Systems Biology Research Group

MetaScope User’s Guide

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***Getting Started***

***Introduction***

MetaScope is a powerful software tool which researchers can use in order to: ⌘ Visualize multiple genome‐scale datasets along with genomic annotations ⌘ Compare and analyze annotation‐anchored experimental data

⌘ Curate and integrate genome‐scale datasets

⌘ Build a new annotation with experimental data and canonical annotation such as transcription unit annotation

*Overview of MetaScope functionality*

General usage of MetaScope includes

⌘ Load genomic annotations

⌘ Load genome‐scale datasets including ChIP‐chip data, expression profiling data, and TSS (Transcription Start Site) data

⌘ Load processed datasets including predicted binding site from ChIP‐chip data, transcription detect signals from expression profiling, and processed TSS data ⌘ Compare and analyze genome‐scale experimental datasets with known genomic annotations

⌘ Curate and integrate processed datasets

⌘ Build a new annotation with processed datasets and/or canonical genomic annotations

*Unique features of MetaScope*

MetaScope supports integrative functions by which multiple genome‐scale datasets can be analyzed, compared and integrated. Those integrative functions include: ⌘ Track operation

④ Make average, difference, or sum

④ Merge features from biological replicates

④ Filter features by features on other track.

④ Adjust score values of features, or width of them

④ Assign ID to features in an orderly manner

⌘ Feature operation

④ Filter out features by score, or leave top features with or without sliding window ④ Merge features in feature level

④ Unite multiple features into one

④ Move or copy features into another track

④ Create, edit or delete features

⌘ Integration function

④ Integrate start and stop codon information with proteomic data to generate potential ORF (pORF) annotation

④ Integrate RNA polymerase (RNAP) ChIP‐chip binding information with transcript detection signals to generate RNAP‐guided transcription segment (RTS)

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④ Integrate RTS with transcription start site data and pORF data to generate transcription unit annotation.

In addition, MetaScope provides overlapping multiple data tracks, splitting one data window into two, workspace management by which user can store information about data files open, track setting, overlapping information and other configuration for each project.

***Documentation***

The most recent version of user’s guide can be found on the website below: http://gcrg.ucsd.edu/Downloads/MetaScope

If you have any question, please contact Donghyuk Kim (dok023@ucsd.edu).

***Document conventions***

A expression “A > B” when describing user interface means “click the first item A; this makes the next item B visible; then click B.”

Examples:

⌘ “File menu > Open Workspace” means “click the File menu first, and then choose Open Workspace.”

⌘ “Average tab > An existing file” means “click the Average tab and then click the An existing file combo box.”

Screen shots in this document were taken at the time this document was written, thus there might be small changes in positions or texts in the user interface, because MetaScope will be updated on a regular basis. MetaScope runs on .NET framework, however there also might be some differences on different versions of Windows operating system.

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***Installation***

***System requirements***

MetaScope runs on .NET framework 4.0 or higher, thus can run on any computer with .NET framework installed. Currently, .NET framework supports only Microsoft Windows operating system, thus MetaScope cannot run on Linux or Mac machines.

.NET framework is freely available on Microsoft website below:

http://www.microsoft.com/downloads/details.aspx?FamilyID=9cfb2d51‐5ff4‐4491‐ b0e5‐b386f32c0992&displaylang=en

Installation of .NET framework may require rebooting of your system once.

The recommended minimum hardware requirements are Pentium 1 GHz or higher with 512 MB RAM or more. However, if large amount of datasets will be loaded and visualized, then a system with Intel Core processor family or higher and 2 GB RAM or more is recommended.

MetaScope is implemented with WPF (Windows Presentation Foundation) graphical library. WPF renders user interfaces in Windows‐based application, and directly utilizes DirectX, rather than relying on the older GDI subsystem. Thus graphic card of the system also affects the overall visualization performance of Metascope.

***Typical installation***

In order to install MetaScope, visit the MetaScope site:

http://gcrg.ucsd.edu/Downloads/MetaScope

Download the “.zip” file containing following 4 files, and unzip those files, and place them whichever folder they need to be placed, as shown in Figure 1.

⌘ MetaScope.exe

⌘ AvalonDoc.dll

⌘ MetaScope.workspace

⌘ MetaScope.Layout.xml

“MetaScope.exe” is the main executable file of MetaScope application. “AvalonDoc.dll” is also a part of MetaScope software, and contains a library for user interface of MetaScope. “MetaScope.workspace” is a default workspace file, which only indicates default user interface layout file “MetaScope.Layout.xml”.

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***Getting familiar with MetaScope***

***Terminology***

*Genomes and chromosomes*

Genome and chromosome can slightly different meaning dependent on the context where they are used. In MetaScope a **chromosome** means any single piece of sequence and single continuous region of genomic positions where that sequence is located. Each chromosome should have the unique chromosome ID, and one example of chromosome ID is NCBI reference sequence ID which starts with “NC\_”.

A **genome** refers to any group of those chromosomes described above.

For example, the genome of *Escherichia coli* has only one chromosome, the NCBI reference sequence ID of which is NC\_000913.

(http://www.ncbi.nlm.nih.gov/nuccore/NC\_000913.2)

Another example is the genome of *Klebsiella pneumoniae* MGH 78578 has one main chromosome (NC\_009648) and 5 plasmids (NC\_009649, NC\_009650, NC\_009651, NC\_009652, NC\_009653) which are considered 5 difference chromosomes in MetaScope.

MetaScope recognizes and categorizes all datasets by chromosome ID given in the GFF files.

*Annotations*

Currently, MetaScope only support data files in GFF format, and does not distinguish experimental raw data, processed data or annotation if they share the same chromosome ID. Anyway, the definition of annotation, or rather genomic annotation, used here is the known or suspected locations of genomic features, such as genes, mRNAs, sRNAs, predicted coding regions, pseudogenes, promoter regions, transcription start sites, RNA polymerase binding regions and others.

*GFF (General feature format)*

According to the Wikipedia, the general feature format is a file format used for describing genes and other features of DNA, RNA and protein sequences. The filename extension associated with such file is “.GFF”, and currently there are two versions of the GFF file format in general use: GFF version 2 and GFF version 3.

The more information about GFF can be found in Wikipedia website, Sanger institute website and Sequence Ontology Project website below:

http://en.wikipedia.org/wiki/General\_feature\_format

http://www.sanger.ac.uk/resources/software/gff/spec.html

http://www.sequenceontology.org/gff3.shtml

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*Data track*

One chromosome tab can contain multiple **data tracks**, each of which corresponds to a set of data features that share the same data type. The data type represents the third column of GFF file. The more information about this column and the overall explanation of GFF file can be found at the websites listed in terminology section of this document.

*Data feature*

**Data feature** is an atomic data structure which are dealt and displayed in MetaScope, and it corresponds to each row in GFF file. Each data feature has 9 distinct fields: sequence ID, source, type, start, end, score, strand, phase, and attribute.

The detailed information and more precise definitions of them can be found at the websites about GFF file, but the brief explanation of them are:

⌘ Sequence ID: This ID means the chromosome ID.

⌘ Source: This field is intended to describe the algorithm or operating procedure that generated this feature.

⌘ Type: This field shows the type of the feature. It can be “gene” or “CDS” for protein coding region or anything else.

⌘ Start: This is the starting position of the data feature in the genome. ⌘ End: This is the ending position of the data feature in the genome. ⌘ Score: This field represents the score of the data feature, which can be used to

indicate the signal of the feature, or E‐value for sequence similarity feature. ⌘ Strand: This is the strand of the data feature: “+” for positive strand, “‐“ for minus strand, and “.” for features that are not stranded.

⌘ Phase: This is for “CDS” features, indicating where the feature begins with reference to the reading frame.

⌘ Attribute: This contains a list of feature attributes in the key‐value format of “tag=value”.

*Horizontal scroll bar*

**Horizontal scrollbar** is located on bottom of **chromosome tab**, and used for navigating across the genomic position.

*Vertical scroll bar*

**Vertical scrollbar** is located on the right side of **chromosome tab**, as shown in Figure 15. It is used for scrolling down or up chromosome tab, in order to shift the range of view over data tracks. When there are few data tracks in one **chromosome tab**, vertical scrollbar is hidden. However, as more data tracks are loaded and displayed in the **chromosome tab**, **vertical scrollbar** shows up automatically.

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**9**

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**Figure 46**

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**Figure 47. C**

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**9**

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**Figure 49. C**

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**9**

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**Figu**

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Figure 52.

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**9**

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**Figure 54**

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**9**

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**Figure 57.**

**Deleting da**

**ata features**

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**9**

This function can be used for processing and analyzing ChIP‐chip binding signals. The second track in Figure 57 shows unprocessed ChIP‐chip data and the third track displays calculated ChIP‐chip binding regions. Grey boxes in the third track represent calculated binding regions with lower P‐values. Thus user might want to remove those binding signals using this function, in order to more focus on more significant binding signals.

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**Figure 58.**

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**Figure 59.**

**Averaging**

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**Figure 61. D**

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**Figure 62. D**

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**Figure 63. S**

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**9**

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**Figure 66**

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**9**

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**Figure 67.**

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**9**

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**Figure 69.**

**RTS tab in**

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