
WEoN Documentation

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Apr 02, 2019

CONTENTS

1	Installation	3
2	Instructions to use WEoN	5
3	Indices and tables	9

WEoN (Weighted Epigenomic Network) is a [Cytoscape](#) app that incorporates a filtering method to determine specific gene regulatory networks. The method uses histone modifications through CHiP-on-chip seq, gene expression through RNA-seq, and chromatin accessibility through DNase-seq to filter out known and inferred regulations (like Transcription factors and regulatory RNAs) from a Gene Regulatory Network (GRN) considered as a gold standard (e.g. a GRN with all known connections, regardless development stage or cell type). The corresponding specific GRN consider weighted information that can be further analyzed to validate the network.

INSTALLATION

First, be aware that WEoN runs a PERL script that filter out regulations unlikely occurring from a gold standard GRN. Please follow the specific instructions for your platform [here](#). Also, the app backend is in transition to python, so please also follow intructions to get python3 [here](#).

There are two different ways to obtain WEoN:

1. **Download from the Figshare repository (Recommended).** WEoN can be downloaded from [Figshare repository](#) along with example data. Then, within Cytoscape, go to: Apps >> App Manager >> Install from File...

OR

2. **Download from the Github repository.** If you are familiar with git, the [Github repository](#) can be cloned and the respective jar file installed from within Cytoscape: Apps >> App Manager >> Install from File...

Additionally, please run `script.sh` or copy the PERL scripts to `/home/$USER/CytoscapeConfiguration/3/apps/installed` (*UNIX), while similar paths exist in MacOS and Windows OS. Please be aware you need a PERL interpreter to execute WEoN backend.

Note: Downloading from the Cytoscape App Store. We'll upload WEoN to the Cytoscape [App Store](#) soon, where it could be downloaded. However, example data could only be obtained from the Figshare repository due to size limitations.

Note: Need Help? If you run into any problems with installation, please leave an issue in the official [Github repository](#).

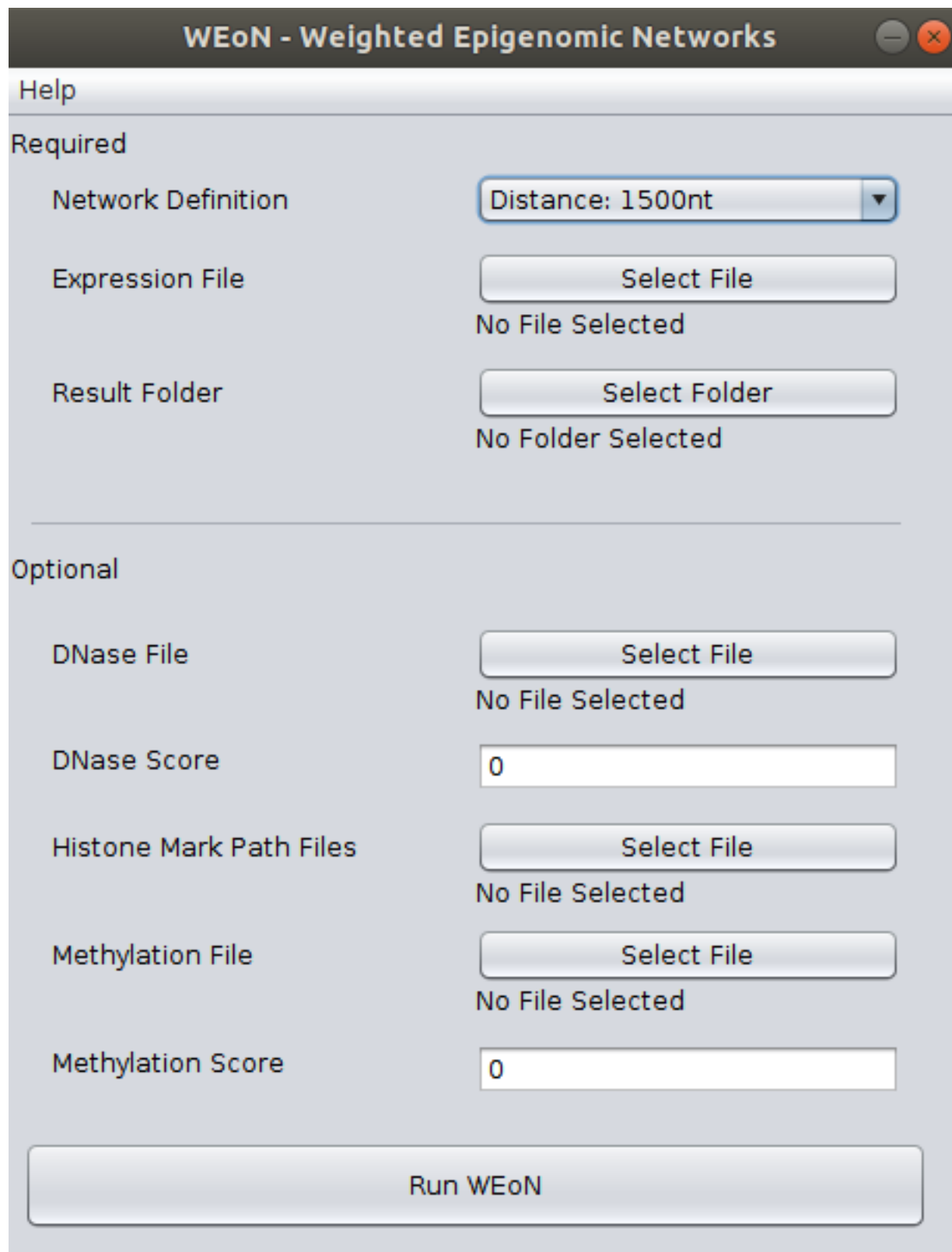
INSTRUCTIONS TO USE WEON

This document contains the principal instructions in order to use the Cytoscape app WEoN (Weighted Epigenetic Networks). To open WEoN, go to Cytoscape Apps menu, then click on WEoN to open it.

We currently applied the method to *Drosophila melanogaster* due to a specific epigenetic code referred to the experimentally determined impact of post- traslational modifications on histones.

1. Interface

The WEoN interface is a simple selector screen that serves as input screen for the backend PERL scripts, therefore parsing correctly the genomic data and calling orderly the scripts to filter out unlikely occurring regulations.



The image shows a software window titled "WEoN - Weighted Epigenomic Networks". It has a standard macOS-style title bar with minimize, maximize, and close buttons. The window is divided into two main sections: "Required" and "Optional".

Required Section:

- Network Definition:** A dropdown menu showing "Distance: 1500nt".
- Expression File:** A button labeled "Select File" with the text "No File Selected" below it.
- Result Folder:** A button labeled "Select Folder" with the text "No Folder Selected" below it.

Optional Section:

- DNase File:** A button labeled "Select File" with the text "No File Selected" below it.
- DNase Score:** A text input field containing the value "0".
- Histone Mark Path Files:** A button labeled "Select File" with the text "No File Selected" below it.
- Methylation File:** A button labeled "Select File" with the text "No File Selected" below it.
- Methylation Score:** A text input field containing the value "0".

At the bottom of the window is a large button labeled "Run WEoN".

2. Required data

WEoN use RNA-seq data to filter out absent transcription factors and miRNAs from the Gold Standard (or

Reference Network). We provide three Gold Standards, which were constructed within a different cutoff of 1500, 2000, and 5000 nucleotides from the Transcription Start Site.

Please select a two-column file separated by tabulations as an `Expression File`. The first column is the gene name while the second is the expression in any unit, like counts, RPKM, or FPKM. WEoN use an internal dictionary to match gene names from the Gold Standard and the Expression File. Data must be a single experiment or the average value of the experimental replica.

We provide `expression_test.tsv` as an example `Expression File`. Please click on the corresponding `Select File` button and navigated to the containing folder. Also, provide a path (with write permission) from the `Select Folder` button: click on and navigate.

Note: The resulting Gene Regulatory Network will be stored at the user selected path from the `Select Folder` button. Although, the GRN will be loaded automatically when WEoN finish the filtering processes, the user can reuse the GRN.

3. Optional data

`DNase file` and `Methylation file` are four-columns files separated by tabulations. Each column correspond, in order, to the chromosome where was mapped the sequence, the initial coordinate, the ending coordinate, and the score for the mapped feature. Both files has an associated `Score` block which the user can use a threshold value where all lower scores are dismissed. Default is zero, meaning all mapped features in the `DNase` and `Methylation` files will be used in the filtering process.

The `Histone Mark Path Files` allows the introduction of a single file that determine the absolute path to ChIP-seq experiments for each histone post- translational modification. The file is a four-column text as follow:

mark	state	annotation	location
H3K27me3	-	promoter	/absolute/path/to/example_data/
↪H3K27me3_0-4hr.bed			
H3K27ac	+	promoter	...
H3K36me2	+	promoter	...
H3K36me3	+	promoter	...
H3K4me1	+	promoter	...
H3K4me2	+	promoter	...
H3K4me3	+	promoter	...
H3K79me2	+	promoter	...
H3K9ac	+	promoter	...
H3K9me2	+	promoter	...
H3K9me3	+	promoter	...
H3S10ph	+	promoter	...
H4K16ac	+	promoter	...
H4K20me3	-	promoter	...

Note: We will improve the annotation of histone marks associating each mark to an experimentally validated effect on specific DNA sequences like promoters. For the current release of WEoN, the 3rd column don't interfere with the filtering process.

4. Execute filtering

Click on `Run WEoN`, wait, and load the time/tissue specific GRN into Cytoscape clicking on `Create View`.

Note: Feel free to contact directly through the [Github repository](#) or to Dr. Alberto Martin's e-mail.

INDICES AND TABLES

- `genindex`
- `modindex`
- `search`