TopControl: A Tool for Candidate Disease Gene Prioritization based on Topological Features

The TopControl tool utilizes several other tools such as TFmiR, MDS and MCDS. To run TopControl, the following steps need to be considered:

1. Derive the set of differentially expressed (DE) genes from a dataset that consists of rows related to genes and columns corresponding to samples across disease and normal conditions using one of the differential expression analysis methods.

2. Apply the TFmiR web server on the DE set to construct the full differential co-regulatory network. DE genes and miRNAs which interact with each other form the third layer of candidates. The set of miRNAs is added to the list of candidates based on the TFmiR strategy as explained in the paper.

3. Apply the ILP formulation of minimum dominating set (MDS) available at `https://github.com/maryamNazarieh/KeyRegulatoryGenes` on the full network to get the set of dominators.

4. Apply the ILP formulation or the heuristic program for determining minimum connected dominating set (MCDS) available at `http://apps.cytoscape.org/apps/mcds` on the LCC network to get the set of connected dominators.

5. Run the R code available at the following link to output the set of candidates at layer 4 and layer 5. Genes and miRNAs from the third layer form the fourth layer if they take part in one of the three sets, MDS, MCDS or hub set. The set of candidates in the fourth layer which are selected by all three methods such as MDS, MCDS, and hubs are selected in the fifth layer and sorted in descending order based on the log_2(fold changes) of expression between two conditions.

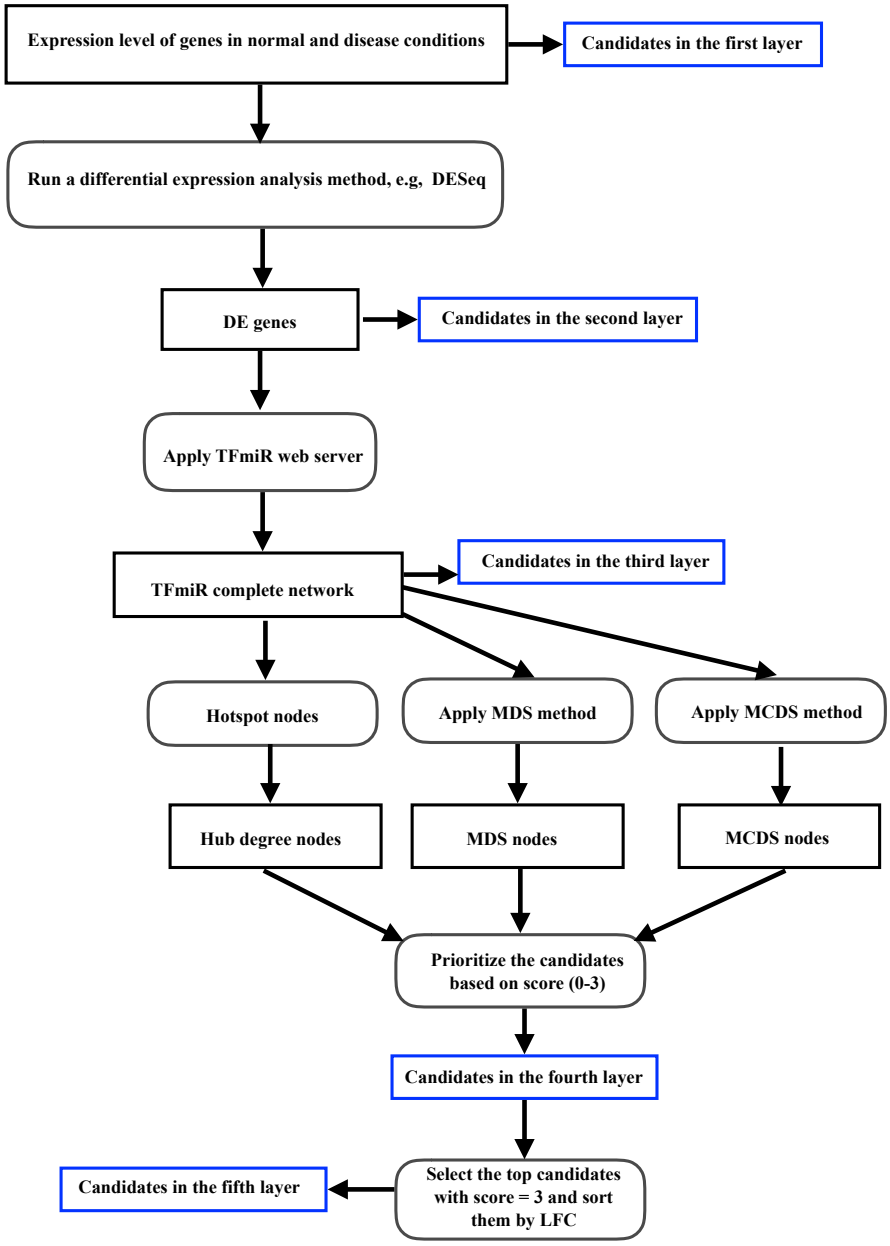

Figure 1: Dependency of TopControl on TFmiR, MDS and MCDS. TopControl integrates three sets of hubs, MDS and MCDS as candidates in the fourth layer. The set of genes and miRNAs that are selected by all the above-mentioned methods make up the candidates in the fifth layer.