ENDEAVOUR, an application to prioritize candidate disease genes.

Demonstration using the Usher syndrome.

Genome-wide experimental methods to identify disease / pathway genes (such as linkage analysis and association studies) often generate large list of candidate genes from which only a few are interesting. ENDEAVOUR (http://www.esat.kuleuven.be/endeavour) is able to prioritize such a list, i.e., to give a rank to each gene according to its similarity with the disease / pathway of interest.

The aim of this demonstration is to prove that ENDEAVOUR can efficiently prioritize a chromosomal region in which a disease causal gene is expected to lie. For that purpose, we will work with the Usher syndrome, a genetic disorder that involves both hearing impairment and retinitis pigmentosa.

Our application, ENDEAVOUR, ranks all the candidate genes according to their similarities with the genes already known to be involved in the disease. In order to mimic the discovery of a new gene involved in the Usher syndrome, we remove one gene from the list of known genes (the left-out gene) and use it as a candidate together with its neighborhood – the chromosomal band. The prioritization shows that this left-out gene is then ranked in the top of the candidate list.

More recently, a chromosomal region linked to the Usher syndrome has been reported. However, the causal gene has not been found yet. A standard prioritization shows that the top-ranking genes are indeed good candidates for further wet-lab validation.

To conclude, we present a general view of what the tool is for and how to do it by exploring many of the functionalities that the user-friendly interface provides and by using a real biological situation.

Overview of the demonstration:

Introduction (~3 min):
- What is gene prioritization?
- How does ENDEAVOUR work?
- Let us take a real biological situation.

On-line prioritization (~20 min):
- Starting the application.
- General description.
- Loading the training genes.
- Training the model.
- Loading the test genes.
- Scoring and results.
- Saving / Loading as XML.

Conclusion (~2 min).