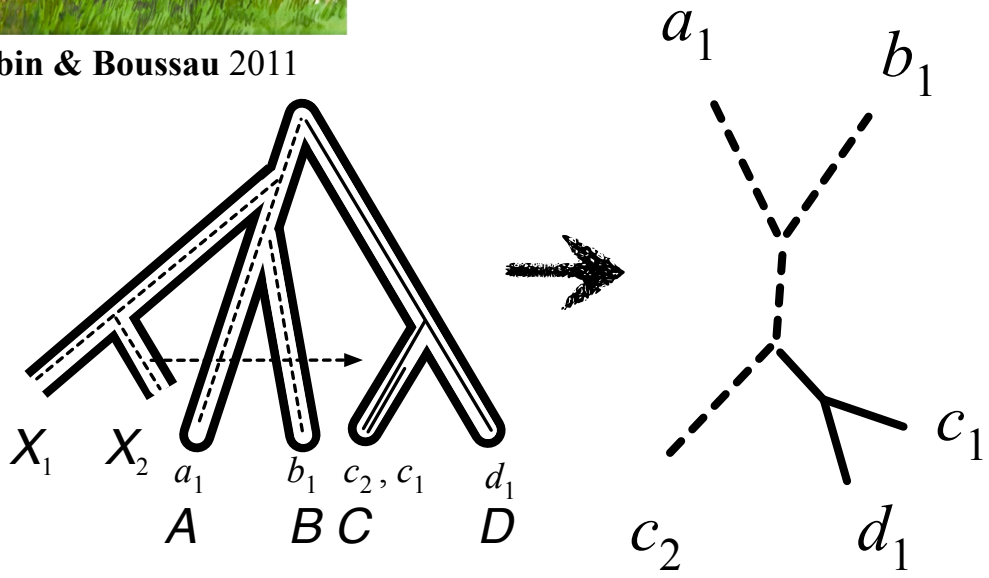


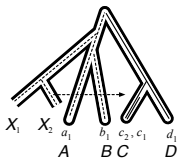
The combination of speciation dynamics and gene birth and death generates gene trees

σ speciation/extinction rate
δ gene duplication rate
τ gene transfer rate
λ gene loss rate

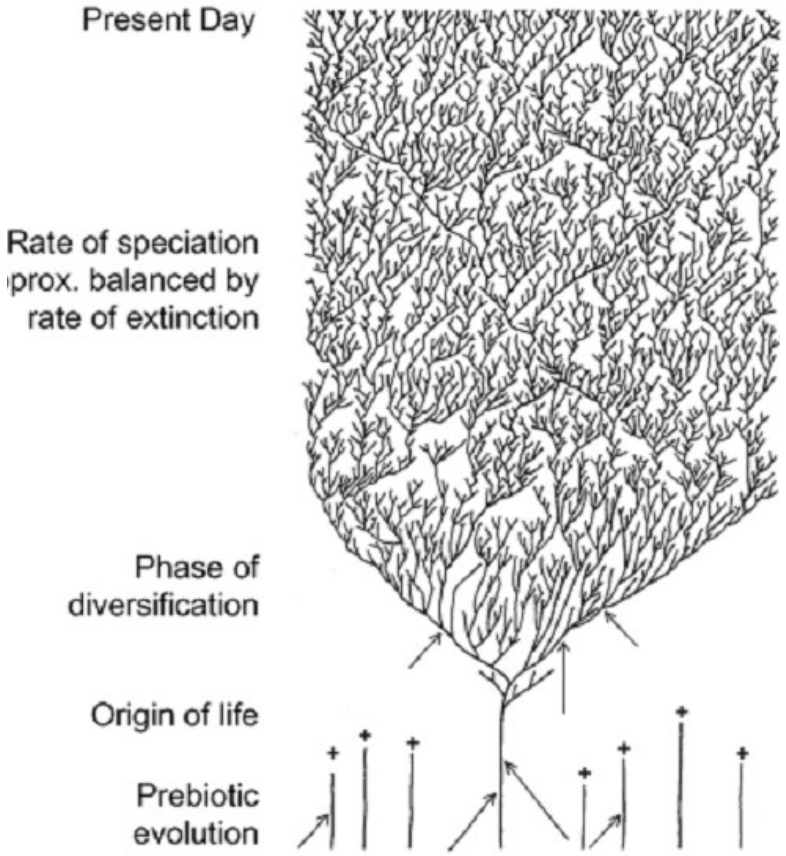
Daubin & Boussau 2011

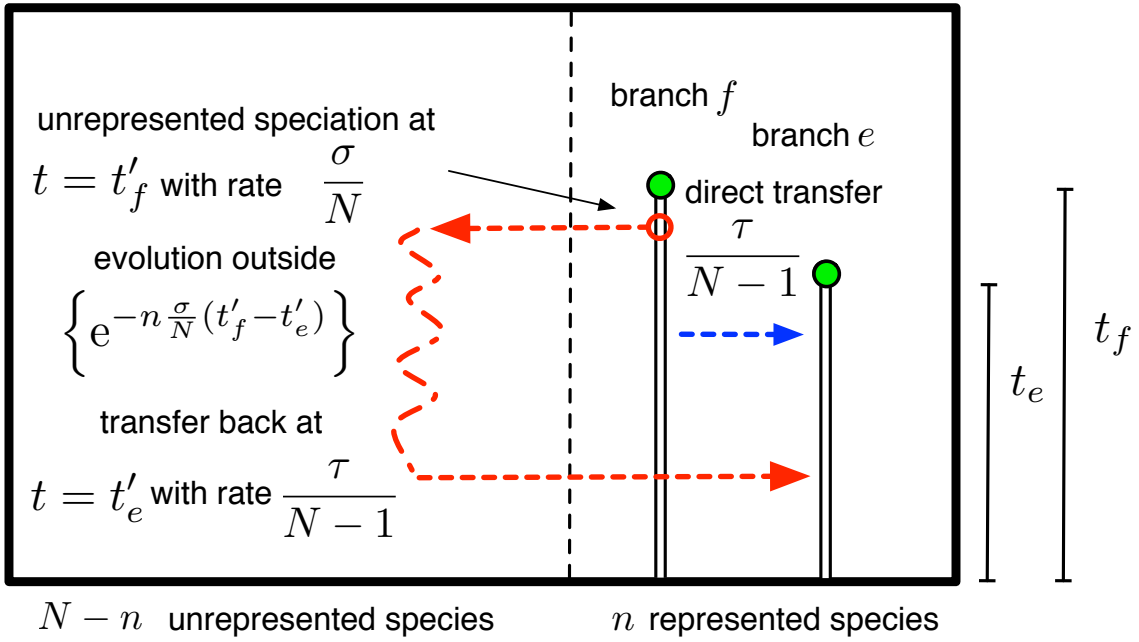






..(almost) all transfers are from the dead..





Gogarten lab

$$T_{\text{direct}} \approx \int_0^{\frac{N}{n\sigma}} \frac{\tau}{N} \mathrm{d}t'_e = \frac{1}{N}\frac{\tau}{2n}\left[\frac{2N}{\sigma}\right],$$

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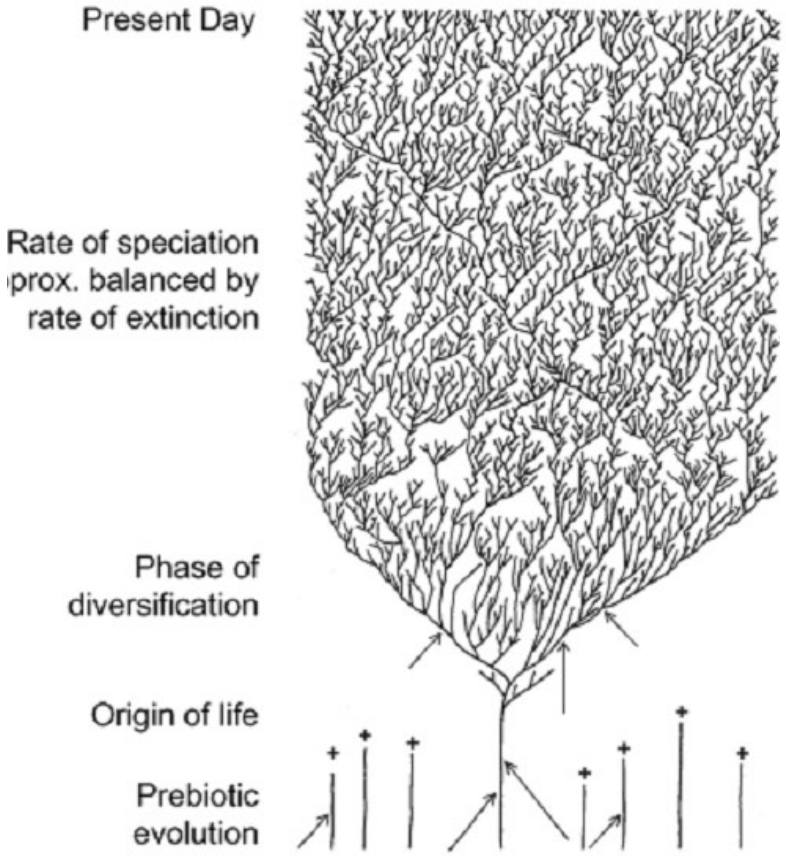

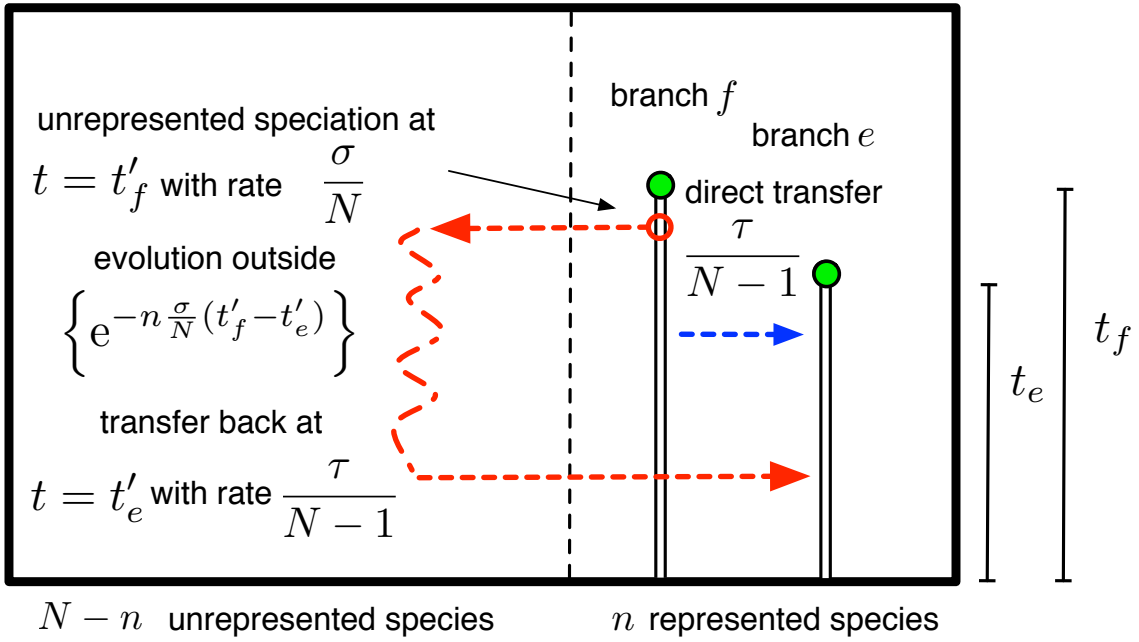

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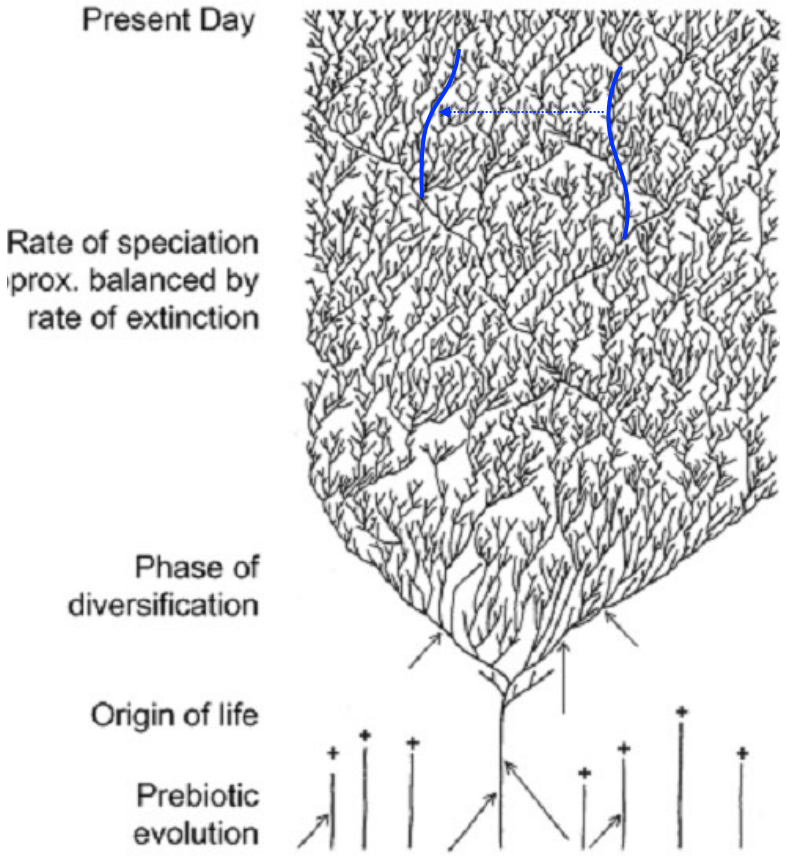

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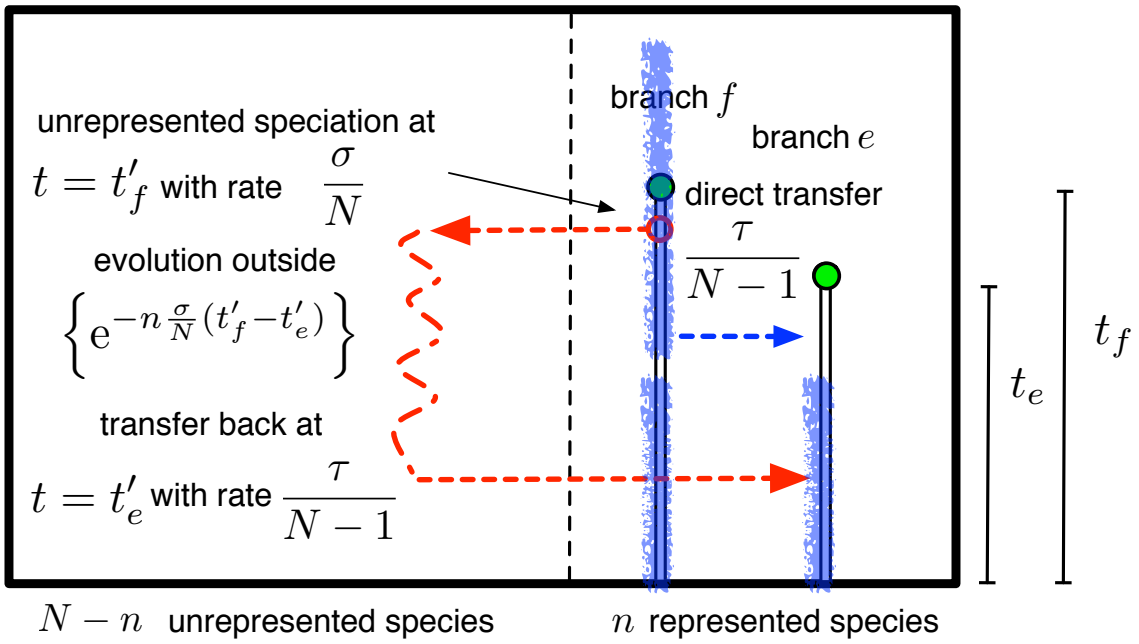

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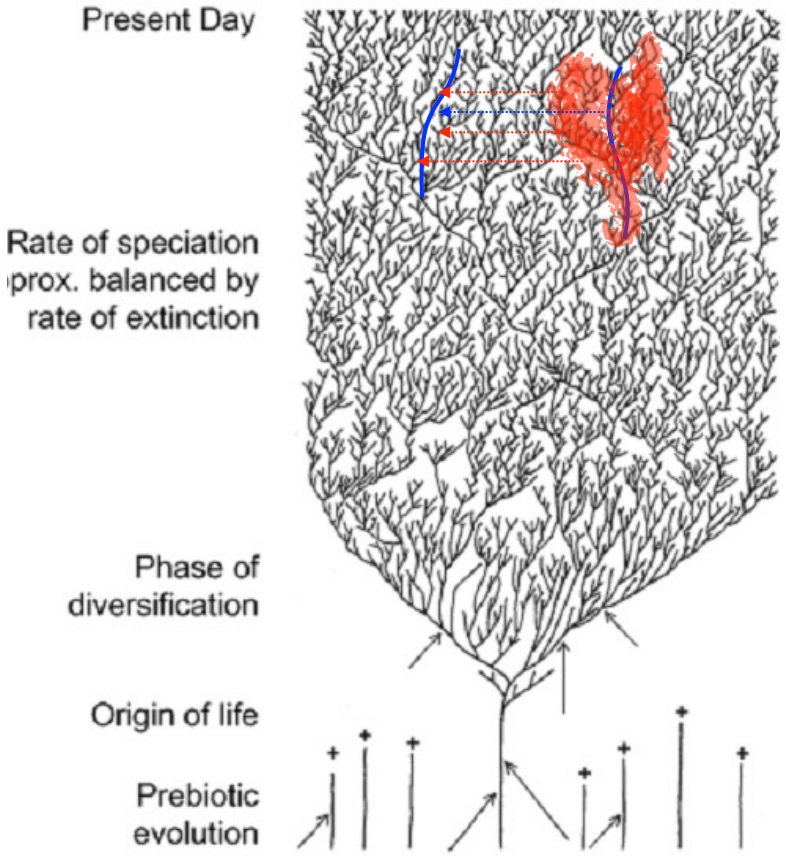

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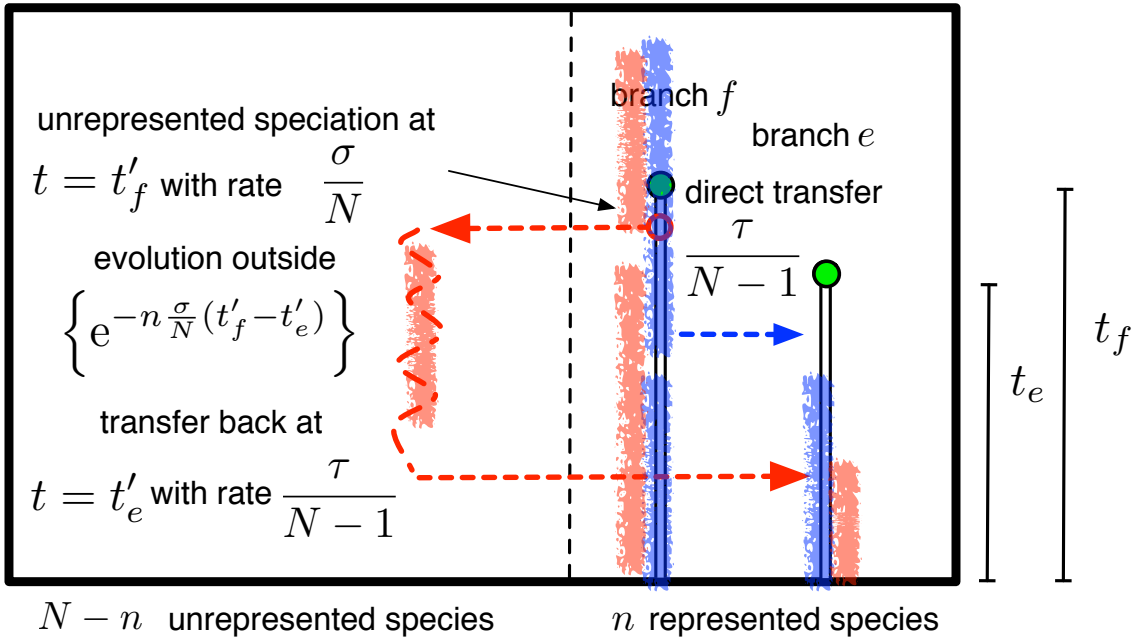

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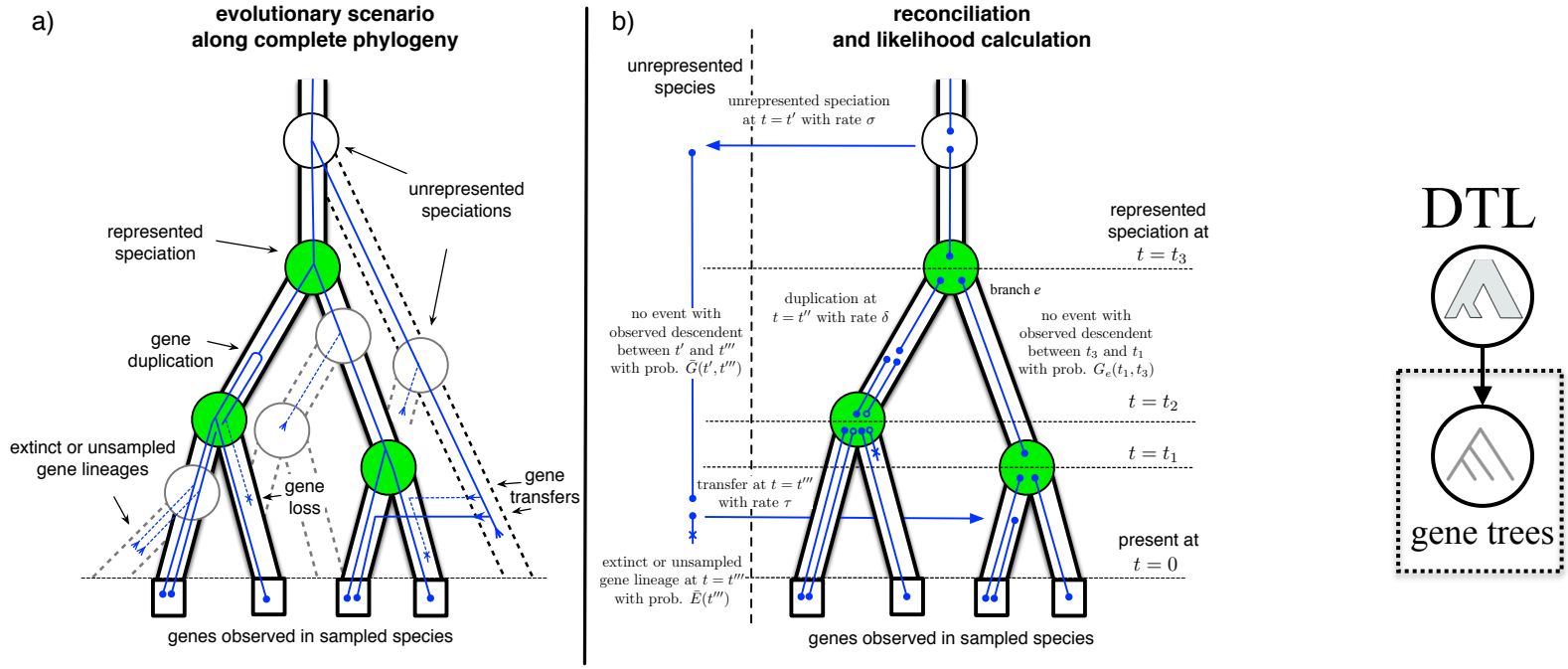
.. but gene trees are generated along the species tree

Calculating the likelihood $P(\text{gene tree} \mid \text{species tree})$ requires

summing over all possible ***gene birth and death events*** along a given ***species tree.***

calculating $p(G_i|S)$ **is possible if** $n \ll N$



implemented in ALE:

http://github.com/ssolo/ALE

Szöllősi, Tannier, Lartillot & Daubin *Systematic Biology* (2013)
Lateral Gene Transfer from the Dead

Szöllősi, Rosikiewicz, Boussau, Tannier & Daubin *Systematic Biology* (2013)
Efficient exploration of the space of reconciled gene trees

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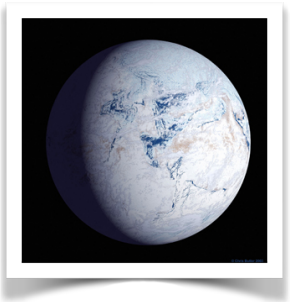
A corollary of the observation that LGT events record evolutionary paths along the complete species tree is that the phylogenies of **genes from a limited sample of extant species carry information about extinct lineages, and therefore about the size and dynamics of ancient biodiversity.**

Can we detect mass extinction events?



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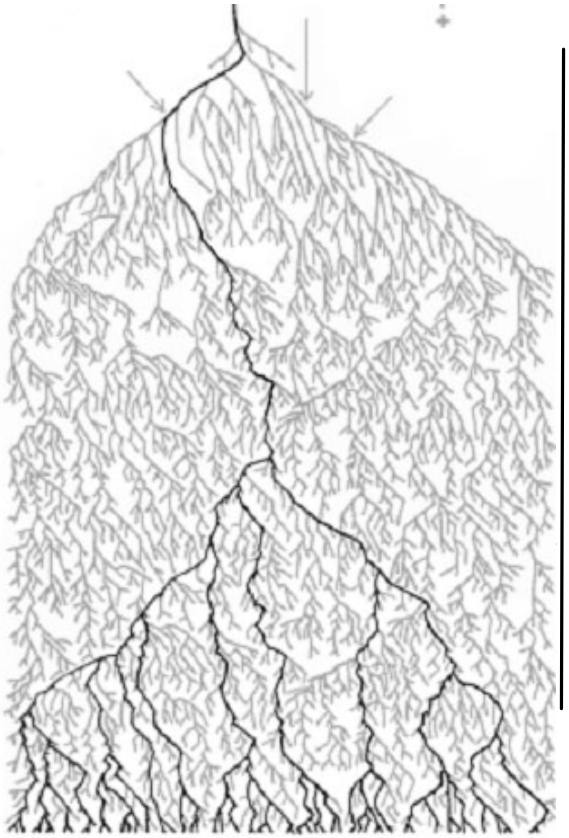

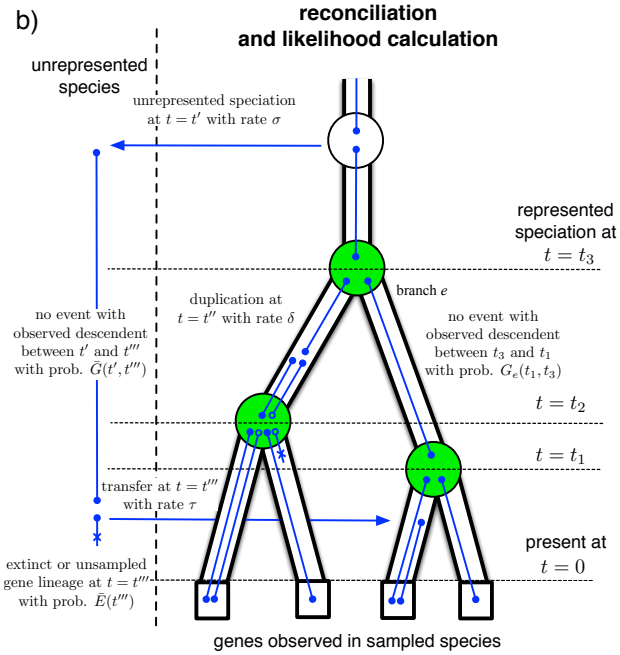

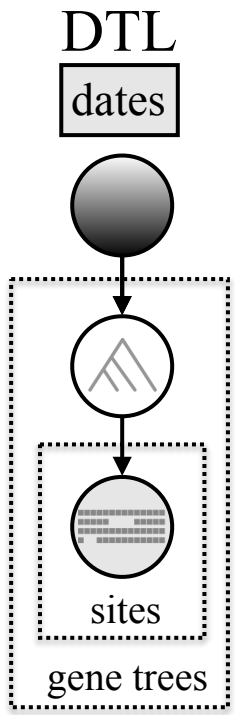

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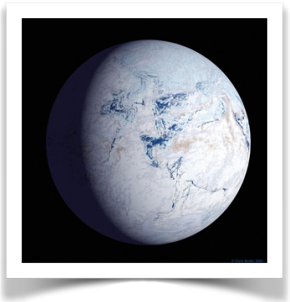

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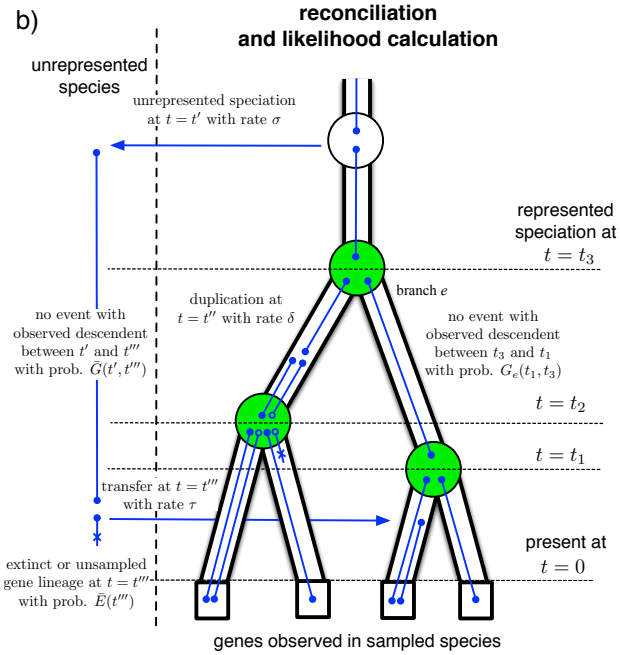

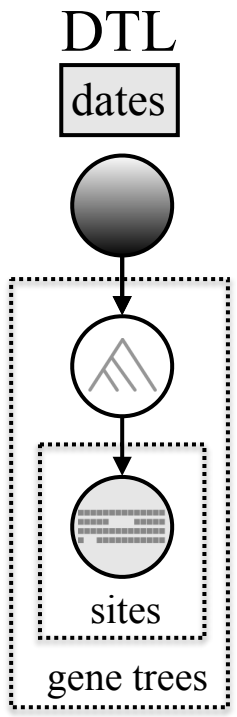

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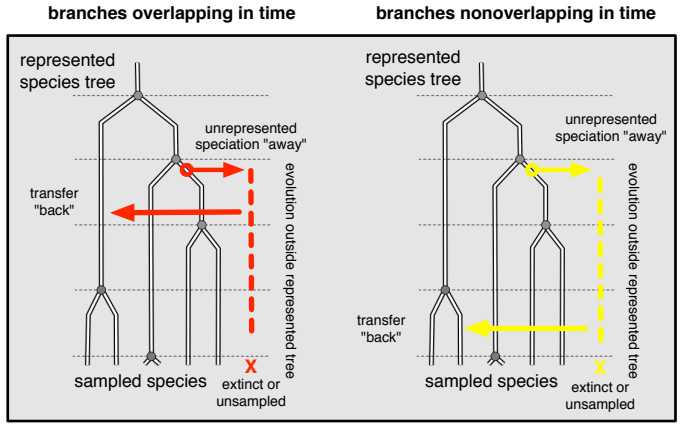
Routes to cyanobacterial genomes

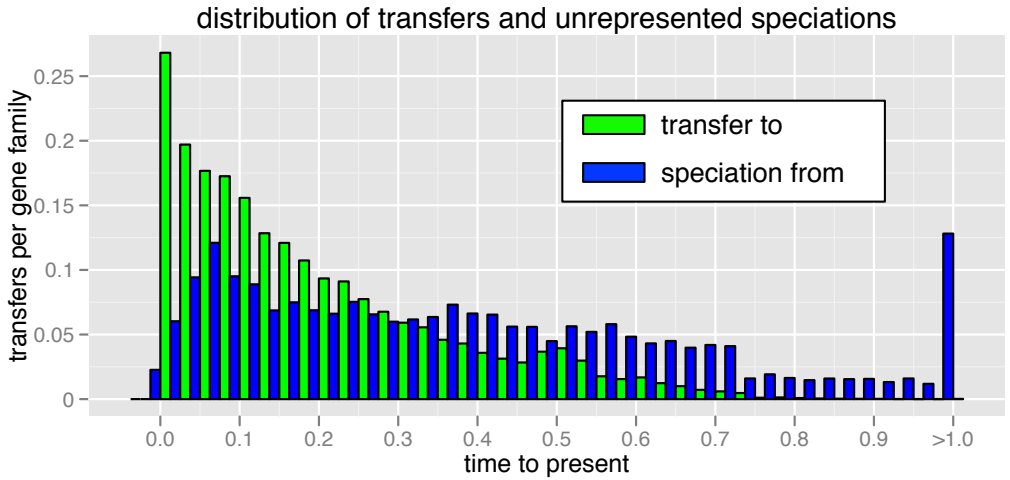
474 single copy families from 36 cyanobacteria

28% of Ts between non-overlapping branches

6% from above the root of Cyanobacteria



a)



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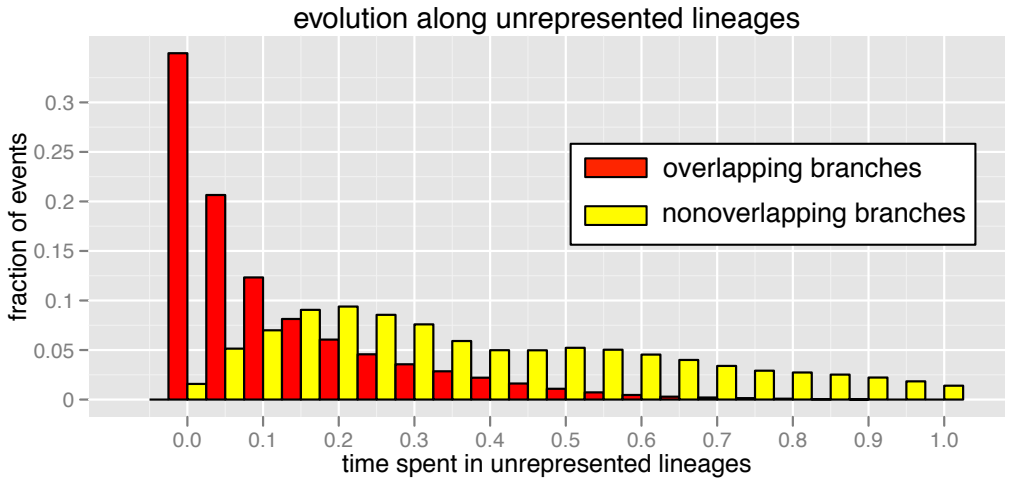

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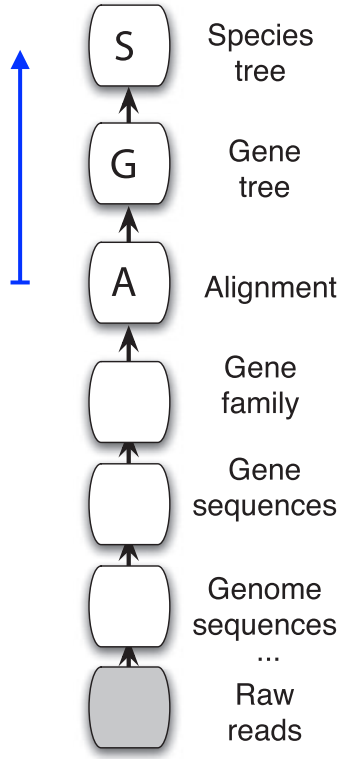
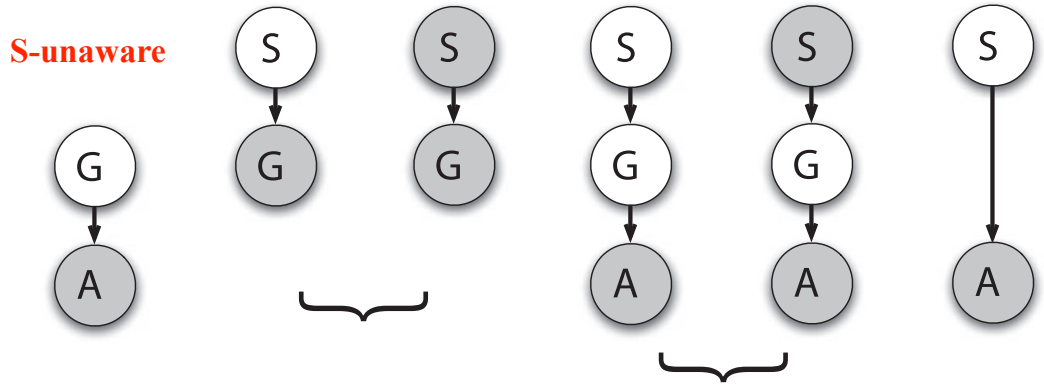
fast models of gene family evolution with DT&L

Species tree-awareness

Phylogenomics inference pipeline



Gene tree-species tree models published in the literature



S-unaware

P(A|G)
- PhyML [Guindon & Gascuel, 2003];
- RAxML [Stamatakis et al., 2005];
- MrBayes [Ronquist et al., 2012];
- BEAST [Drummond et al., 2012];

P(G|S)
- BEST [Edwards et al., 2007];
- DLCoal [Rasmussen & Kellis, 2012];
- MP-EST [Liu et al., 2010];
- ODT [Szöllősi et al., 2012];
- ASTRAL [Mirarab et al. 2014]

S-aware

P(A|G,S)
- *BEAST [Heled & Drummond, 2008];
- Prime-GSR [Akerborg et al., 2009];
- IMa2 [Hey, 2011];
- PHYLDOG [Boussau et al., 2013];
- Prime-DLRS [Sjöstrand et al., 2012];
- **AleRax**
- ALE [Szöllősi et al., 2013b];

P(A|S)
- SNAPP [Bryant et al., 2012];
- ALE [Szöllősi et al., 2013b];

Szöllősi,.., Boussau 2015 Syst. Biol.

Efficiently integrating over the space of reconciled gene trees

AleRax

using ~~ALE~~ we can approximate the integral in the DTL version of the Felsenstein equation:

$$P(A|S, \text{rates}) = \int_G p(A|G)p(G|S, \text{rates})$$

Felsenstein 1988

AleRax: A tool for gene and species tree co-estimation and reconciliation under a probabilistic model of gene duplication, transfer, and loss

Benoit Morel,[1,2], Tom A. Williams,[3] Alexandros Stamatakis,[4,1,2] and Gergely J. Szöllősi,[5,6,7]

[1]Computational Molecular Evolution group, Heidelberg Institute for Theoretical Studies, Heidelberg, Germany
[2] Institute for Theoretical Informatics, Karlsruhe Institute of Technology, Karlsruhe, Germany
[3] School of Biological Sciences, University of Bristol, Bristol, UK
[4] Biodiversity Computing Group, Institute of Computer Science, Foundation for Research and Technology - Hellas
[5] ELTE-MTA "Lendület" Evolutionary Genomics Research Group, Pázmány P. stny. 1A., H-1117 Budapest, Hungary
[6] Institute of Evolution, Centre for Ecological Research, Konkoly-Thege M. út 29-33. H-1121 Budapest, Hungary
[7] Model-Based Evolutionary Genomics Unit, Okinawa Institute of Science and Technology Graduate University, Okinawa, Japan.

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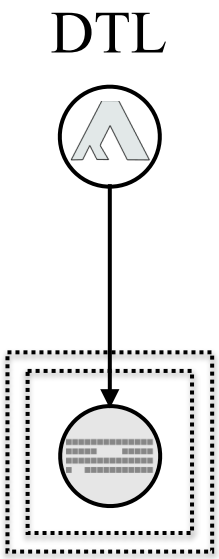

https://github.com/BenoitMorel/AleRax.git

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Join us for a postdoc at the interface of computational & evolutionary biology! Use probabilistic models & machine learning to model coevolution, reconstruct the Tree of Life, understand somatic evolution or pursue your own project..

Model-Based Evolutionary Genomics Unit
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Okinawa Institute of Science and Technology

gergely.szollosi@oist.jp