**TREMEL Help**

**Search Box(es)**

The user can query TREMEL with either genes, transcription factors (TFs) or terms, or a combination of up to 3 entities of any type. The entity type can be selected from the drop down list to the right of each search box. Clicking the "+" button to the left of the first search box opens an additional search box. A maximum of 3 search boxes are allowed. The gene and TF queries need to be the official symbols designated by the National Center for Biotechnology Information (NCBI). Only one symbol is allowed per search box. The term query can be any single keyword. All queries are case insensitive. The output of the tool consists of two panels.

**Top Panel: 3-D interactive plot**

The top panel is comprised of a 3-dimensional interactive plot that shows all Annotated Transcriptional Modules (ATMs) containing the search box entities, as points. The axes of the plot correspond to the Non-negative Tensor Factorization (NTF) approximation rank *k*, the ATM #, and the rank of the queried entity (first search box only) in the ATMs. An ATM can be selected in the panel by clicking on its corresponding point in the 3-D plot. The color of the selected point changes to red and the colors of the remaining points corresponding to all other ATMs are depicted in terms of similarity to the selected ATM. The most similar ATMs are colored in shades of red while the least similar ones are colored in shades of blue. The similarity between any two ATMs is calculated as the Jaccard coefficient between the sets of genes and TFs in the respective ATMs. Upon initial search completion, one ATM is preselected and colored in red. This initial selection is performed in a manner such that the ATM with the lowest queried entity rank is picked. Ties are resolved in favor of the ATM with the lowest NTF approximation rank.

**Bottom Panel: ATM contents**

The bottom panel contains several sub-panels, each corresponding to an ATM point in the first panel. The top sub-panel corresponds to the selected ATM, and the remaining ATMs are ordered according to their similarity to the selected ATM. Each sub-panel displays the ranked genes, TFs and terms of the corresponding ATM, as well as the enriched GO categories and KEGG pathways. Clicking a sub-panel expands it to display its contents, and closes the previously open sub-panel. The contents of only one sub-panel are viewable at a time.

**Search:**

1. Select entity type from pulldown menu: Gene, TF, or Term.
2. Enter gene/TF symbol or any keyword.
3. Click 'TREMEL Search' to submit.
4. Click [+/-] to add additional search fields.

**Visualization:**

1. Click on any point in the plot to display the terms, genes and TFs included in that ATM along with the enriched GO categories and KEGG pathways.
2. The selected point is displayed in red. Other points are colored in shades of red and blue based on the similarity to the selected module.
3. Rotate the plot by left-clicking and dragging the mouse.
4. Customize the plot using right-click menu options.