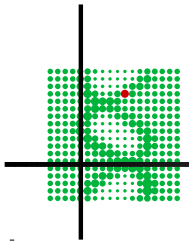

An Improved Algorithm for the Macro-evolutionary Phylogeny Problem

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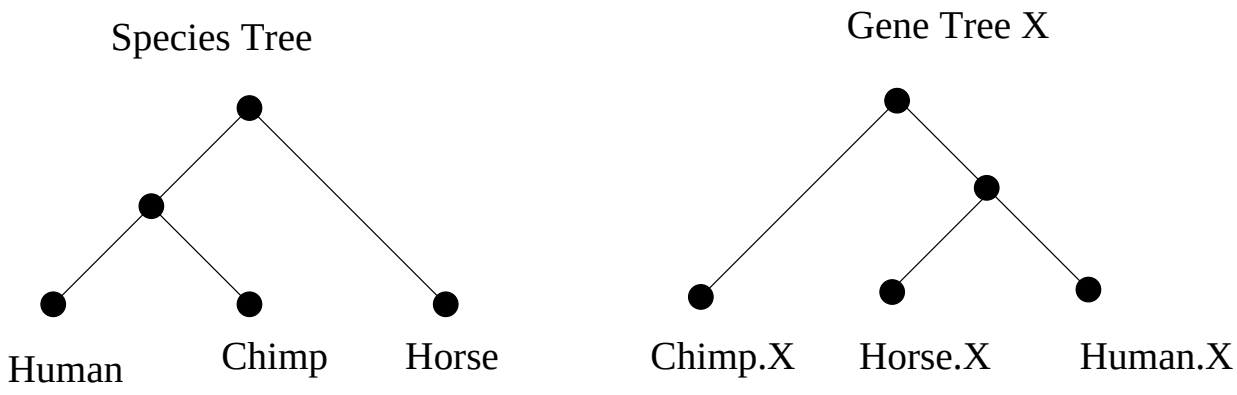
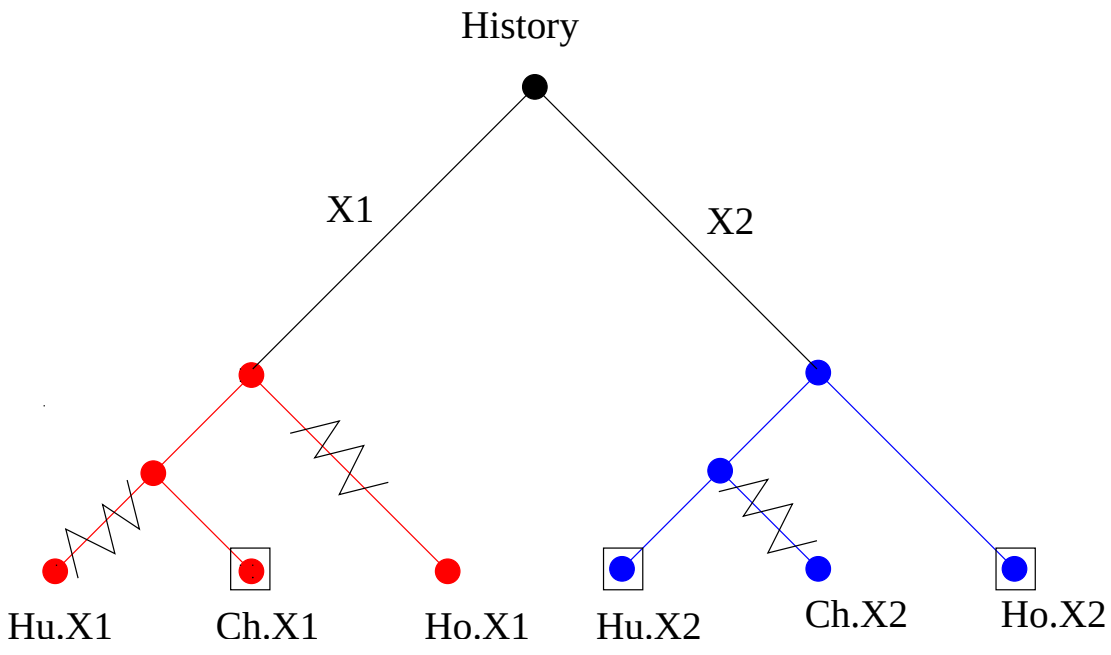
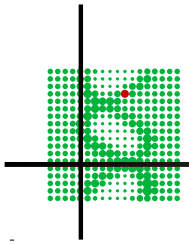
CPM 2006, Barcelona

Gene trees, species trees and gene duplications





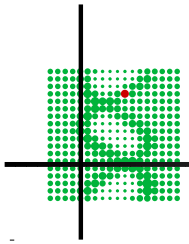


Gene trees, species trees and gene duplications

- Topology of gene trees and species trees are usually different.

- The evolutionary history of a gene family should be determined by:
  - **micro-evolutionary events** (sequence evolution)
  - **macro-evolutionary events** (gene duplication and loss)

- Tree Reconciliation Algorithm (Page 1994)



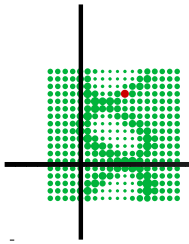
Durand et al. (RECOMB2005)

- A Hybrid Micro-Macroevolutionary Approach to Gene Tree Reconstruction

Two phase approach:
Phase 1: A gene tree based only on micro-evolutionary model is constructed.
Phase 2: Refining the tree w.r.t. a macroevolutionary model.

- regions with strong sequence support are left intact.
- other regions are rearranged w.r.t to the **D/L score**.

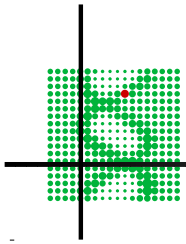
D/L score: $c_\lambda L + c_\delta D$, the weighted sum of the number of duplications, D, and the number of of losses, L, in the tree.



The Macro-Evolutionary Phylogeny Problem

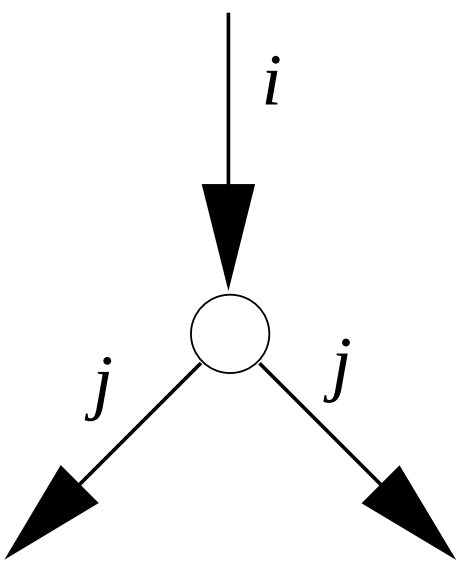
- **Input:** A rooted species tree, T_S with s leaves; a list of multiplicities $m_1, ..., m_s$, where m_l is the number of gene family members found in species l; weights c_λ and c_δ.

- **Output:** The set of all rooted gene trees $\{T_G\}$ with $\Sigma_{l=1}^{s} m_l$ leaves such that D/L Score of T_G is minimal.



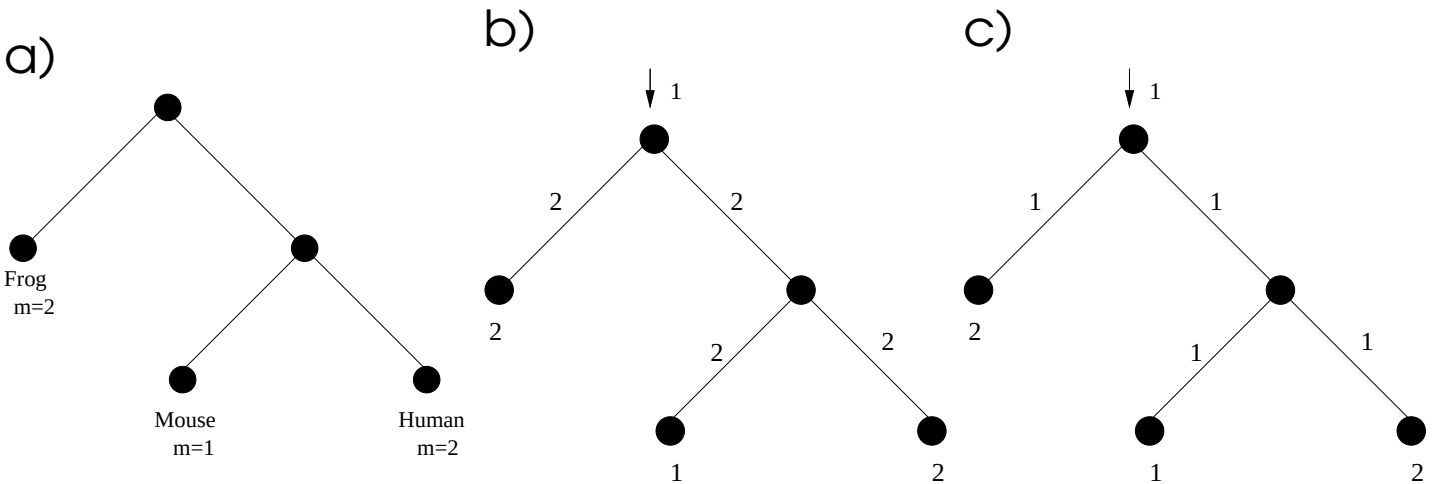
The Macro-Evolutionary Phylogeny Problem

- The output can be represented only by annotation of the species tree by the number of gene copies in different nodes.
- each duplication increases the number of gene copies by one.
- each loss decreases the number of the gene copies by one.
- the entering number of genes in root should be one.

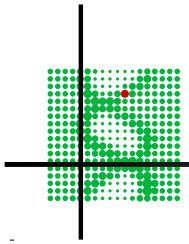


- if $i < j$ then $j - i$ duplications
- if $i = j$ then speciation
- if $i > j$ then $i - j$ losses

Minimal D/L score history



- a) species tree
- b) a history with one duplication and one loss
- c) a history with two duplications.



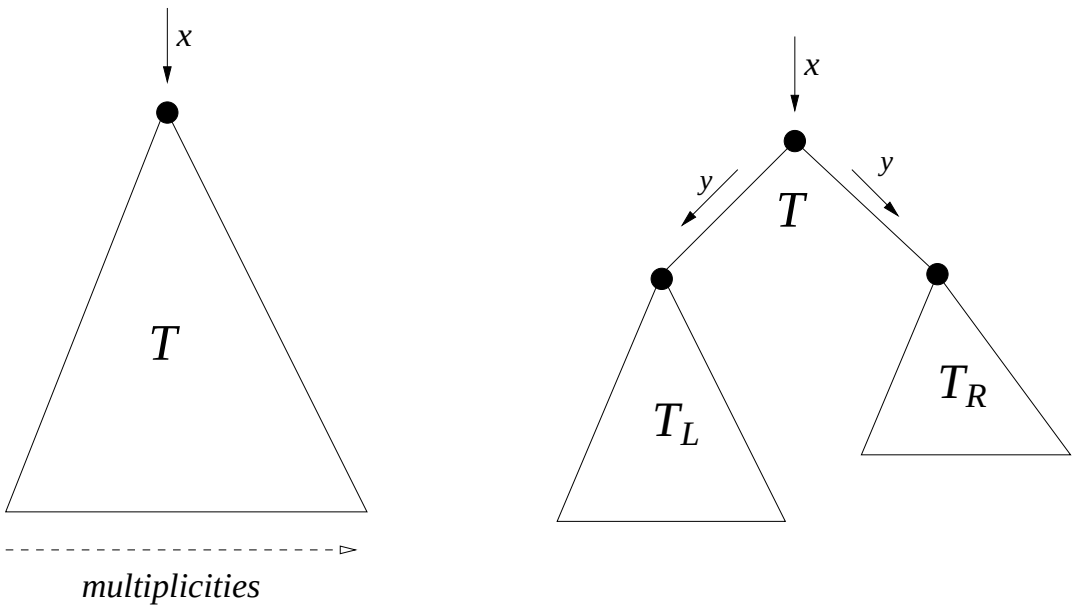
Past Work vs. Present Work

- Durand et al. (Recomb 2005)
  - Dynamic Programming for filling a table $COST[i, j, v]$
  - Finding the optimal solution using this table $COST$.

- This work
  - Dynamic Programming with a reduced dimension
  - Using combinatorial properties of optimal generation function $g(x, T)$.

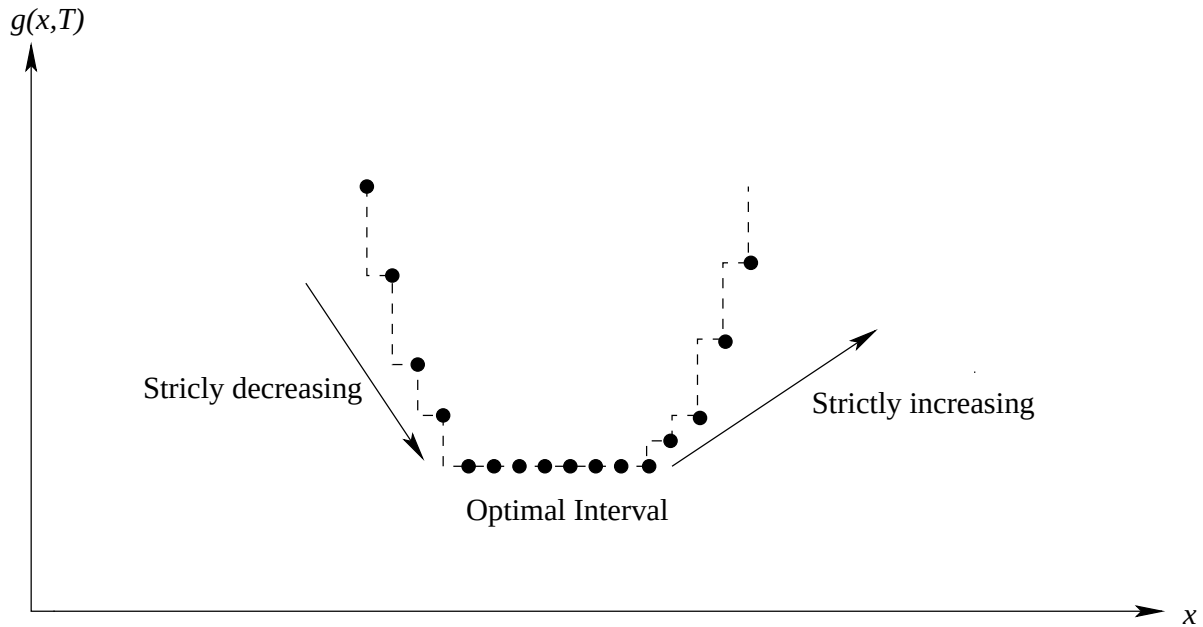
Definition of $g(x, \mathcal{T})$

- $g(x, \mathcal{T})$ the minimum D/L score of $\mathcal{T}$ where its root has x entering copies of genes.

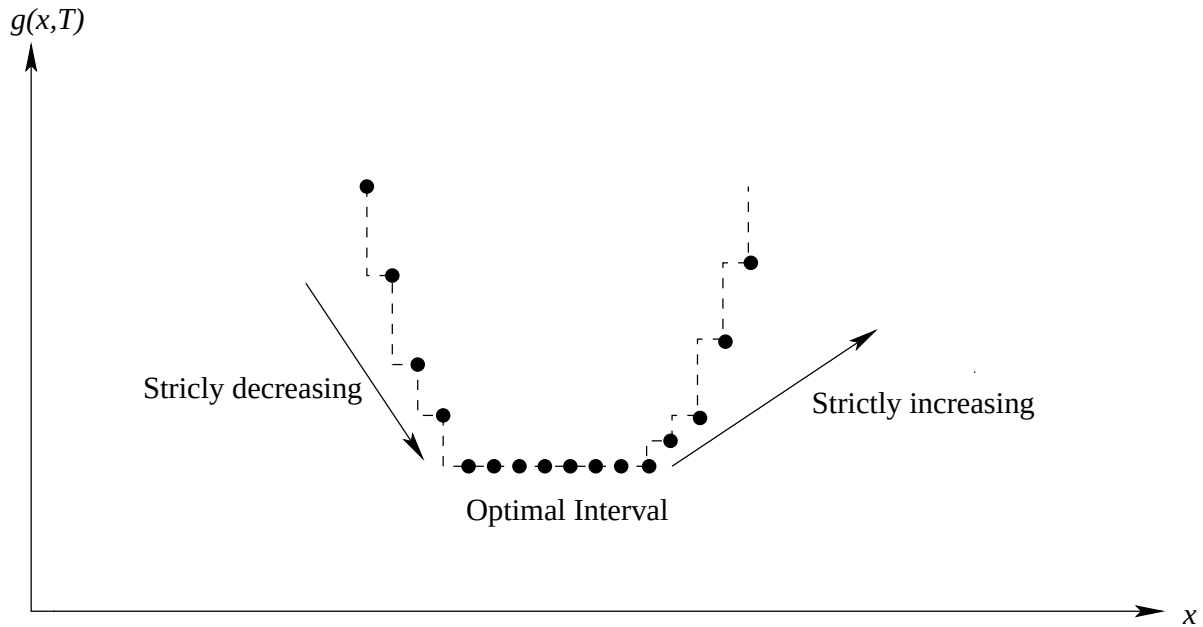


$$g(x, \mathcal{T}) = \min \begin{cases} g(x+1, \mathcal{T}) + c_\delta & \text{(Duplication)} \\ g(x-1, \mathcal{T}) + c_\lambda & \text{(Loss)} \\ g(x, \mathcal{T}_L) + g(x, \mathcal{T}_R) & \text{(Speciation)} \end{cases}$$

General Structure of $g(x, \mathcal{T})$



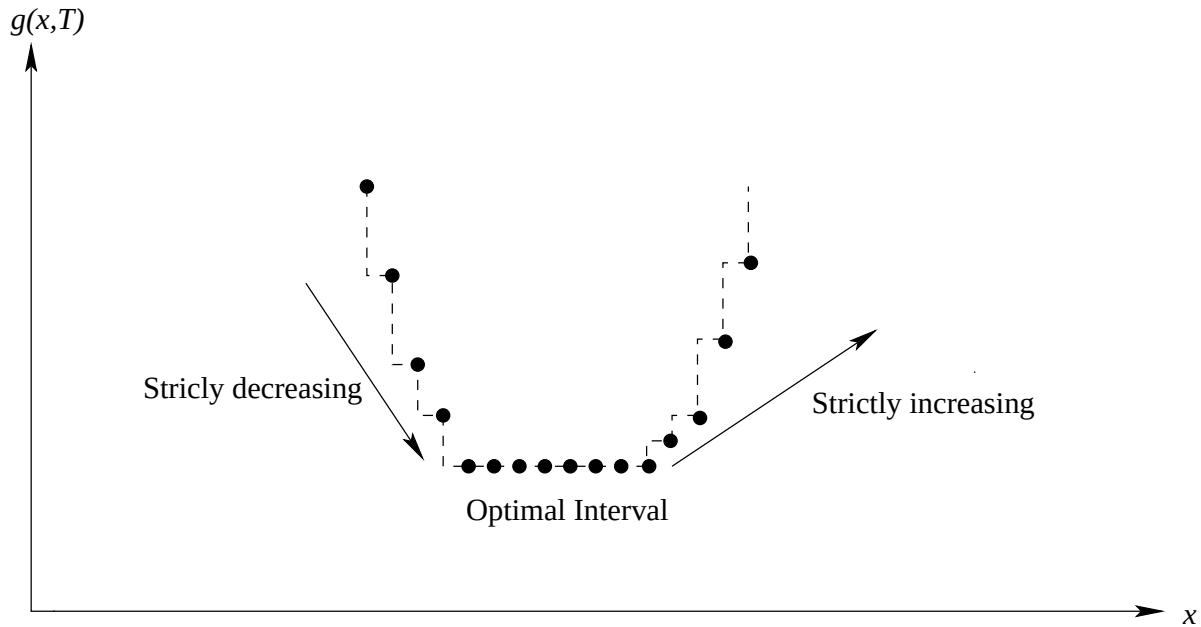
General Structure of $g(x, \mathcal{T})$



$g(x, T)$ in range $(-\infty, \infty)$:

- is firstly strictly decreasing,
- adapts its minimum on an interval,
- and then it is strictly increasing.

General Structure of $g(x, \mathcal{T})$

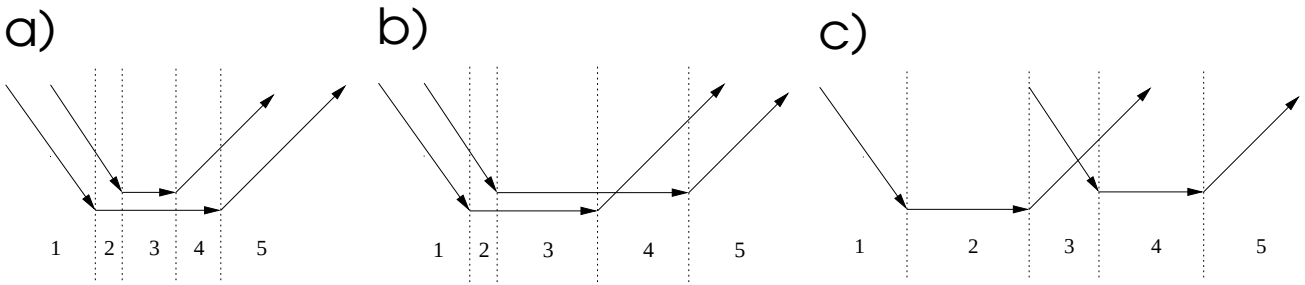


$g(x, T)$ in range $(-\infty, \infty)$:

- is firstly strictly decreasing,
- adapts its minimum on an interval,
- and then it is strictly increasing.

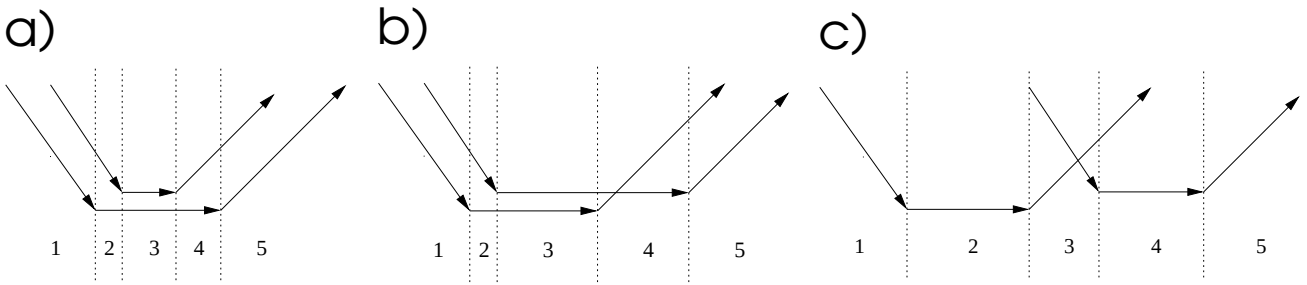
$g(x, T)$ is convex; $\Delta g(x, T) = g(x, T) - g(x-1, T)$ is increasing.
for very large x, $\Delta g(x, T) = c_\lambda$ and for very small x and $\Delta g(x, T) = -c_\delta$.

Possible Configurations of $g(x, \mathcal{T}_L)$ and $g(x, \mathcal{T}_R)$

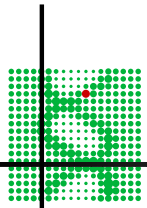


- a) Interval 3 is the optimal interval of $g(x, \mathcal{T})$.
- b) Interval 3 is the optimal interval of $g(x, \mathcal{T})$.
- c) The optimal interval of $g(x, \mathcal{T})$ is included in 3.

Possible Configurations of $g(x, \mathcal{T}_L)$ and $g(x, \mathcal{T}_R)$



- In interval (2,3,4), $g(x, \mathcal{T}) = g(x, \mathcal{T}_L) + g(x, \mathcal{T}_R)$.
- In interval (1), $g(x, \mathcal{T}) = \min\{g(x, \mathcal{T}_L) + g(x, \mathcal{T}_R), g(x+1, \mathcal{T}) + c_\delta\}$
- In interval (5), $g(x, \mathcal{T}) = \min\{g(x, \mathcal{T}_L) + g(x, \mathcal{T}_R), g(x-1, \mathcal{T}) + c_\lambda\}$



Algorithm

Gencost(Tree T)

1. **if** T *is a leaf* **then**

  1.1 **for** $i \leftarrow 1$ **to** m **do**

    1.1.1 **if** $i \geq label(T)$ **then** $g[i,T] \leftarrow (i - label(T)) \times c_\lambda$

    1.1.2 **if** $i < label(T)$ **then** $g[i,T] \leftarrow (label(T) - i) \times c_\delta$

  1.2 **exit**

2. *GenCost(T_L); GenCost(T_R);*

3. $[l_1, l_2] \leftarrow OPT(T_L)$; $[r_1, r_2] \leftarrow OPT(T_R)$

4. $t_1 \leftarrow \min\{l_1, r_1\}$; $t_2 \leftarrow \min\{l_2, r_2\}$

5. **for** $i \leftarrow t_1$ **to** t_2 **do** $g[i,T] \leftarrow g[i,T_L] + g[i,T_R]$

6. **for** $i \leftarrow t_2 + 1$ **to** m **do** $g[i,T] \leftarrow \min\{g[i-1,T] + c_\lambda, g[i,T_L] + g[i,T_R]\}$

7. **for** $i \leftarrow t_1 - 1$ **downto** 1 **do** $g[i,T] \leftarrow \min\{g[i+1,T] + c_\delta, g[i,T_L] + g[i,T_R]\}$

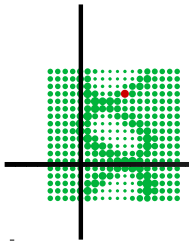


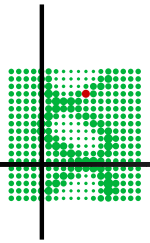
Table of Time Complexities

	One optimal answer	k optimal answer
Durand et al. 2005	$O(nm^2)$	$O(nm^2 + nmk)$
This work	$O(nm)$	$O(nm + nk)$
This work (unit costs)	$O(n)$	$O(nk)$

n the size of the species tree.

m the maximum number of gene copies in a species.

$-c_\delta \leq \Delta g(x, T) \leq c_\lambda$, so m can be replaced by $\min\{m, c_\delta + c_\lambda\}$



Summary and Future Work

- We proposed an algorithm running $O(m)$ times faster than the previous algorithm. In some gene families like kinases m can be a large number (several hundreds).

- We are currently working on including horizontal gene transfers into the model. should be considered in the macro-evolutionary problem.

ET CE SOIR ..... **ALLEZ LES BLEUS**