

A tutorial for metaOmic

Contents

| | | |
|----------|-----------------------------------|----------|
| 1 | Introduction | 1 |
| 2 | Preliminaries | 2 |
| 2.1 | Citing MetaOmics | 2 |
| 2.2 | Installation | 2 |
| 2.3 | Question and bug report | 2 |
| 3 | Prepare data | 3 |
| 3.1 | Raw data | 3 |
| 3.2 | Clinical data | 3 |
| 4 | MetaOmics suit GUI | 4 |
| 4.1 | Setting | 4 |
| 4.2 | Preprocessing | 5 |
| 4.3 | Saved Data | 7 |
| 5 | Toolsets | 8 |
| 5.1 | MetaQC | 8 |
| 5.2 | MetaDE | 8 |
| 5.3 | MetaPath | 8 |
| 5.4 | MetaClust | 8 |
| 5.4.1 | About | 9 |
| 5.4.2 | Tune K | 9 |
| 5.5 | MetaPCA | 10 |
| 5.6 | MetaKTSP | 10 |
| 5.7 | MetaDCN | 10 |
| 5.8 | MetaLA | 10 |

1 Introduction

MetaOmics is a GUI for meta-analysis implemented using R shiny. Current version includes MetaQC for quality control, MetaDE for differential expression analysis, MetaPath for pathway enrichment analysis, MetaClust for sparse clustering analysis, MetaPCA for principal component analysis, MetaKTSP for

classification analysis, MetaDCN for differential co-expression network analysis, MetaLA for liquid association analysis.

In this tutorial, we will go through installation and usage step by step using a real example.

The metaOmics suit software is publicly available at <https://github.com/metaOmic/metaOmics>. Individual R packages are also available on GitHub and the url will be introduced in each individual package section.

2 Preliminaries

2.1 Citing MetaOmics

MetaOmics implements many meta-analytic methodology by their authors. Please cite appropriate papers when you use result from MeteOmics suit, by which the authors will receive professional credit for their work.

- MetaOmics suit itself can be cited as:
- MetaQC: Kang, D. D., Sibille, E., Kaminski, N., and Tseng, G. C. (2012). Metaqc: objective quality control and inclusion/exclusion criteria for genomic meta-analysis. *Nucleic acids research*, 40(2):e15–e15.
- MetaDE: **multiple?**
- MetaPath: Shen, K. and Tseng, G. C. (2010). Meta-analysis for pathway enrichment analysis when combining multiple genomic studies. *Bioinformatics*, 26(10):1316–1323.
- MetaClust: Huo, Z., Ding, Y., Liu, S., Oesterreich, S., and Tseng, G. (2016). Meta-analytic framework for sparse k-means to identify disease subtypes in multiple transcriptomic studies. *Journal of the American Statistical Association*, 111(513):27–42.
- MetaPCA: not published yet.
- MetaKTSP: not published yet.
- MetaDCN: not published yet.
- MetaLA: not published yet.

2.2 Installation

The full instruction of how to install, start are available at <https://github.com/metaOmic/metaOmics>. **Do we need to duplicate the description here?**

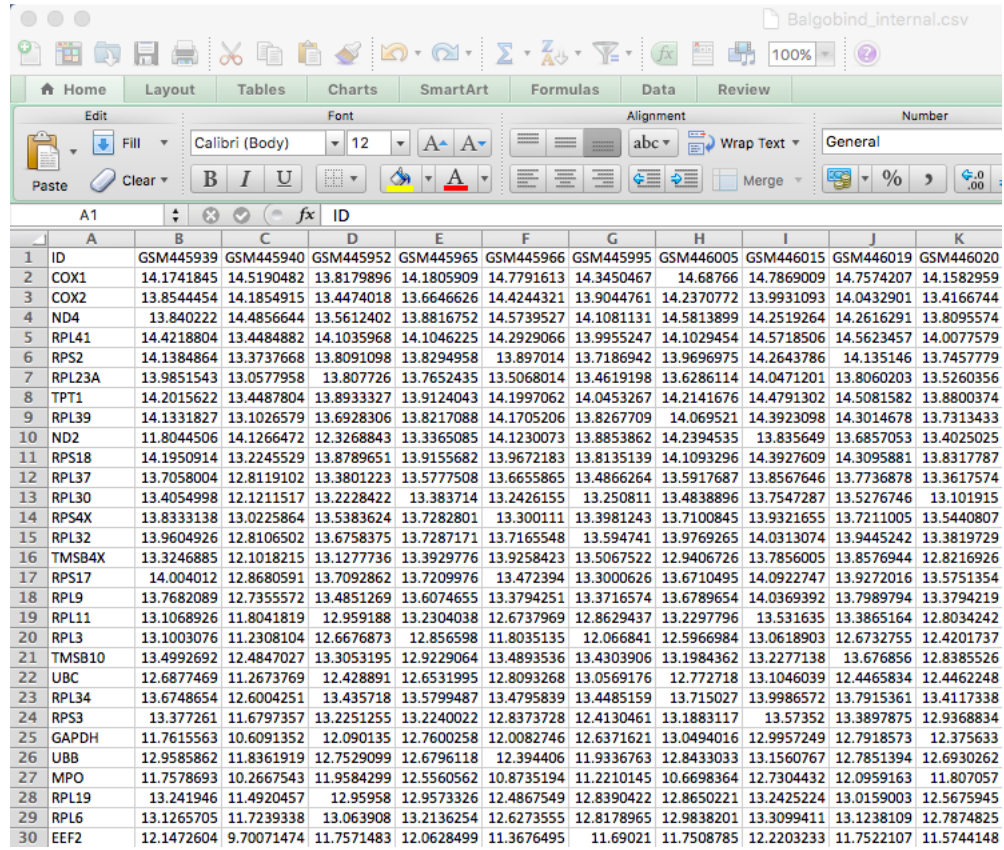
2.3 Question and bug report

Ask Anzhe what is the appropriate way to maintain the package?

3 Prepare data

3.1 Raw data

Data should be prepared as the example in Figure 1. First column should be feature ID (e.g. gene symbol) and the rest of the columns are samples. The first row is sample ID. Valid data type includes continuous, count.



| | A | B | C | D | E | F | G | H | I | J | K |
|----|--------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 1 | ID | GSM445939 | GSM445940 | GSM445952 | GSM445965 | GSM445966 | GSM445995 | GSM446005 | GSM446015 | GSM446019 | GSM446020 |
| 2 | COX1 | 14.1741845 | 14.5190482 | 13.8179896 | 14.1805909 | 14.7791613 | 14.3450467 | 14.68766 | 14.7869009 | 14.7574207 | 14.1582959 |
| 3 | COX2 | 13.8544454 | 14.1854915 | 13.4474018 | 13.6646626 | 14.4244321 | 13.9044761 | 14.2370772 | 13.9931093 | 14.0432901 | 13.4166744 |
| 4 | ND4 | 13.840222 | 14.4856644 | 13.5612402 | 13.8816752 | 14.5739527 | 14.1081131 | 14.5813899 | 14.2519264 | 14.2616291 | 13.8095574 |
| 5 | RPL41 | 14.4218804 | 13.4484882 | 14.1035968 | 14.1046225 | 14.2929066 | 13.9955247 | 14.1029454 | 14.5718506 | 14.5623457 | 14.0077579 |
| 6 | RPS2 | 14.1384864 | 13.3737668 | 13.8091098 | 13.8294958 | 13.897014 | 13.7186942 | 13.9696975 | 14.2643786 | 14.135146 | 13.7457779 |
| 7 | RPL23A | 13.9851543 | 13.0577958 | 13.807726 | 13.7652435 | 13.5068014 | 13.4619198 | 13.6286114 | 14.0471201 | 13.8060203 | 13.5260356 |
| 8 | TPT1 | 14.2015622 | 13.4487804 | 13.8933327 | 13.9124043 | 14.1997062 | 14.0453267 | 14.2141676 | 14.4791302 | 14.5081582 | 13.8800374 |
| 9 | RPL39 | 14.1331827 | 13.1026579 | 13.6928306 | 13.8217088 | 14.1705206 | 13.8267709 | 14.069521 | 14.3923098 | 14.3014678 | 13.7313433 |
| 10 | ND2 | 11.8044506 | 14.1266472 | 12.3268843 | 13.3365085 | 14.1230073 | 13.8853862 | 14.2394535 | 13.835649 | 13.6857053 | 13.4025025 |
| 11 | RPS18 | 14.1950914 | 13.2245529 | 13.8789651 | 13.9155682 | 13.9672183 | 13.8135139 | 14.1093296 | 14.3927609 | 14.3095881 | 13.8317787 |
| 12 | RPL37 | 13.7058004 | 12.8119102 | 13.3801223 | 13.5777508 | 13.6655865 | 13.4866264 | 13.5917687 | 13.8567646 | 13.7736878 | 13.3617574 |
| 13 | RPL30 | 13.4054998 | 12.1211517 | 13.2228422 | 13.383714 | 13.2426155 | 13.250811 | 13.4838896 | 13.7547287 | 13.5276746 | 13.101915 |
| 14 | RPS4X | 13.8333138 | 13.0225864 | 13.5383624 | 13.7282801 | 13.300111 | 13.3981243 | 13.7100845 | 13.9321655 | 13.7211005 | 13.5440807 |
| 15 | RPL32 | 13.9604926 | 12.8106502 | 13.6758375 | 13.7287171 | 13.7165548 | 13.594741 | 13.9769265 | 14.0313074 | 13.9445242 | 13.3819729 |
| 16 | TMSB4X | 13.3246885 | 12.1018215 | 13.1277736 | 13.3929776 | 13.9258423 | 13.5067522 | 12.9406726 | 13.7856005 | 13.8576944 | 12.8216926 |
| 17 | RPS17 | 14.004012 | 12.8680591 | 13.7092862 | 13.7209976 | 13.472394 | 13.3000626 | 13.6710495 | 14.0922747 | 13.9272016 | 13.5751354 |
| 18 | RPL9 | 13.7682089 | 12.7355572 | 13.4851269 | 13.6074655 | 13.3794251 | 13.3716574 | 13.6789654 | 14.0369392 | 13.7989794 | 13.3794219 |
| 19 | RPL11 | 13.1068926 | 11.8041819 | 12.959188 | 13.2304038 | 12.6737969 | 12.8629437 | 13.2297796 | 13.531635 | 13.3865164 | 12.8034242 |
| 20 | RPL3 | 13.1003076 | 11.2308104 | 12.6676873 | 12.856598 | 11.8035135 | 12.066841 | 12.5966984 | 13.0618903 | 12.6732755 | 12.4201737 |
| 21 | TMSB10 | 13.4992692 | 12.4847027 | 13.3053195 | 12.9229064 | 13.4893536 | 13.4303906 | 13.1984362 | 13.2277138 | 13.676856 | 12.8385526 |
| 22 | UBC | 12.6877469 | 11.2673769 | 12.428891 | 12.6531995 | 12.8093268 | 13.0569176 | 12.772718 | 13.1046039 | 12.4465834 | 12.4462248 |
| 23 | RPL34 | 13.6748654 | 12.6004251 | 13.435718 | 13.5799487 | 13.4795839 | 13.4485159 | 13.715027 | 13.9986572 | 13.7915361 | 13.4117338 |
| 24 | RPS3 | 13.377261 | 11.6797357 | 13.2251255 | 13.2240022 | 12.8373728 | 12.4130461 | 13.1883117 | 13.57352 | 13.3897875 | 12.9368834 |
| 25 | GAPDH | 11.7615563 | 10.6091352 | 12.090135 | 12.7600258 | 12.0082746 | 12.6371621 | 13.0494016 | 12.9957249 | 12.7918573 | 12.375633 |
| 26 | UBB | 12.9585862 | 11.8361919 | 12.7529099 | 12.6796118 | 12.394406 | 11.9336763 | 12.8433033 | 13.1560767 | 12.7851394 | 12.6930262 |
| 27 | MPO | 11.7578693 | 10.2667543 | 11.9584299 | 12.5560562 | 10.8735194 | 11.2210145 | 10.6698364 | 12.7304432 | 12.0959163 | 11.807057 |
| 28 | RPL19 | 13.241946 | 11.4920457 | 12.95958 | 12.9573326 | 12.4867549 | 12.8390422 | 12.8650221 | 13.2425224 | 13.0159003 | 12.5675945 |
| 29 | RPL6 | 13.1265705 | 11.7239338 | 13.063908 | 13.2136254 | 12.6273555 | 12.8178965 | 12.9838201 | 13.3099411 | 13.1238109 | 12.7874825 |
| 30 | EEF2 | 12.1472604 | 9.70071474 | 11.7571483 | 12.0628499 | 11.3676495 | 11.69021 | 11.7508785 | 12.2203233 | 11.7522107 | 11.5744148 |

Figure 1: A example data format

3.2 Clinical data

Clinical data should be prepared as the example in Figure 2. First column should be sample ID and each row represents a sample. The rest of the columns are clinical information.

| | A | B | C | D | E |
|----|-----------|----------|---|---|---|
| 1 | | label | | | |
| 2 | GSM445939 | inv(16) | | | |
| 3 | GSM445940 | inv(16) | | | |
| 4 | GSM445952 | inv(16) | | | |
| 5 | GSM445965 | inv(16) | | | |
| 6 | GSM445966 | inv(16) | | | |
| 7 | GSM445995 | inv(16) | | | |
| 8 | GSM446005 | inv(16) | | | |
| 9 | GSM446015 | inv(16) | | | |
| 10 | GSM446019 | inv(16) | | | |
| 11 | GSM446020 | inv(16) | | | |
| 12 | GSM446030 | inv(16) | | | |
| 13 | GSM446032 | inv(16) | | | |
| 14 | GSM446033 | inv(16) | | | |
| 15 | GSM446035 | inv(16) | | | |
| 16 | GSM446036 | inv(16) | | | |
| 17 | GSM446037 | inv(16) | | | |
| 18 | GSM446038 | inv(16) | | | |
| 19 | GSM446039 | inv(16) | | | |
| 20 | GSM446047 | inv(16) | | | |
| 21 | GSM446056 | inv(16) | | | |
| 22 | GSM446088 | inv(16) | | | |
| 23 | GSM446102 | inv(16) | | | |
| 24 | GSM446119 | inv(16) | | | |
| 25 | GSM446120 | inv(16) | | | |
| 26 | GSM446127 | inv(16) | | | |
| 27 | GSM446143 | inv(16) | | | |
| 28 | GSM446147 | inv(16) | | | |
| 29 | GSM445923 | t(15;17) | | | |
| 30 | GSM446023 | t(15;17) | | | |
| 31 | GSM446027 | t(15;17) | | | |

Figure 2: A example clinical data format

4 MetaOmics suit GUI

4.1 Setting

After starting metaOmics, the first page is the metaOmics setting page in Figure 3. There are 4 tabs on top of the page: Setting, Preprocessing, Saved Data and Toolsets. Below the 4 tabs, the first header is the session information. **Why do we need session information?** The second header is Directory for Saving Output Files. By clicking ..., user can set default working directory, in which all the meta-analysis results will be saved. User can view their current working directory on the top right corner. The third header is Toolsets, here users can view if individual packages are installed. If the packages are installed, there is a checked installed status. Otherwise, users can install individual package by clicking install blue button.

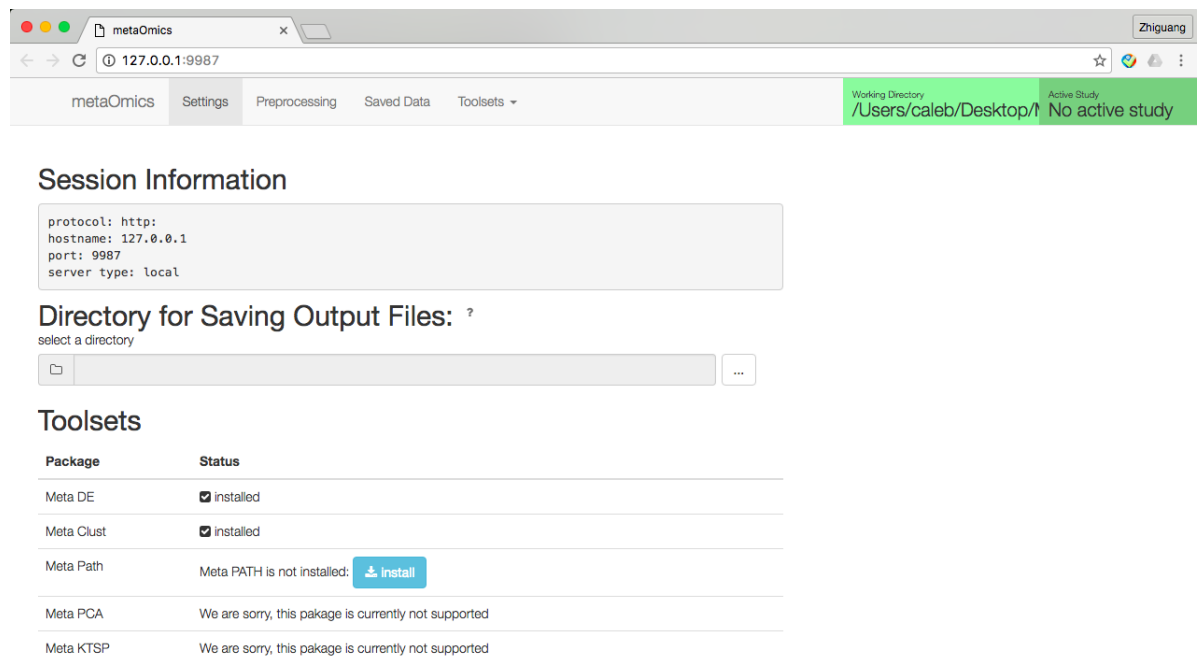


Figure 3: GUI setting page

4.2 Preprocessing

If users go to the Preprocessing page as Figure 4, they are able to upload genomic data via the tab “Choosing/Upload Expression Data”. The data should be prepared according to Section 3. Users may optionally upload Clinical Data, depending on purpose. [Check data requirement table?](#) After uploading is complete, users can preview their data on the right hand side of the page as Figure 5. There are several Expression Data Parsing Option available on the left panel.

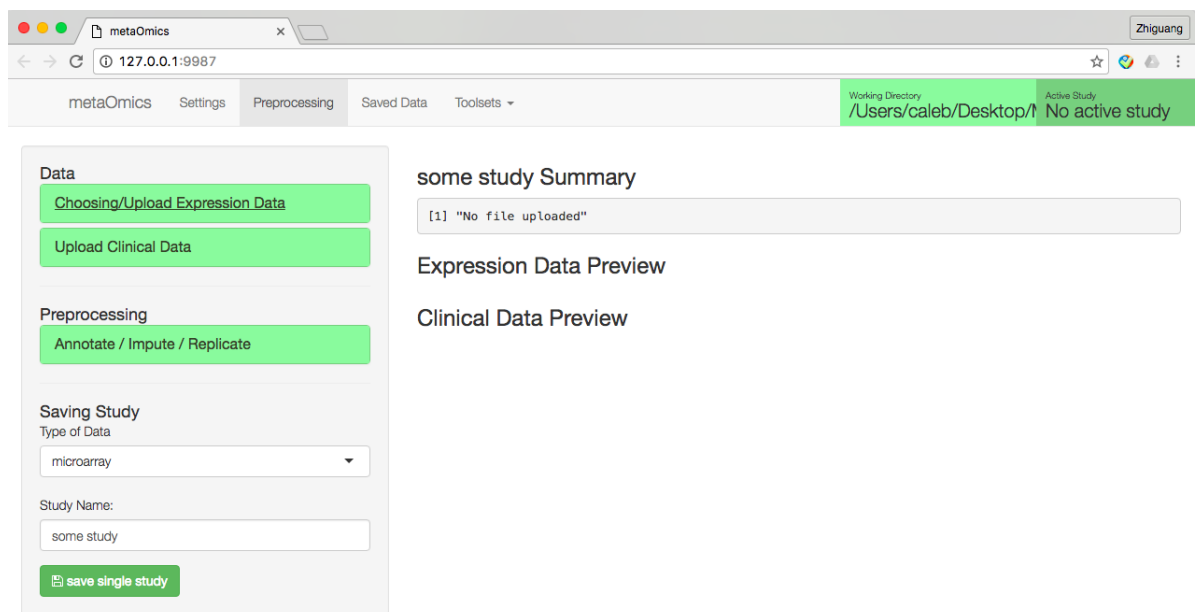


Figure 4: GUI Preprocessing page

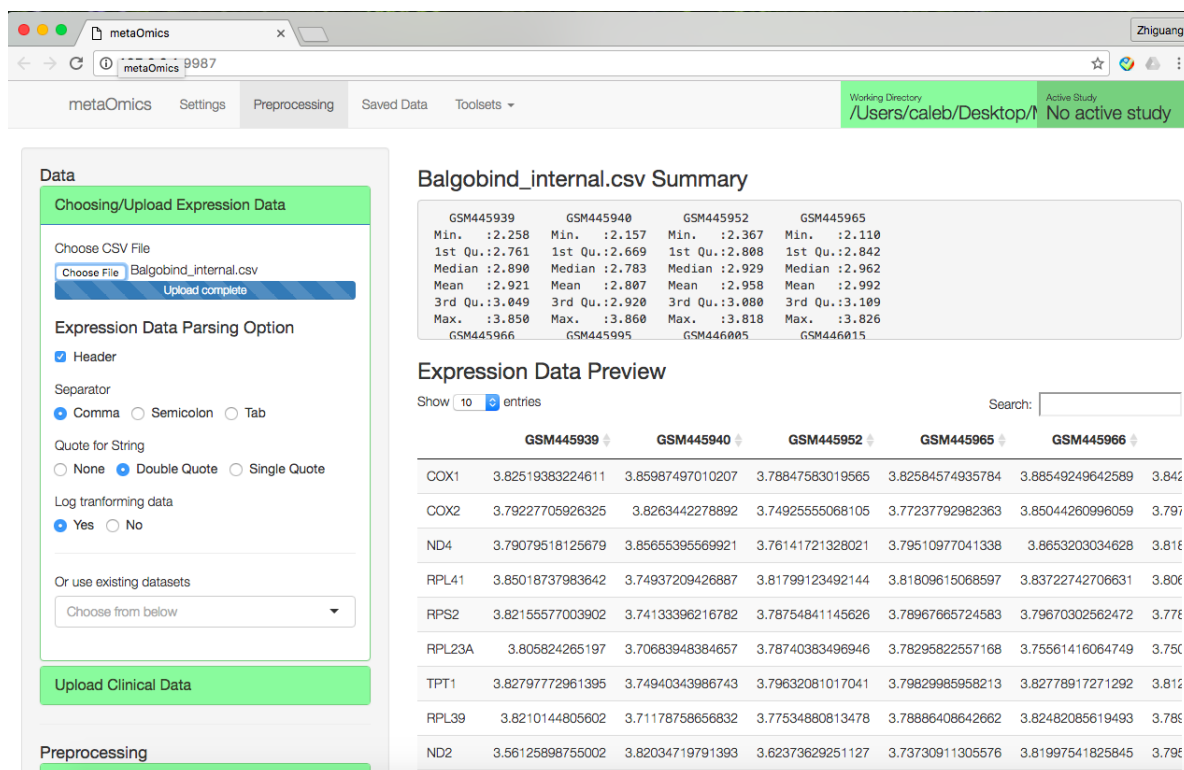


Figure 5: GUI Preprocessing page

The MetaOmics suit also provide handlers for feature annotation, missing value imputation and multiple probe same genes. Then users could specify type of data and study name. Then click “save single study” button, single study will be saved.

4.3 Saved Data

After uploading multiple studies w/o clinical data, Users can turn to the Saved Data tab. Users should select multiple datasets as Figure 6.

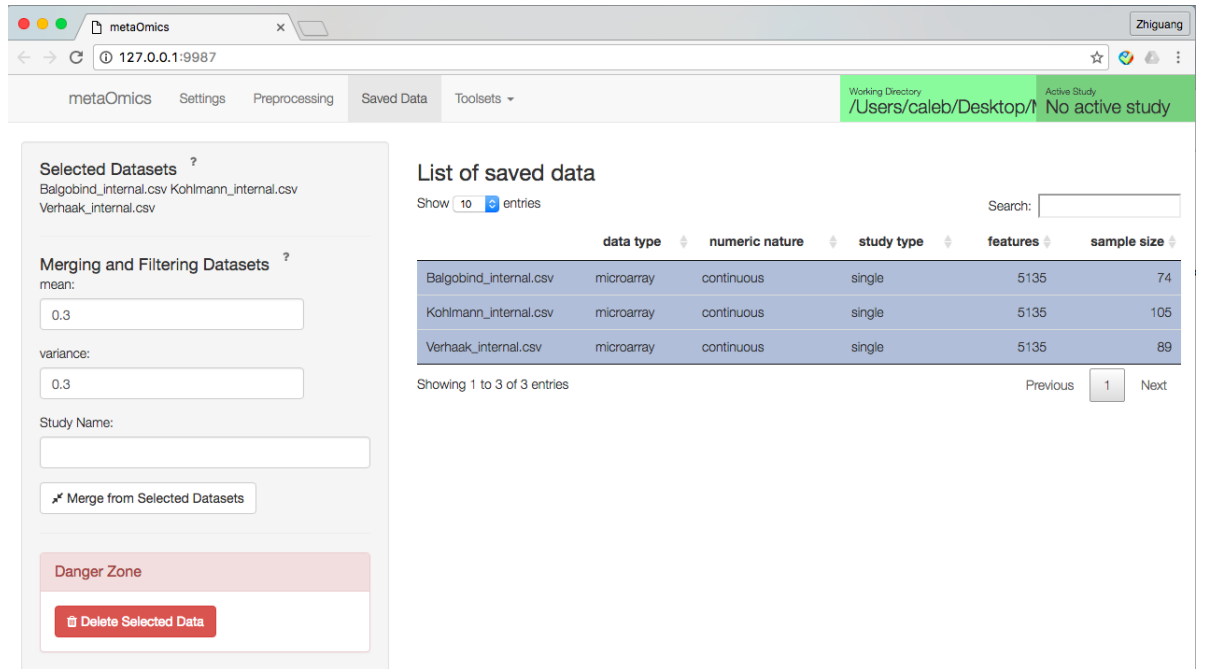


Figure 6: GUI Preprocessing page

Users can select filtering criteria, enter merged study name and click on the Merge from Selected Datasets. A merged dataset will appear on the left “List of saved data” panel. The last thing users need to do before using meta-analytic toolsets is select merged data and click on “Make merged Active Dataset” - A big green button. Then the merged data becomes active study and shows up on the top right corner.

5 Toolsets

5.1 MetaQC

5.2 MetaDE

5.3 MetaPath

5.4 MetaClust

By clicking toolsets and then metaClust, users are directed to metaClust home page as Figure 7.

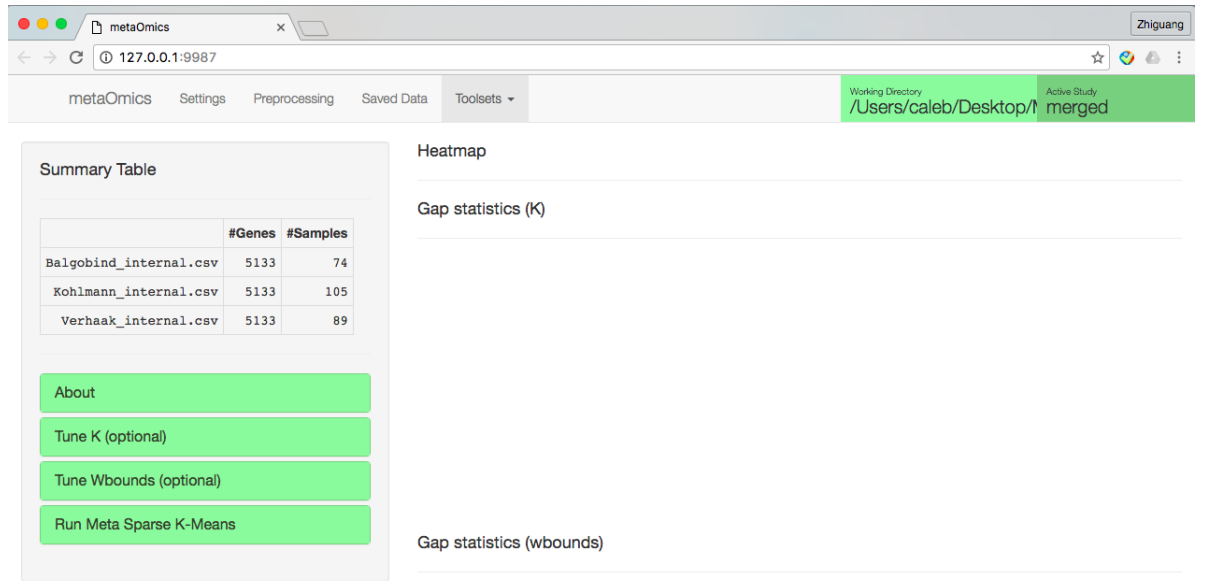


Figure 7: GUI Preprocessing page

On the top left panel users can see data summary Table. Below there are 4 tabs.

5.4.1 About

About tab includes basic introduction of metaClust. Starting with multiple studies, we could run MetaSparseKmeans with pre-specified number of clusters (K) and gene selection tuning parameter (Wbounds). If you are not sure about what are good K and Wbounds, please try Tune K and Tune Wbounds panel.

5.4.2 Tune K

If the users are not sure what is number of clusters, they can start to use the Tune K panel as in Figure 8.

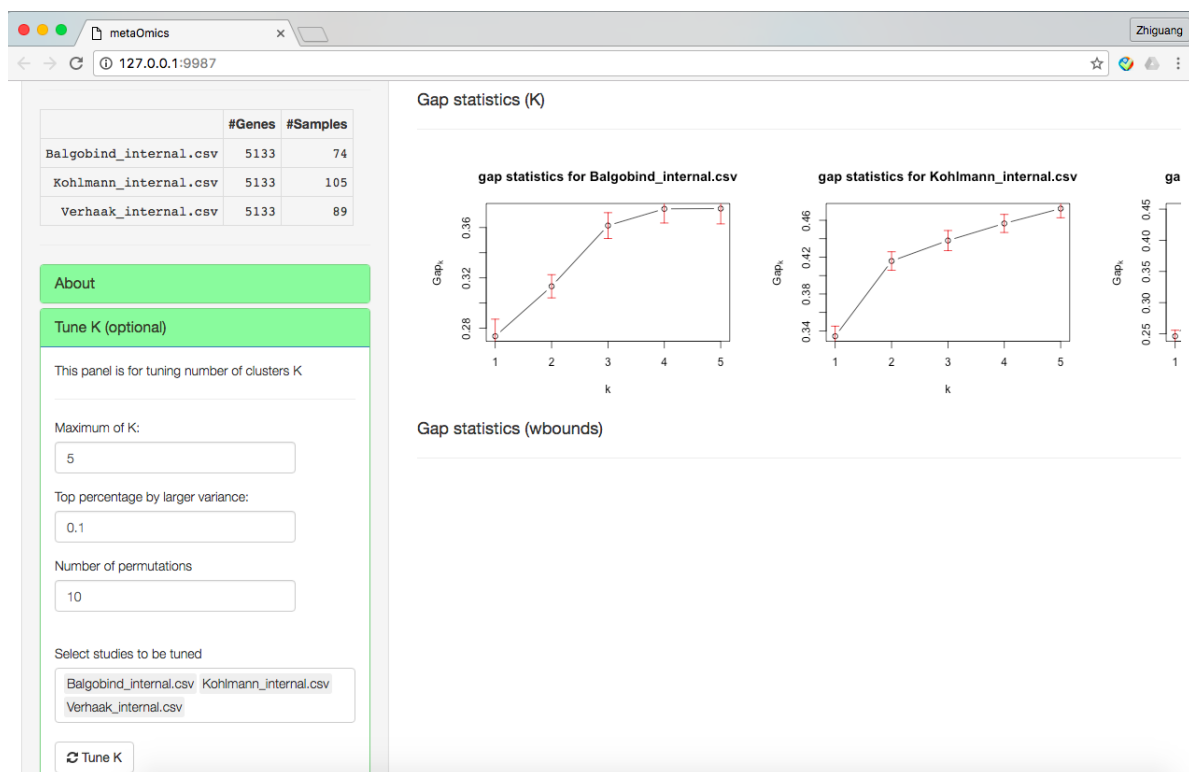


Figure 8: GUI Preprocessing page

5.5 MetaPCA

5.6 MetaKTSP

5.7 MetaDCN

5.8 MetaLA

References

- Huo, Z., Ding, Y., Liu, S., Oesterreich, S., and Tseng, G. (2016). Meta-analytic framework for sparse k-means to identify disease subtypes in multiple transcriptomic studies. *Journal of the American Statistical Association*, 111(513):27–42.
- Kang, D. D., Sibille, E., Kaminski, N., and Tseng, G. C. (2012). Metaqc: objective quality control and inclusion/exclusion criteria for genomic meta-analysis. *Nucleic acids research*, 40(2):e15–e15.

Shen, K. and Tseng, G. C. (2010). Meta-analysis for pathway enrichment analysis when combining multiple genomic studies. *Bioinformatics*, 26(10):1316–1323.