Clustering Genes into Topological Classes

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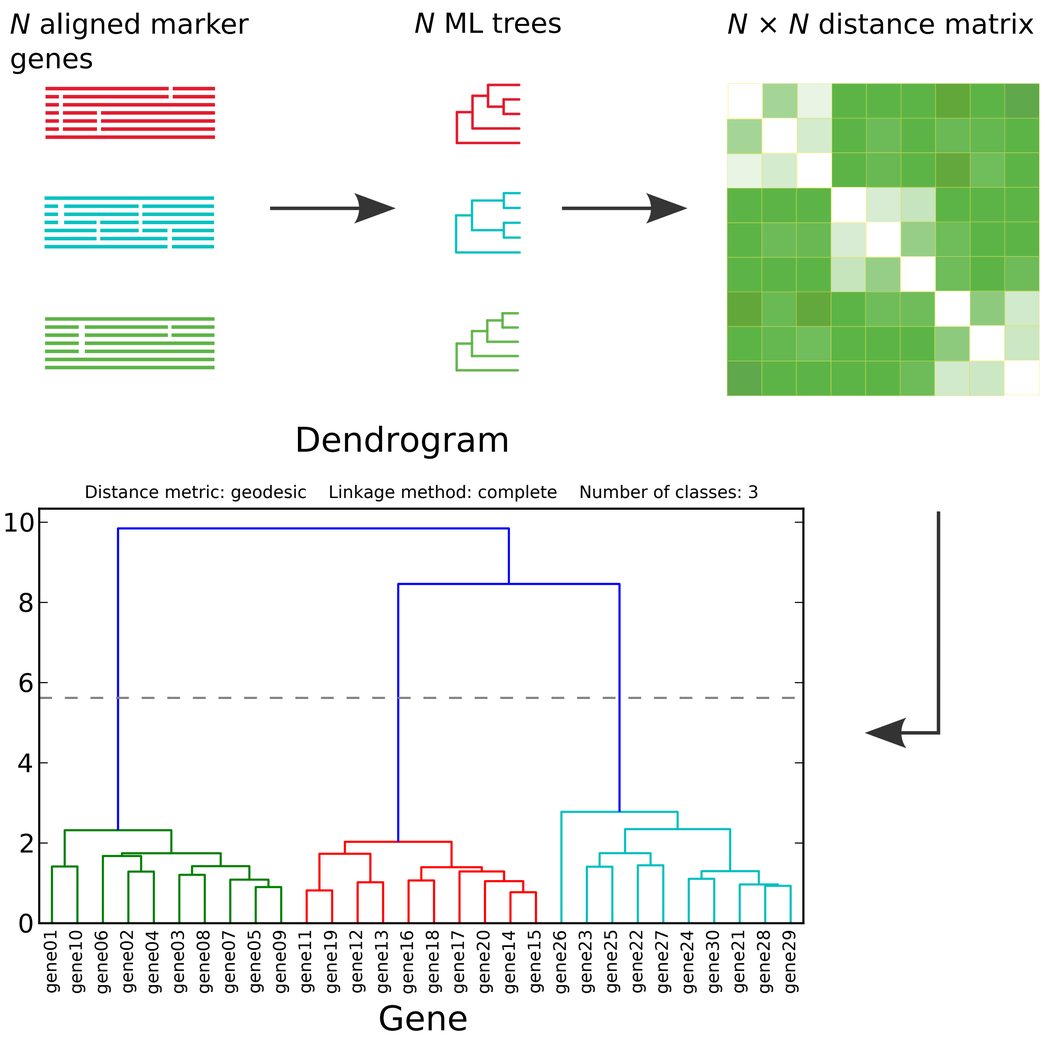
Outline:

To uncover evolutionary relationships between species, we can no longer assume that all genetic loci in a genomic dataset support the same underlying tree topology. Effects such as incomplete lineage sorting, introgression and horizontal transfer can cause incongruence to occur between gene trees. Here, we explore ways to identify multiple topologies present in the data by clustering trees reconstructed from individual loci into classes with common underlying topologies.

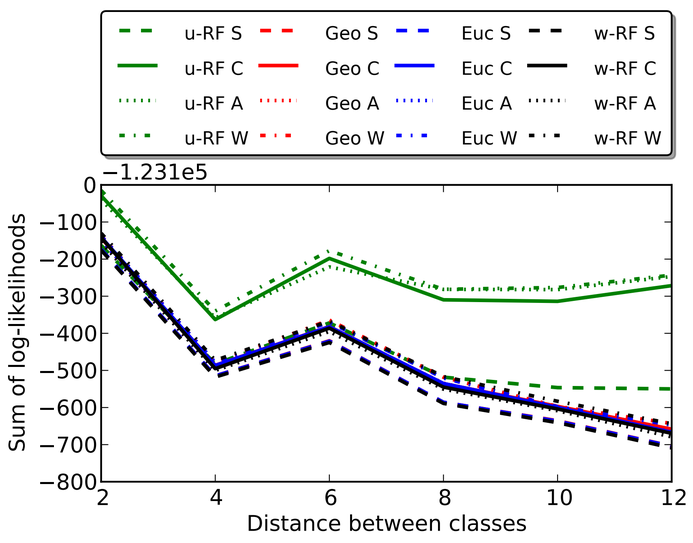
Methods:

Our method uses the distances between the genes' inferred trees as a basis for hierarchical clustering.
For each alignment the tree is inferred by maximum likelihood using PhyML. Distances between the trees are estimated according to one of a choice of commonly used tree distance metrics: the weighted and unweighted Robinson-Foulds distances (Robinson and Foulds, 1979, Robinson and Foulds, 1981), Felsenstein's Branch Length distance (Kuhner and Felsenstein, 1994), and the Geodesic distance (Billera, Holmes and Vogtmann, 2001). The resulting distance matrix is used as input to hierarchical clustering based on one of Single-linkage, Complete-linkage, UPGMA, and Ward's method.



Assessment of clustering performance

Using simulated data we assessed which combination of distance metric and clustering linkage method were best able to recover underlying class structure.

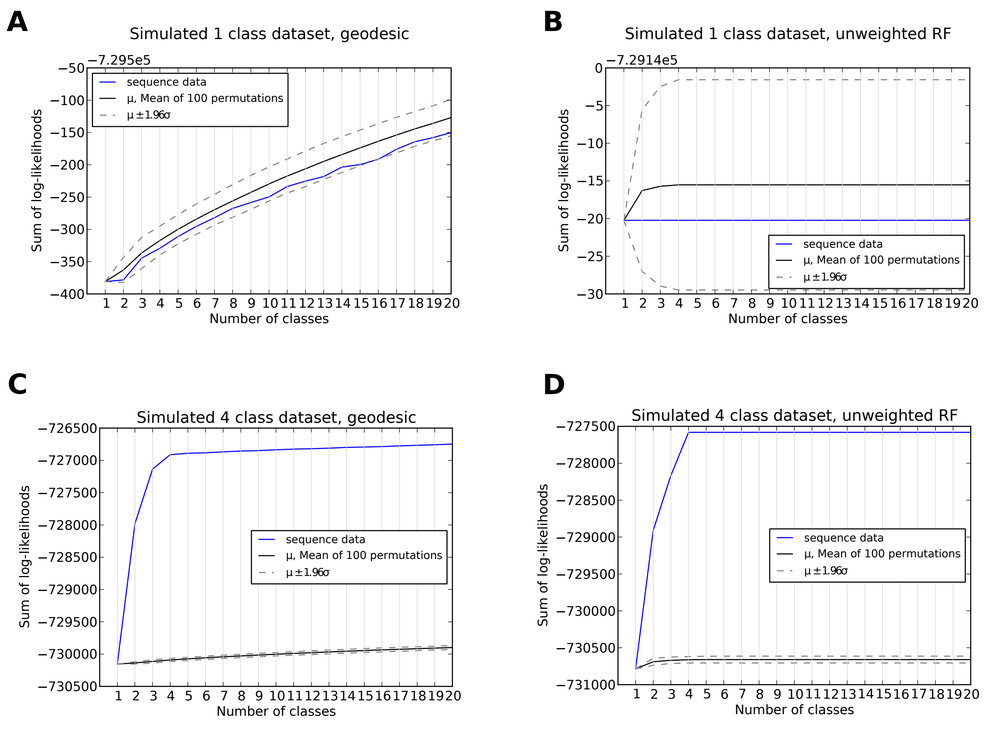


- Simulate 100 sets of 30 alignments from 3 trees; 3 topological classes of ten genes each.
- Cluster the alignments using all combinations of distance and linkage measures.
- Assess results by the sum of the likelihood scores for each class after tree inference with PhyML.
- Done 6 times for different distances between the underlying trees (unweighted RF distance), on the assumption that close trees represent a more difficult case.
- Distance metrics which use branch lengths outperform theunweighted RF distance, unless it is combined with single-linkage clustering, and single-linkage performs best overall.

Determining the number of classes

Simulated Data

We used a random permutation procedure to assess the number of classes present in a dataset. We simulated two datasets - 106 genes with 1 underlying topology, and 106 genes from 4 underlying topologies. For each dataset we also produced 100 randomly permuted copies; all the aligned columns from all the alignments were shuffled, and partitioned back into 106 alignments, to remove any class structure present in the dataset. We clustered the datasets and their permuted copies into 1 - 20 classes, and recorded their summed likelihood scores.

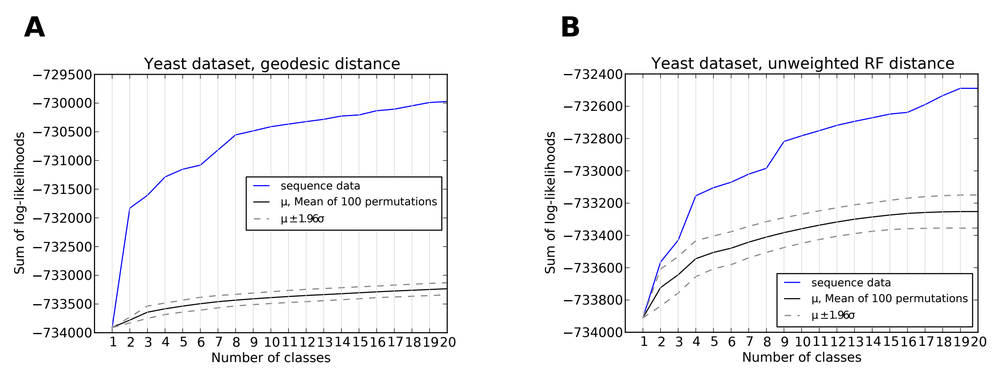


A: 1 underlying class, geodesic distance; B: 1 underlying class, unweighted RF distance; C: 4 underlying classes, geodesic distance; D: 4 underlying classes, unweighted RF distance.

When one class is present, the score of the unshuffled dataset lies within the distribution of the shuffled datasets.
When more than one class is present, the score of the unshuffled dataset is higher than the distribution of the shuffled datasets. For these simulated data, the curve levels off after the true number of classes is reached.

Real Data

We analysed a set of 106 genes from yeasts (Rokas et al., 2003) using this random permutation approach.



These data appear to show some class structure, but it is not clear from this approach how many classes should be chosen.
Future work will tackle the problem of choosing the number of classes using a Bayesian model-selection approach, and explore alternative clustering strategies.

References

Billera, Holmes and Vogtmann, 2001. "Geometry of the Space of Phylogenetic Trees." *Advances in Applied Mathematics* 27 (4) (November): 733-767.
Kuhner and Felsenstein, 1994. "A Simulation Comparison of Phylogeny Algorithms Under Equal and Unequal Evolutionary Rates." Molecular Biology and Evolution 11 (3) (May): 459-468.
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Rokas, Williams, King and Carroll, 2003. "Genome-Scale Approaches to Resolving Incongruence in Molecular Phylogenies." *Nature* 425 (6960): 798-804.