**Main Figures**

Figure 1: Overview of the computational pipeline.

Figure 2: The common modules identified from the fly brain scRNA-seq dataset.

A. Heatmap of the average co-expression strength for the common modules.

B. The scatter plot for the mean value of co-expression strength and uniformity of each module. Each point represents an identified common module.

C. Top (up to 10) significant biological processes enriched by the identified common modules.

Figure 3: The module activity matrix across cells clusters and age groups in the scRNA-seq dataset.

A. Heatmap of module activity across cell clusters. Each module is scored within each single cell through AUCell algorithm (Aibar et al. 2017). The mean activity score per cell cluster is shown. The row- and column-wise clustering is performed with ‘hclust’ function in R with the ‘ward.D2’ method.

B. Heatmap of module activity for selected cell clusters across age groups.

Figure 4: The common modules identified from the fly head snRNA-seq dataset.

A. Heatmap of the average co-expression strength for the common modules.

B. The scatter plot for the mean value of co-expression strength and uniformity of each module. Each point represents an identified common module.

C. Top (up to 10) significant biological processes enriched by the identified common modules.

Figure 5: The common modules identified from the fly head snRNA-seq dataset.

A. Heatmap of the overlap between common modules obtained from single-cell dataset and single-nucleus dataset. The number of genes per module is indicated in the row and column labels. The color represents the percentage of overlapped gene in the smaller module under comparison. The number in each cell represents the number of overlapped gene. Common modules identified from the single-cell data are in rows while those from the single-nucleus are in columns

B. A representative network of module 2 from the snRNA-seq dataset. Each node represents a gene and the edge width represents mean co-expression strength.

**Supplementary Figures**

Figure S1: Summary of dataset pre-processing

The number of cells per cell cluster before and after data pre-processing, the number of expressed genes per cell cluster, the number of cell clusters one gene was detected as effectively expressed.

Figure S2: Visualizations of the common modules from the scRNA-seq dataset

A. Representative networks of common modules from the scRNA-seq dataset. Each node represents a gene and the edge represents mean co-expression strength. The color of each node represents the sum of its edge weights.

B. Heatmap of the overlap between common modules. The number of genes per module is indicated in the row and column labels. The color represents the percentage of overlapped gene in the module under comparison. The number in each cell represents the number of overlapped gene.

Figure S3: Heatmap of distribution of modules in cell clusters from the snRNA-seq dataset. Each row represents a cell cluster and each column corresponds to a module. It a module is detected in a cell cluster given its adjusted P value, it’s colored blue. Otherwise, it’s colored red.

Figure S4: Visualizations of the common modules from the snRNA-seq dataset

A. Representative networks of common modules from the snRNA-seq dataset. Each node represents a gene and the edge represents mean co-expression strength. The color of each node represents the sum of its edge weights.

B. Heatmap of the overlap between common modules. The number of genes per module is indicated in the row and column labels. The color represents the percentage of overlapped gene in the module under comparison. The number in each cell represents the number of overlapped gene.

Figure S5: The module activity matrix across cells clusters in the snRNA-seq dataset.

Heatmap of module activity across cell clusters. Each module is scored within each single cell through AUCell algorithm (Aibar et al. 2017). The mean activity score per cell cluster is shown. The row- and column-wise clustering is performed with ‘hclust’ function in R with the ‘ward.D2’ method.

Figure S6: Performance of the seven gene co-expression related metrics.

The percentage of pairs of correlated genes found in the two datasets under comparison as a function of the number of top edges sorted by their absolute measurement values. Each row represents one metric. Each column represents one comparison for datasets with different number of cells.

Figure S6: Visualization of the two simulation schemes and performance of our pipeline with different values.