Algorithms for Genome Rearrangements

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Lecture 11 - Tools for Real Data Analysis using Genome Rearrangements

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Introduction

How do we apply models of rearrangement in real data?

1. Transform real DNA intro *gene families* to allow the application of rearrangement models.
2. With a suitable representation of all the genomes (permutations, for instance), apply rearrangement models.
   1. Pairwise distances and distance-based phylogeny (z.b., Neighbour Joining)
   2. Multiple Genome Rearrangement – Find trees that minimize the number of rearrangement events

Real Dataset

We will use 7 *Yersinia pestis* genomes. There are more than 200 strains of YP that have been sequenced:
`http://www.ncbi.nlm.nih.gov/genome/153`

- Yersinia pestis Antiqua
- Yersinia pestis CO92
- Yersinia pestis KIM 10
- Yersinia pestis Nepal516
- Yersinia pestis Pestoides F
- Yersinia pestis Z176003
- Yersinia pestis biovar Microtus str. 91001

Each strand has a link to the corresponding NCBI page, where the GenBank file can be downloaded.

Alignment and detection of syntenic regions

To find the conserved regions on each genome, we will use Mauve `http://gel.ahabs.wisc.edu/mauve/`

- Preprocess and generate .sslist files for each .gb (GenBank) input file:

  ```
  progressiveMauve --mums --output=mauve-output.xmfa *gb
  ```

- Align all genomes and generate a *permutation file*:

  ```
  mauveAligner --output=all.mauve
  --permutation-matrix-output=permutation.txt
  Yersinia_pestis_{Antiqua,CO92,KIM_10,Nepal516,Pestoides_F,Z176003,
  biovar_Microtus_str_91001}.Chr.{gb,gb.sslist}
  ```

The file `permutation.txt` contains one line for each genome, with a permutation from 0 to the number of blocks (79 in this case).

Rearrangement Scenarios and Distance Phylogeny

To calculate the pairwise distance between all genomes we will use UniMoG:
`http://bibiserv.techfak.uni-bielefeld.de/dcj/welcome.html`

To execute it: `java -jar UniMoG.jar &`

- Copy file with permutation and edit it, adjusting to UniMoG format (name of genomes, spacing, etc.)
- Run a DCJ scenario in UniMoG.
- Copy distance matrix in a file

The output contains example DCJ scenarios between all the genomes and also a distance matrix, in phylip format.

Distance Phylogeny

We will use SplitsTree `http://www.splitstree.org/`.

First, we need to convert the format from

```
7
Antiqua
CO92      25
KIM_10    24 17
Nepal     22 16 11
Pestoides 31 23 22 23
Z176003   24 9 18 17 24
Biovar    36 27 28 27 32 28
```

to

```
7
Antiqua 0 25 24 22 31 24 36
CO92 25 0 17 16 23 9 27
KIM_10 24 17 0 11 22 18 28
Nepal 22 16 11 0 23 17 27
Pestoides 31 23 22 23 0 24 32
Z176003 24 9 18 17 24 0 28
Biovar 36 27 28 27 32 28 0
```

Converting Distance matrix

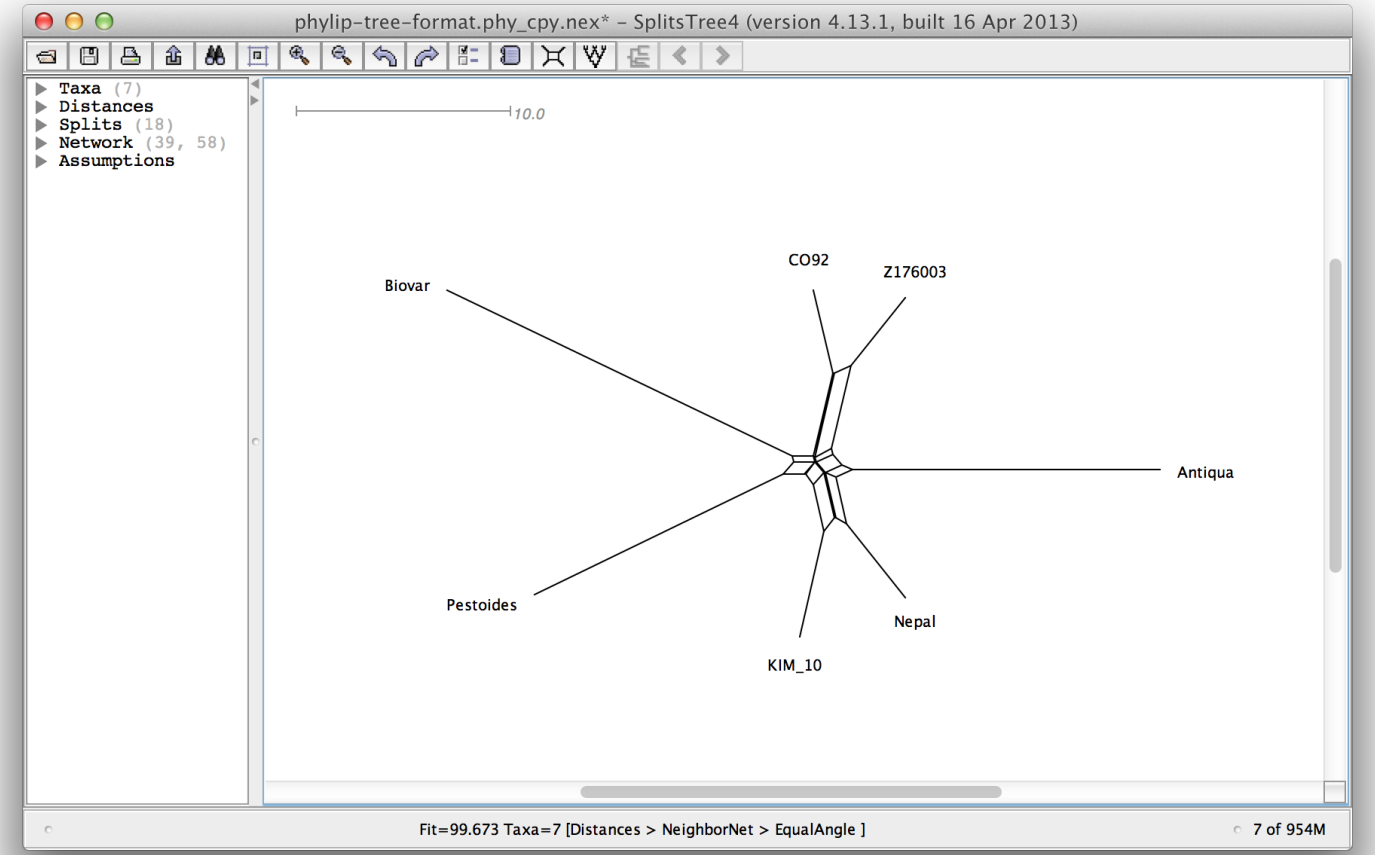
There are of course several ways of doing this. I did a R-script:

```
mat <- read.table("dcj-dist.phy",fill=TRUE,col.names=paste("V",1:8),skip=1,row.names=1)
mat[is.na(mat)] <- 0
mat <- mat + t(mat)
write.table(mat, file="dcj.phy",col.names=FALSE, quotes=FALSE)
```

Then add a first line with the number of genomes, in this example, 7.

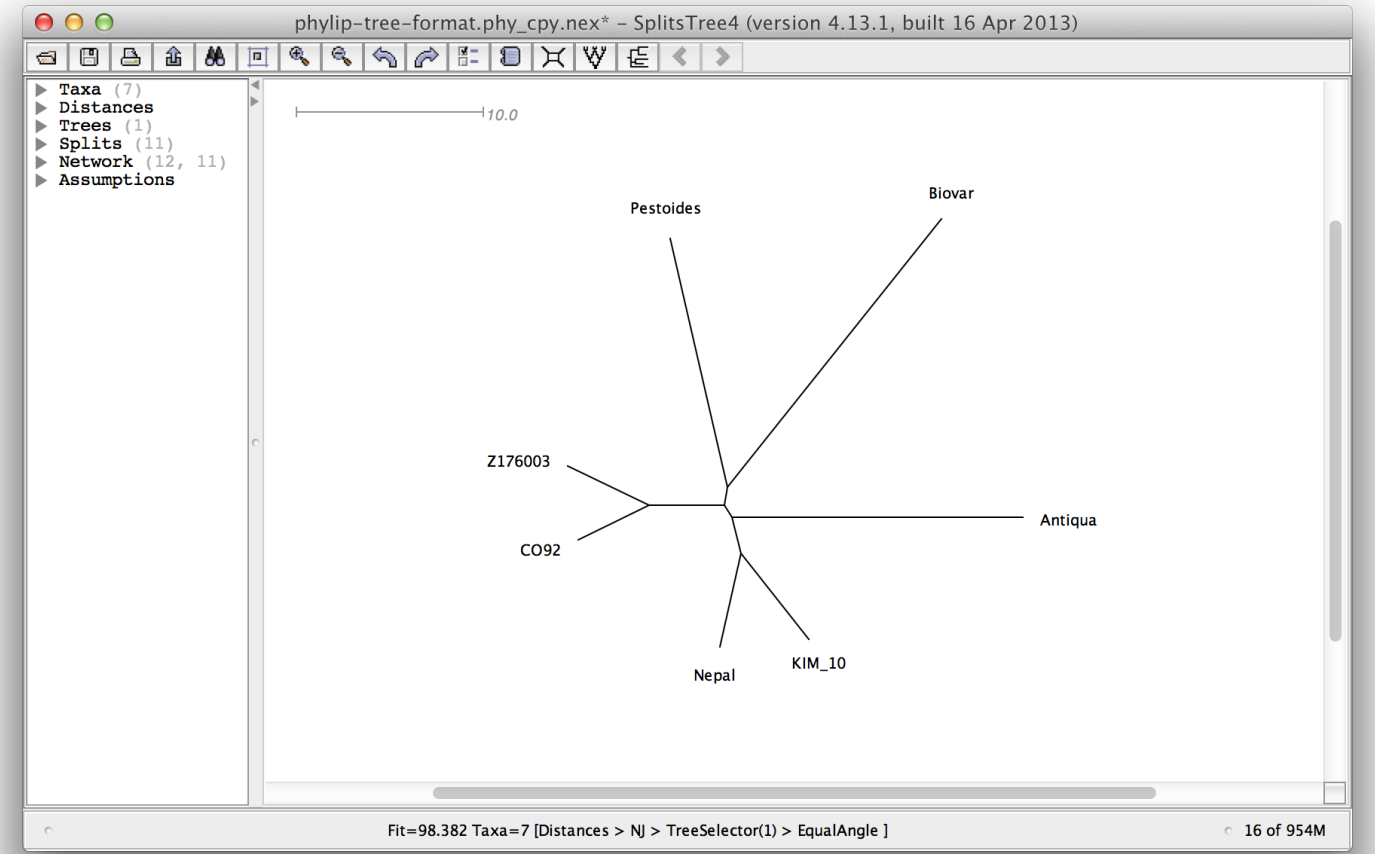
Phylogenetic Trees with SplitsTree

Opening the file `dcj.phy` in SplitsTree automatically generates a SplitTree representation:



Phylogenetic Trees with SplitsTree

In the menu `Trees/NJ` it is possible to find the Neighbour Joining tree:



Multiple Genome Rearrangement

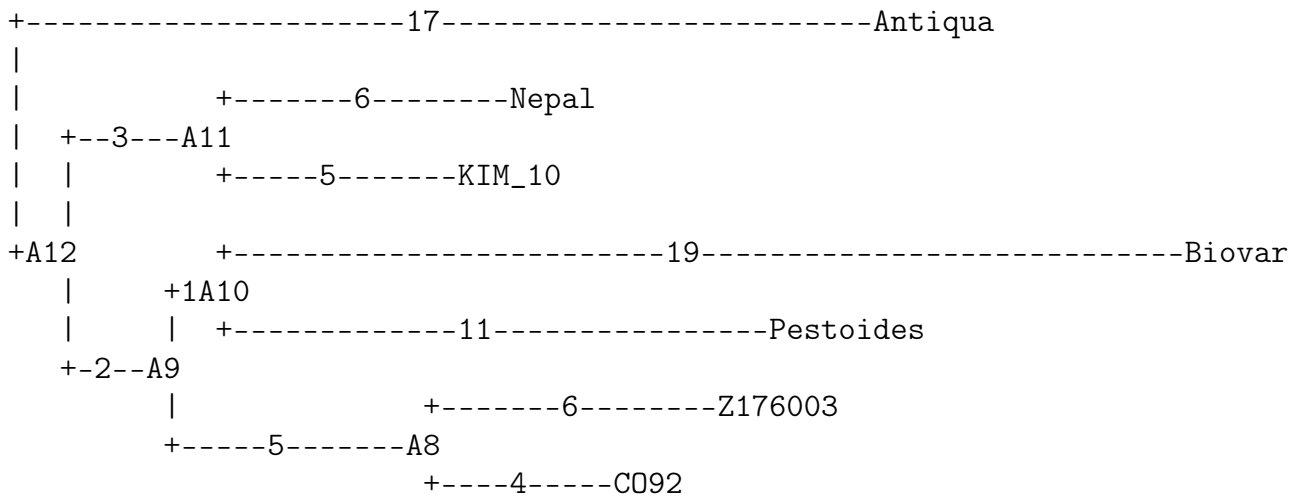
- Another way to find a phylogenetic tree with rearrangement data is to solve the *Multiple Genome Rearrangement* problem.
- Since it is a NP-Hard problem, we can only do it with a small dataset. In our case, 7 genomes with +- 50 genes is small enough.
- We will use a software called MGR (yes, not very creative) `http://grimm.ucsd.edu/MGR/`
- The input is the same as UniMoG, but the 0's have to be removed.

```
MGR -f permuttions.txt -C -H 1
```

The `-C` flag tells that the genomes are unichromosomal circular, and `-H 1` applies an heuristic for the Median problem, solving it much faster.

MGR Output

The output is the best tree found (not necessarily the optimal), with branch lenghts corresponding to the number of rearrangement events:



The output also contains the permutations of the internal nodes (A8, A9, ..., A12), giving a possibility for the gene arrangement for ancestral genomes.