

An efficient algorithm for gene/species trees parsimonious reconciliation with losses, duplications, and transfers

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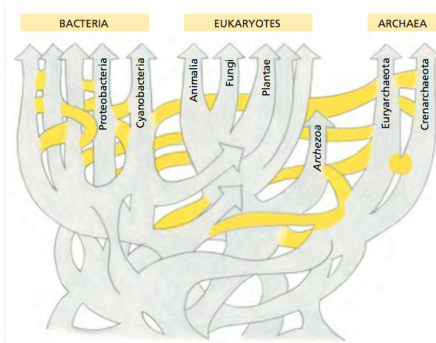
3- LBBE, CNRS - Univ. Lyon 1, France.

4- ISEM, CNRS - Univ. Montpellier 2, France.

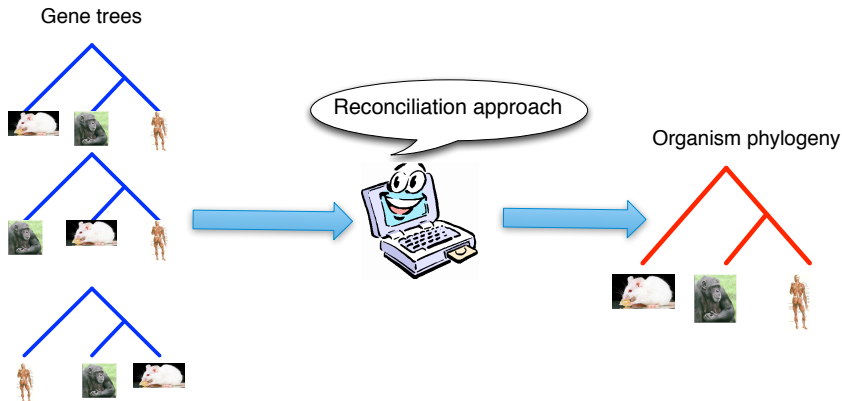
JOBIM, Montpellier
September 2010

Concept of the Tree of Life

- **For:** Kurland et al. 2003, Puigbò et al. 2009
- **Moderate:** Galtier et Daubin 2008
- **Against:** Baptiste et al. 2005; Koonin 2007



Inferring a Tree of Life by retrieving signals from gene trees



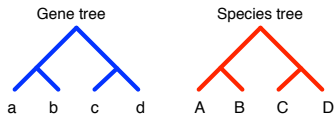
Reconciliation

- Parsimony and probabilistic app. [LAGERGREN ET AL.; GORECKI ET AL.]
- Used to identify orthologous sequences (functional annotation)
- Similar concepts in Ecology and Biogeography [PAGE ET AL.]

Reconciliation depicts coevolution

(Some) Macro Evolutionary Events

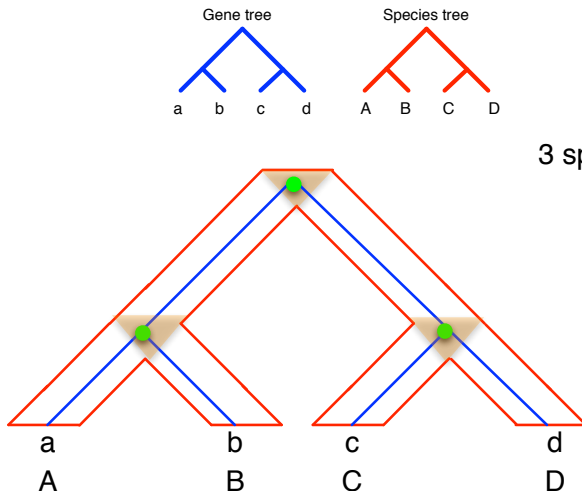
Speciation (\mathbb{S}), Duplication (\mathbb{D}), Transfer (\mathbb{T}), and Loss (\mathbb{L})



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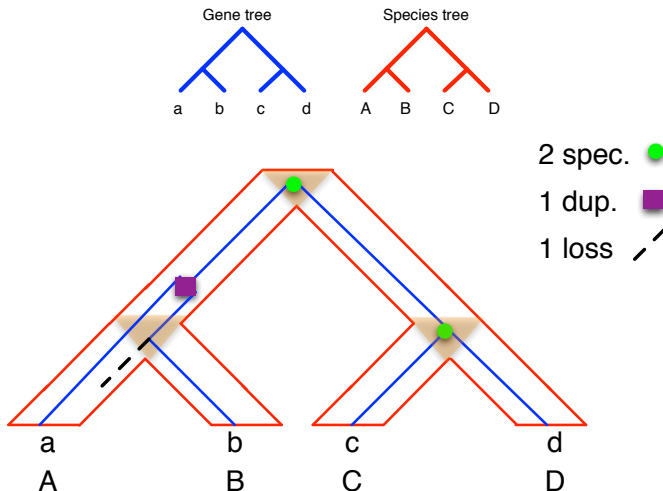
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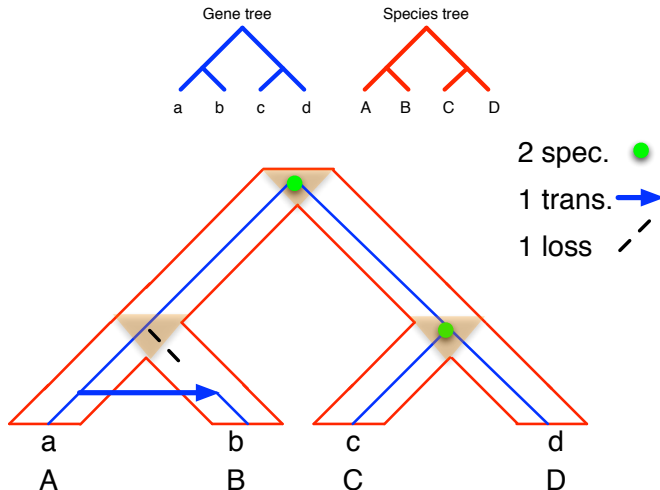
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The Most Parsimonious Reconciliation problem

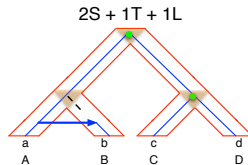
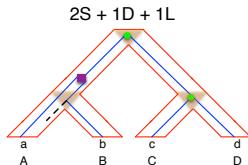
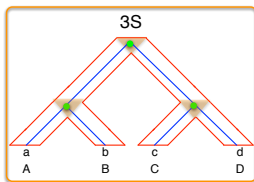
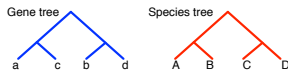
- Input: **costs** for each event (\mathbb{D} , \mathbb{T} , \mathbb{L} , \mathbb{S}) and gene / species **trees**
- Output: a reconciliation that has a **Minimal cost** and is **Time consistent**
(May be more than one optimal reconciliation)

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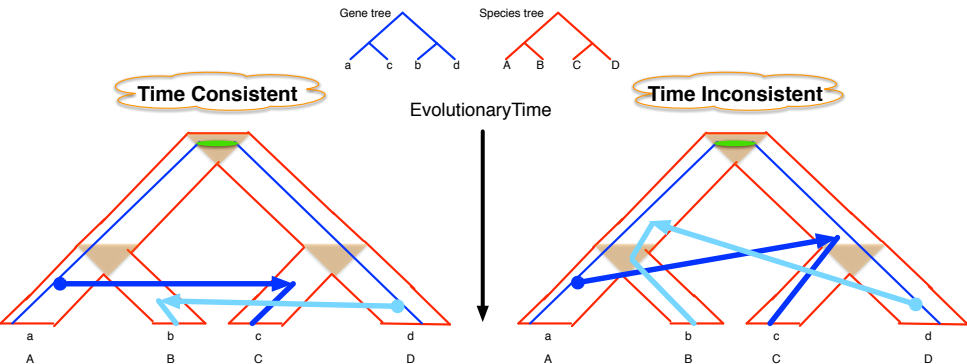
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Previous approaches & models

Species Graph

[Gorecki]

Locations of (possible) transfers are defined in advance in S .

Inconvenients of reconciliation models

- Don't **directly** account for losses [HALLETT & LAGERGREN 04]
- Can lead to **time inconsistent reconciliations**
(Tarzan & Jane software) [MERKLE ET AL 05-10]
- **Don't guarantee optimality!!!**

Dated species tree S

Lagergren's group 09-10, Lyubetsky et al 09, Merkle et al 05-10, Gorbunov et al 09, Libeskind-Hadas 09

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Our contribution

An efficient model for MPR problem

- Considering a **dated** species tree S .
- Relying on **6 atomic events**, each one being fast to investigate

A dynamic programming algorithm

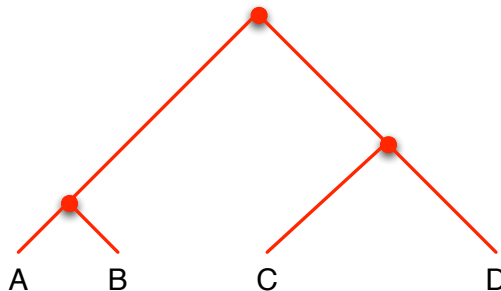
- Based on a **small subdivision** S' of S
- **Fast**: runs in time $O(|S'| \cdot |G|)$
- Previous algorithms in $O(|S|^4 \cdot |G|^4)$ and $O(|S'|^3 \cdot |G|)$

Experimental results for the relevance of parsimony

Is parsimony relevant to infer the evolutionary scenario of a gene family?

An Efficient Reconciliation Model

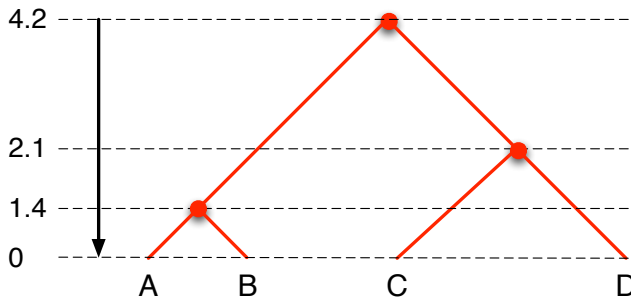
- Date species tree [LARTILLOT ET AL. 2004, AKERBORG ET AL. 2008, ETC.].
- Discretize evolutionary time into slices.
- Allow transfers within the same time slice.



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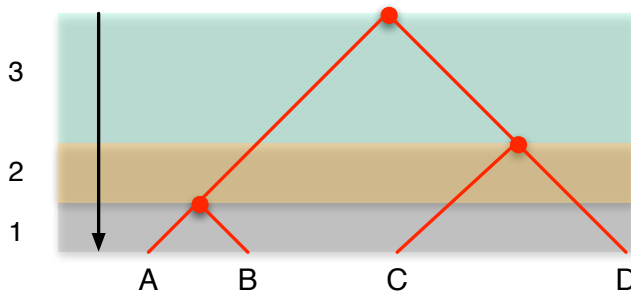
Time Dates



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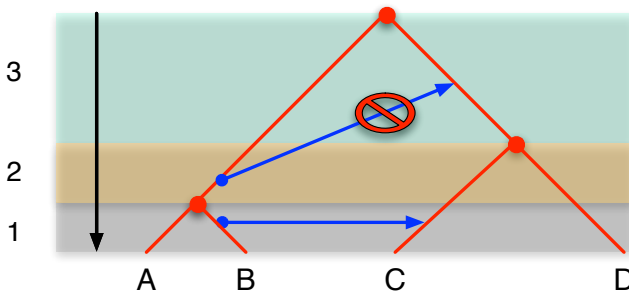
Time Slices

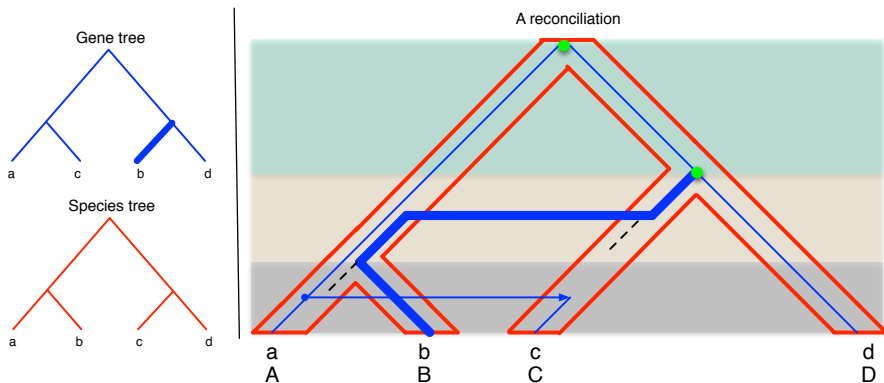


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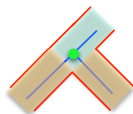




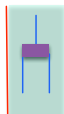
An Efficient Reconciliation Model

Six *Atomic events*, where losses are implicitly considered (**Parsimony**)

Speciation (\mathbb{S})



Duplication (\mathbb{D})



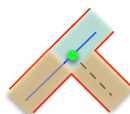
Transfer (\mathbb{T})



No event (\emptyset)



Speciation + Loss (\mathbb{SL})



Transfer+Loss (\mathbb{TL})



Theorem

A Most Parsimonious Reconciliation is computed in time $\Theta(|G| \cdot |S'|)$

Two Datasets DS_1 and DS_2

Details of the simulation process

- 10 species trees on 100 species (Birth and Death with a ratio = 1.25)
- Gene Tree + Real Reconciliation generated (with rates \mathbb{L}_R , \mathbb{T}_R and \mathbb{D}_R)
- Based on realistic loss rates [CSUROS AND MIKLOS]
- Gene trees have between 59 and 93 leaves

DS_1 : “Simulate” a relatively Large Time Scale (archaeal or bacterial phylum)

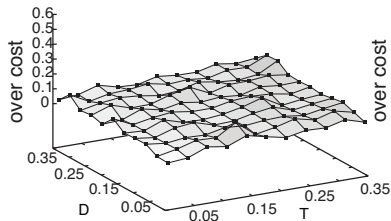
- Fixed rate $\mathbb{L}_R = 0.7$ and tree height $h = 1$
- 11 values for \mathbb{T}_R and \mathbb{D}_R in $[0.01, 0.35]$
- 6,050 $G = (5 G) \times (10 S) \times (11 \times 11 \text{ rate pairs})$

DS_2 : “Simulate” Different Time Scales and Vary the Importance of \mathbb{T} vs. \mathbb{D}

- Four different tree heights $h \in [0.2, 0.4, 0.8, 1.6]$
- Fixed ratio $\mathbb{L}_R / (\mathbb{D}_R + \mathbb{T}_R + \mathbb{L}_R) = 0.7$ [CSUROS AND MIKLOS]
- 11 values for $\mathbb{T}_R \in [0, 0.3]$ and $\mathbb{D}_R = 0.3 - \mathbb{T}_R$ fixed.
- 8,800 $G = (20 G) \times (10 S) \times (4 \times 11 \text{ rate pairs})$

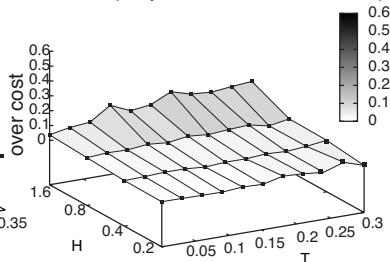
Efficiency of parsimony according to costs

DS_1 (Large Time Scale)



(a)

DS_2 (Importance of T vs. D)



(b)

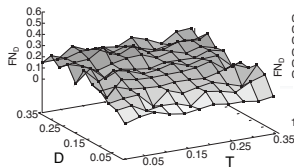
Over cost of the real scenario w.r.t. MPR

- Small for all \mathbb{D} and \mathbb{T} rates (DS_1)
- Increases with the height of the gene trees (DS_2)
- Parsimony might be considered as a credible criterion

Great!

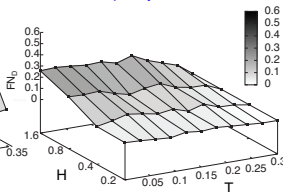
Accuracy of parsimony to retrieve \mathbb{D} events

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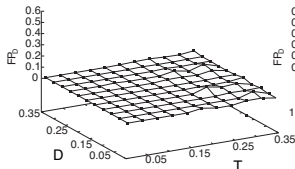


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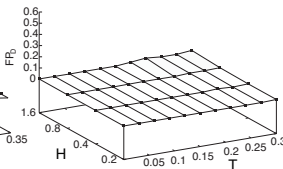
DS_2 (Importance of T vs. \mathbb{D})



(b)



(c)



(d)

False Negatives / Positives: Node of G + Branche in S'

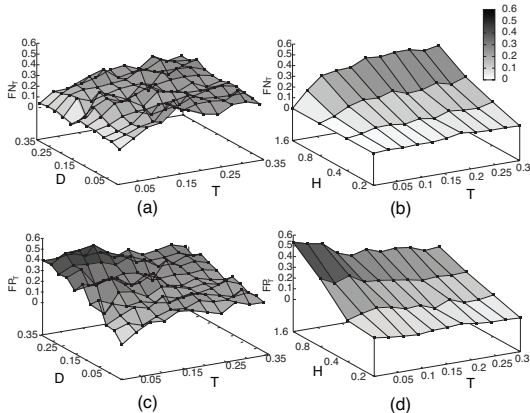
- Reasonably few forgotten duplications (homoplasy and several MPRs?)
- *Very* few False Positives

Not bad!

Accuracy of parsimony to retrieve \mathbb{T} events

DS_1 (Large Time Scale)

DS_2 (Importance of \mathbb{T} vs. \mathbb{D})



False Negatives / Positives: Node of $G + 2$ Branches in S'

Large number of \mathbb{D} leads to non-trivial errors in \mathbb{T} prediction

Huh huh... :(

Transfers among archaeal genomes

Input data

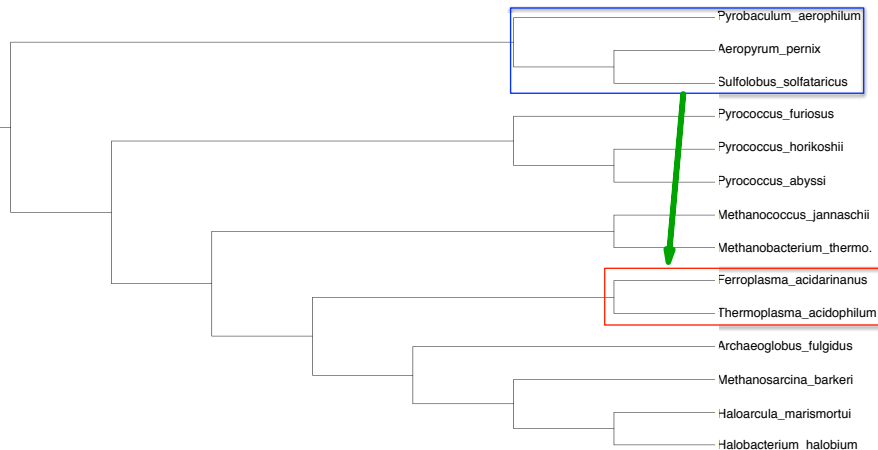
- Dated species tree: 14 archaeal (53 ribosomal proteins)
3 dates for (Ferroplasma A., Thermoplasma A.) clade. [TIMETREE]
- Gene tree: ribosomal proteins
2 roots. [MATTE ET AL. 2002; TOFIGH ET AL. 2010]
- **6 cases**

Our approach vs. *Tofigh et al.* (May propose Time Inconsistent transfer)

- Our approach: 5 transfers + 3 losses
- *Tofigh et al.*: 5 transfers / duplications (Losses = “a posteriori”)

What is the relevancy of these transfers?

From Crenarchaeota to the plasma



Apparently correct (both roots of G , \neq direction)

- Other transfers proposed in the same dir. and with different methods
- Same ecological niche

Conclusion

Our Most Parsimonious Reconciliation algorithm

- Proposes Time-Consistent transfers;
- Directly account for losses (discriminate among different scenarios).
- Much faster (cpu / complexity) than previous ones [GORBUNOV ET AL. 09].
- Program available: www.lirmm.fr/phylariane/

Experimental conclusions

- Parsimony cost fits nicely with real one.
- Few duplications not recovered and almost no incorrect ones predicted.
- Transfers less correctly predicted ($\approx 20 - 30\%$ errors).

What next?

- Enumerating and counting MPRs. [DOYON ET AL. 2009]
- Links between MPR and ML reconciliations
- Polytomous trees (low supported clades) [VERNOT ET AL. 2008]

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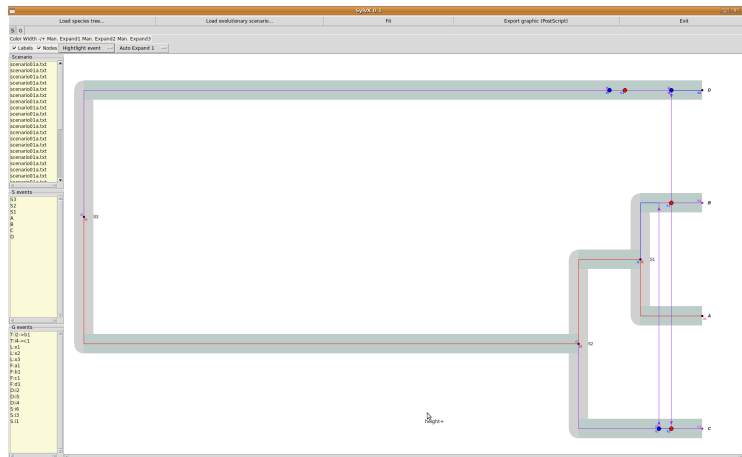
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Phyl-ARIANE project

SylvX - reconciliation viewer/editor

- Automatic computation and manual modifications of reconciliations
- Graphical operators & analyses: re-rooting, zooming, filtering events

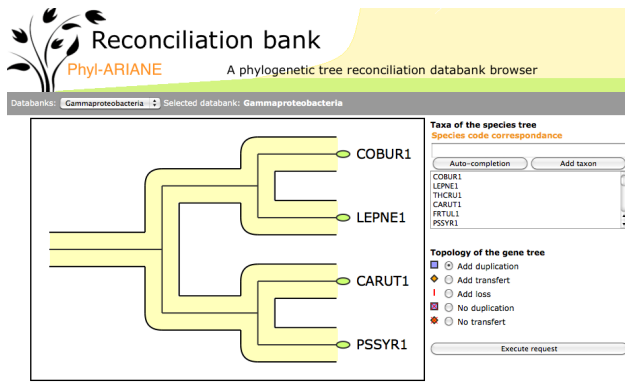


Phyl-ARIANE project

Reconciliation bank browser (gamma and beta proteobacteria)

Query a databank for

- evolutionary events (duplications, losses, and transfers);
- reconciliation patterns.



Reconciliation bank
Phyl-ARIANE A phylogenetic tree reconciliation databank browser

Databanks: **Gammaproteobacteria** Selected databank: **Gammaproteobacteria**

Taxa of the species tree
Species code correspondence

Auto-completion Add taxon

COBUR1
LEPNE1
THCRU1
CARUT1
FRTUL1
PSSYR1

Topology of the gene tree

☒ Add duplication
☒ Add transfert
☒ Add loss
☒ No duplication
☒ No transfert

Execute request

Acknowledgment



Phyl-ARIANE

Phylogenomics: integrated algorithms and visualizations for analyzing the evolution of life

<http://www.lirmm.fr/phylariane/>

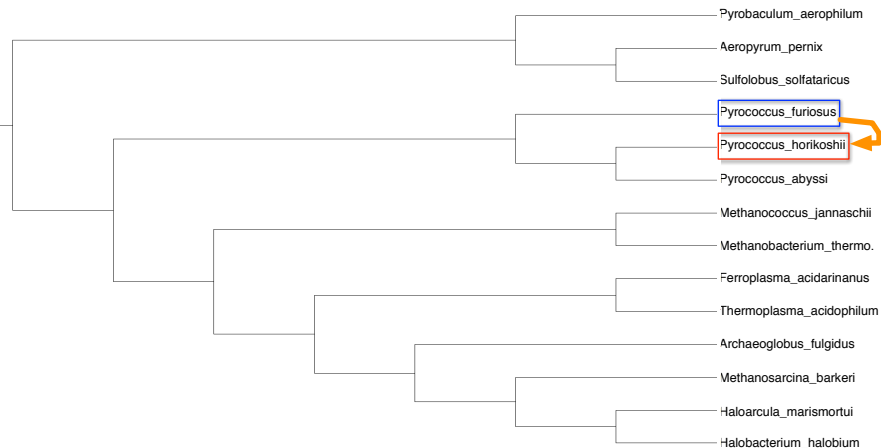
Thanks

- Eric Tannier & Vincent Daubin, Lyon (FR)
- Céline Brochier for the gene tree and her help on the Archaeal dataset
- Mukul S. Bansal for the dataset of Guigo et al. 1996

Funding

Phylariane ANR project, Région LR, CNRS, ...

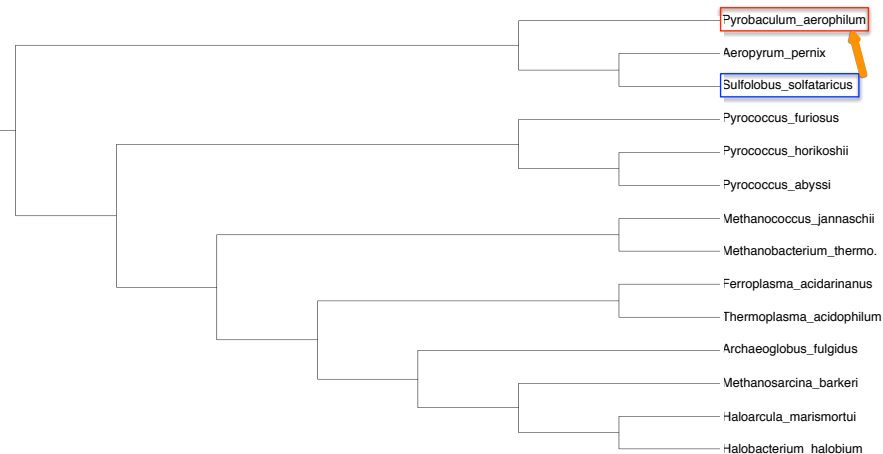
From *Pyrococcus furiosus* to *Pyrococcus horikoshii*



Seem to be correct (both roots of G)

- High bootstrap values in species and gene trees.
- But small sequences and branch lengths (gene tree).

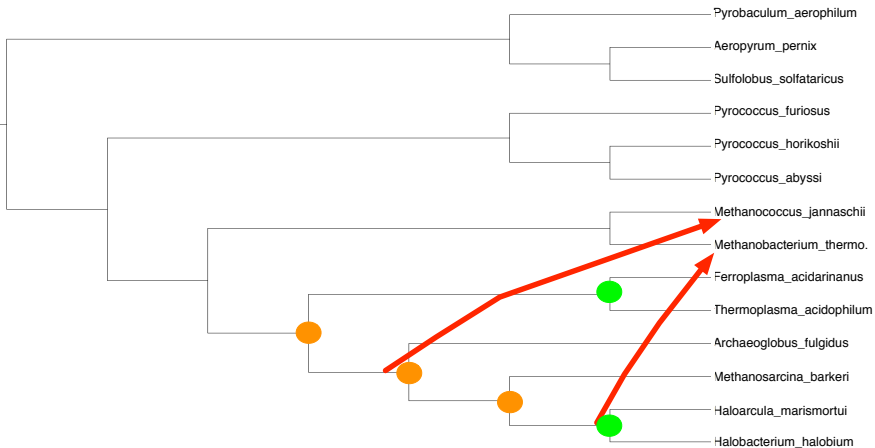
From *Sulfolobus solfataricus* to *Pyrobaculum aerophilum*



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- High bootstrap values in species and gene trees.
- More studies to do.

Reconciling trees with lack of resolution

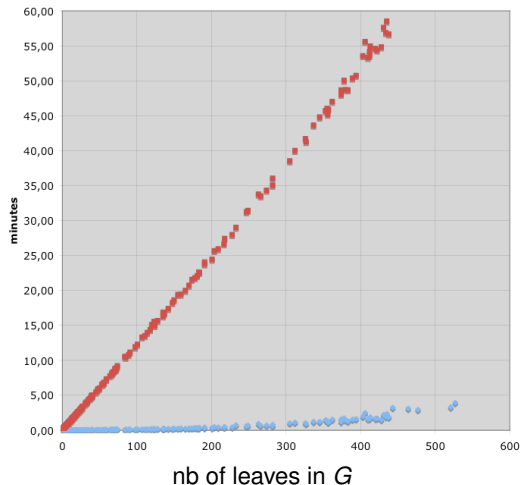


Artificial transfers (probably)

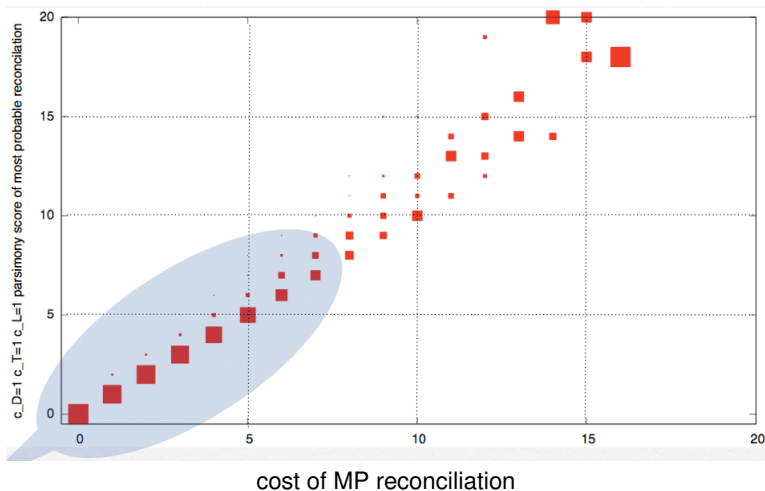
- Low bootstrap values in species and gene trees.
- Collapsing unsupported nodes erases discrepancies between trees.

Running times

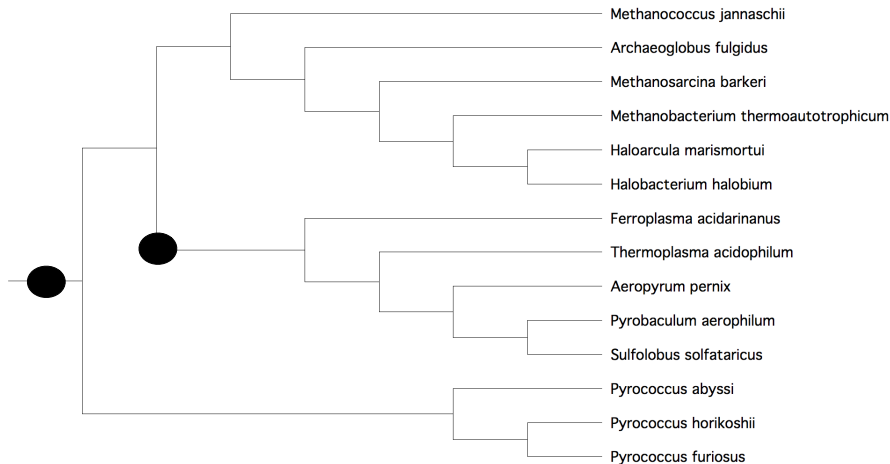
Comparison with an implementation of [Gorbunov et al 09]:
from dozens minutes to less than 2 sec (between 1.09s and 1.38s)



Relationship between the MP and ML criteria



Two roots for the (rpl12e) ribosomal proteins



Dynamic Programming Algorithm

Properties

- $\mathbb{S}\mathbb{L}$ is an optimal scenario where one gene goes extinct after an \mathbb{S} event (Idem for $\mathbb{T}\mathbb{L}$ and \mathbb{T})
- Any $\mathbb{T}\mathbb{L}$ event is (possibly) followed by a different event.
- The model allows to progress either in S' (its time) or in G .
- The best landing place is independent of the donor branch.

Maximum Likelihood approach

Similar algorithm applies to ML

[SZÖLLÖZI ET AL IN PREP.]

Vertebrates: Whole Genome Duplications

Episode Clustering Problem (without transfer)

Given S and $\{G_1, \dots, G_n\}$, minimize the number of locations in S where all duplications can be placed.

53 gene trees form 16 vertebrates

[GUIGO ET AL. 1996]

	# Dup	# Spots of S	# WGD	MPR wrt. Guigo
Guigo et al.	46	4	5	
MPR ($\mathbb{D}_C, \mathbb{L}_C \geq 1$)	46	6	9	80%
MPR ($\mathbb{D}_C = 1, \mathbb{L}_C = 0$)	46	6	9	95%

Episode Clustering Problem

On this dataset, **Whole-Genome-Duplications** can be retrieved and located solely with **Most-Parsimonious-Reconciliation** classical approaches.

Whole Genome Duplications

