GRAPPA

A High-Performance Computational Tool For Phylogeny Reconstruction From Gene-Order Data

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Collaborators and Sponsors

In collaboration with

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Overview

- Gene-Order Data
- Difficulties in Using Gene-Order Data
- Breakpoint Analysis
- GRAPPA: Breakpoint and Inversion Analyses
- Speed!
- Capabilities and Extensions

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Phylogenies from Gene Orders

Distances are hard to compute!

Inversion distances can be computed in linear time (Bader/Moret/Yan), but others can only be approximated.

Models are primitive!

The Nadeau-Taylor model is the most basic possible. No formal ML approach has been suggested.

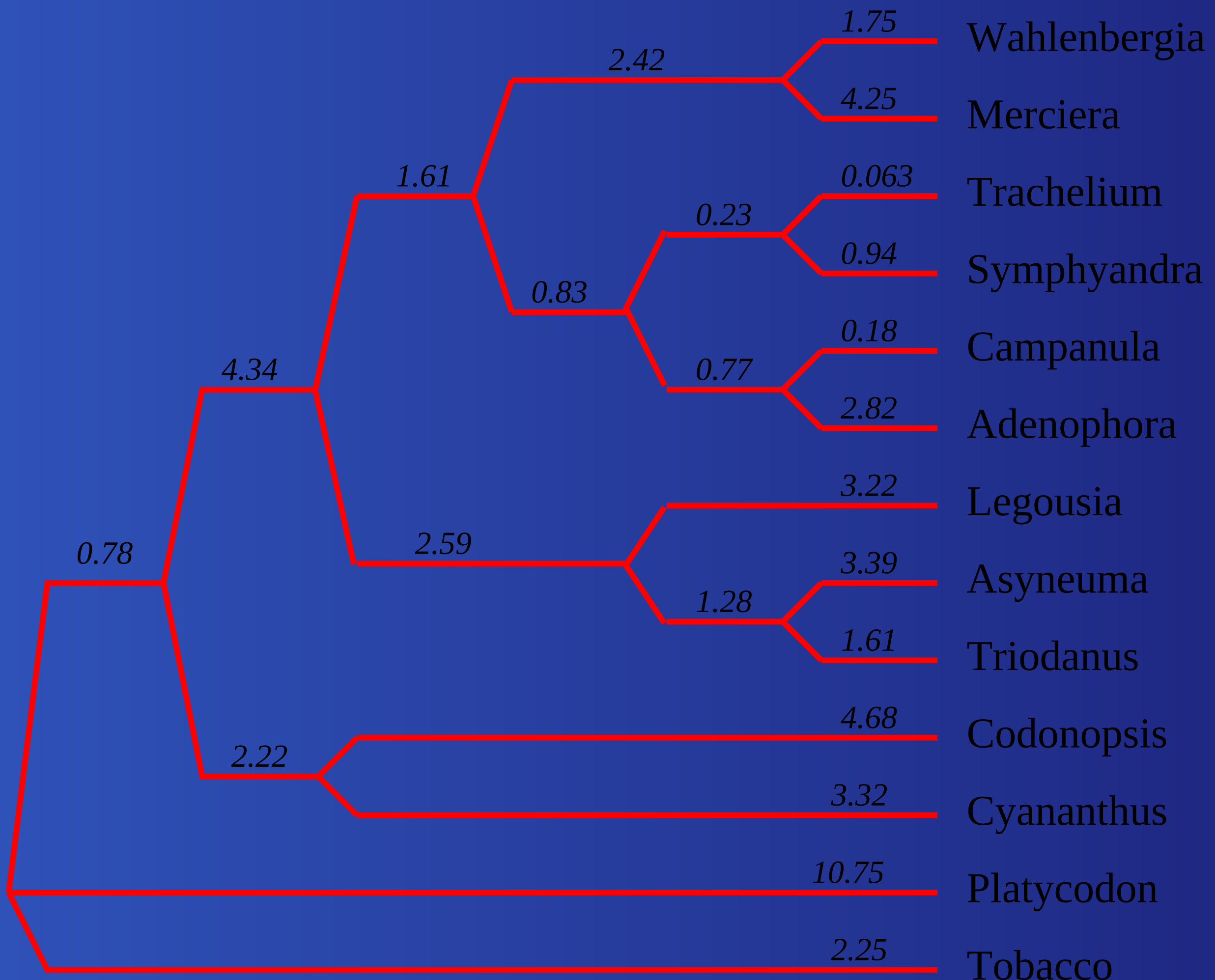
An Example: the Bluebell Family

Robert Jansen's group at UT Austin provided full gene sequences for the chloroplasts of 12 species of Campanulaceae (Bluebells), plus tobacco.

These chloroplasts have a single circular chromosome with about 120 genes.

Target: reconstruct the most parsimonious phylogeny. i.e., the tree that minimizes the total evolutionary distance.

12 Species of *Campanulaceae*



The Bluebell Family (cont'd)

We reimplemented a tool due to D. Sankoff and M. Blanchette using algorithm engineering.

Results: *a speed-up by* **three to four orders of magnitude** *in the serial part of the code and a total speed-up by over* **one million** *when run on the 512-processor* Los Lobos *supercluster at UNM.*

Reasons: *cache-awareness, detailed code optimization, better combinatorial optimization, better bounding, and parallelization.*

Breakpoint Analysis: An Overview

An iterative improvement procedure:

```
Initially label all internal nodes with gene orders
Repeat
    For each internal node $v$, with neighbors $A$, $B$, and $C$, do
        Solve the *MPB* on $A, B, C$ to yield label $m$
        If relabelling $v$ with $m$ improves the score of $T$, then do it
until no internal node can be relabelled
```

MPB: Median Problem for Breakpoint

Given 3 gene orders, represented as 3 signed permutations π_1, π_2, *and* π_3, *find a 4th permutation* π_m *that minimizes the sum of the distances*

$$d(\pi_1, \pi_m) + d(\pi_1, \pi_m) + d(\pi_1, \pi_m)$$

where each distance is the number of breakpoints, *i.e., the number of adjacencies present in one permutation but not in the other.*

We can similarly define the Median Problem for Inversions *or other distance measures.*

MPB: an example

Let the (circular) permutations be

```
1  -2   4   3
1   2  -3  -4
2  -3  -4  -1
```

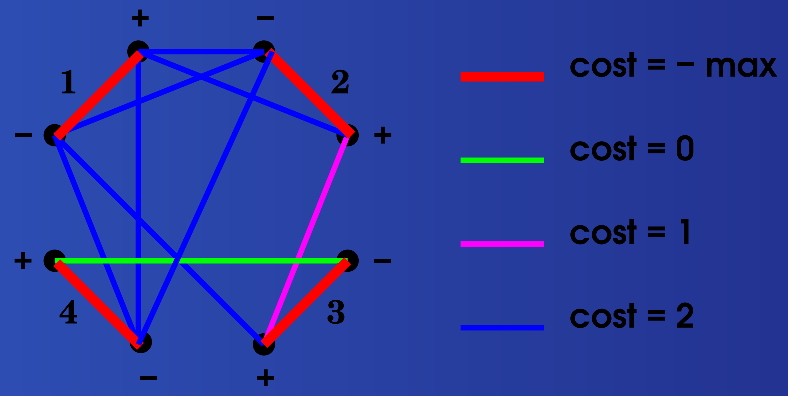
A possible median is -1 2 -3 -4, with cost 5

```
d( ( 1  -2   4   3 ) , ( -1  2  -3  -4 ) ) = 3
d( ( 1   2  -3  -4 ) , ( -1  2  -3  -4 ) ) = 2
d( ( 2  -3  -4  -1 ) , ( -1  2  -3  -4 ) ) = 0
```

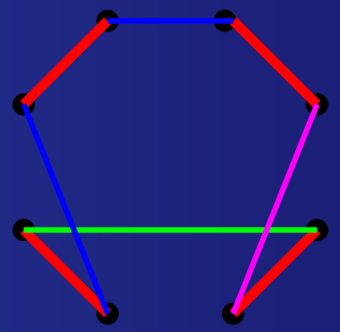
MPB (cont'd)

Sankoff showed to to convert this problem to the Travelling Salesperson Problem.

+1 −2 +4 +3
+1 +2 −3 −4
+2 −3 −4 −1



edges not shown have cost = 3



an optimal solution corresponding to genome +1 +2 −3 −4

Adjacency A B becomes an edge from A to −B

The cost of an edge A −B is the number of genomes that do NOT have the adjacency A B

High-Performance Algo. Engineering

Running time and quality of solutions as the paramount goal.

Includes parallelism (both shared-memory and message-passing), but most impact comes from refining the serial part of the code.

Cache-aware programming is a key to performance with high-performance machines, which have deep memory hierarchies.

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- Speedup on Los Lobos is over 100,000,000!

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- Already parallelized to run under MPI

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- Includes EDE distance correction
- Computes greedy insertion trees under perfect elimination ordering (often better than NJ trees)

Extensions

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- Stronger upper bounds to enable a true branch-and-bound exploration
- More efficient and completely general median solver

Conclusions

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- GRAPPA has confirmed that gene orders have a significant phylogenetic signal (Campanulaceae, other datasets).
- GRAPPA is parsimony-based, which may not be the best criterion (even with distance corrections such as EDE) when distantly-related species are included.