**Supplementary File 1**

**Experimental evaluation and comparison of multi-omics data integration methods for cancer subtyping**

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**1. Recommended k of each method**

In this work, we chose nine typical methods to evaluate, compare, and analyze, including iClusterBayes, LRAcluster, SNF, PFA, NEMO, moCluster, CIMLR, MultiNMF, and PINS. We notice that, in these methods, iClusterBayes, SNF, PINS, NEMO, moCluster, and CIMLR have their criteria to estimate the best number of clusters based on different strategies. For SNF, NEMO, and CIMLR, they estimate the best number of clusters automatically according to eigen-gaps or rotation cost. For PINS, it automatically evaluates the instability of different connectivity matrices to determine the best k. For iClusterBayes and moCluster, they calculate different metrics (deviance ratios and Bayesian information criterion values for iClusterBayes, gap-statistic for moCluster) to generate a plot that is used to choose the best k by users manually. According to the criteria of these methods, we ran these methods using our Dataset #1 Nine-cancer datasets. Table S1 shows every recommended k by different methods.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Methods** | **Data**  **Combination** | **Complete Datasets** | | | | | | | | | **Significant Datasets** | | | | | | | | |
| **B** | **C** | **KC** | **LA** | **LS** | **A** | **KP** | **LI** | **T** | **B** | **C** | **KC** | **LA** | **LS** | **A** | **KP** | **LI** | **T** |
| **iCluster Bayes** | **m\_mi** | **4** | **3** | **3** | **4** | **3** | **2** | **2** | **2** | **2** | **3** | **2** | **2** | **2** | **3** | **2** | **2** | **2** | **2** |
| **m\_me** | **4** | **3** | **4** | **4** | **3** | **2** | **2** | **2** | **2** | **3** | **2** | **3** | **3** | **3** | **2** | **3** | **3** | **2** |
| **m\_cnv** | **4** | **3** | **3** | **4** | **3** | **2** | **4** | **3** | **2** | **3** | **3** | **2** | **4** | **2** | **2** | **3** | **4** | **2** |
| **mi\_me** | **2** | **3** | **4** | **2** | **2** | **2** | **2** | **2** | **2** | **2** | **2** | **3** | **2** | **2** | **2** | **2** | **2** | **2** |
| **mi\_cnv** | **3** | **3** | **3** | **4** | **3** | **2** | **3** | **4** | **2** | **3** | **2** | **2** | **3** | **2** | **3** | **2** | **2** | **2** |
| **me\_cnv** | **3** | **2** | **4** | **2** | **3** | **2** | **3** | **3** | **2** | **4** | **3** | **3** | **3** | **2** | **2** | **3** | **2** | **2** |
| **m\_mi\_me** | **4** | **3** | **3** | **3** | **3** | **2** | **4** | **4** | **2** | **3** | **2** | **3** | **3** | **3** | **2** | **2** | **4** | **2** |
| **m\_mi\_cnv** | **4** | **4** | **3** | **4** | **3** | **2** | **3** | **4** | **3** | **3** | **3** | **3** | **4** | **2** | **2** | **2** | **3** | **2** |
| **m\_me\_cnv** | **4** | **3** | **4** | **4** | **4** | **2** | **3** | **4** | **2** | **3** | **2** | **3** | **3** | **2** | **2** | **3** | **4** | **2** |
| **mi\_me\_cnv** | **4** | **2** | **4** | **2** | **3** | **2** | **3** | **3** | **2** | **4** | **2** | **2** | **3** | **2** | **2** | **3** | **2** | **2** |
| **m\_mi\_me\_cnv** | **4** | **3** | **4** | **4** | **3** | **2** | **3** | **3** | **2** | **3** | **2** | **3** | **4** | **2** | **2** | **2** | **4** | **2** |
| **SNF** | **m\_mi** | **2** | **2** | **3** | **2** | **2** | **2** | **3** | **2** | **3** | **2** | **3** | **2** | **2** | **2** | **2** | **3** | **2** | **2** |
| **m\_me** | **2** | **3** | **4** | **2** | **3** | **2** | **3** | **3** | **3** | **2** | **3** | **4** | **2** | **2** | **2** | **3** | **2** | **2** |
| **m\_cnv** | **2** | **2** | **4** | **2** | **2** | **3** | **5** | **2** | **2** | **3** | **2** | **4** | **4** | **3** | **3** | **6** | **2** | **2** |
| **mi\_me** | **2** | **2** | **4** | **2** | **2** | **2** | **3** | **5** | **3** | **3** | **3** | **6** | **2** | **2** | **2** | **2** | **4** | **2** |
| **mi\_cnv** | **2** | **2** | **4** | **2** | **2** | **3** | **3** | **2** | **2** | **3** | **2** | **3** | **2** | **2** | **2** | **8** | **2** | **2** |
| **me\_cnv** | **4** | **2** | **3** | **2** | **2** | **3** | **2** | **3** | **2** | **3** | **2** | **4** | **2** | **2** | **3** | **2** | **2** | **2** |
| **m\_mi\_me** | **2** | **3** | **3** | **2** | **2** | **2** | **3** | **2** | **3** | **3** | **3** | **2** | **2** | **2** | **2** | **3** | **2** | **2** |
| **m\_mi\_cnv** | **2** | **2** | **4** | **2** | **2** | **3** | **2** | **2** | **2** | **2** | **2** | **3** | **2** | **2** | **2** | **3** | **4** | **3** |
| **m\_me\_cnv** | **3** | **2** | **3** | **2** | **2** | **3** | **2** | **3** | **3** | **3** | **2** | **3** | **2** | **2** | **3** | **2** | **2** | **2** |
| **mi\_me\_cnv** | **3** | **2** | **3** | **2** | **2** | **3** | **2** | **3** | **3** | **3** | **2** | **3** | **2** | **2** | **2** | **2** | **2** | **2** |
| **m\_mi\_me\_cnv** | **2** | **2** | **3** | **2** | **2** | **3** | **2** | **2** | **3** | **3** | **2** | **3** | **2** | **2** | **2** | **4** | **2** | **2** |
| **PINS** | **m\_mi** | **7** | **18** | **8** | **39** | **16** | **4** | **10** | **12** | **5** | **14** | **14** | **25** | **14** | **22** | **4** | **22** | **28** | **8** |
| **m\_me** | **11** | **5** | **11** | **34** | **32** | **8** | **4** | **11** | **8** | **51** | **30** | **2** | **19** | **21** | **2** | **2** | **3** | **7** |
| **m\_cnv** | **14** | **2** | **2** | **11** | **11** | **7** | **2** | **2** | **5** | **26** | **3** | **8** | **27** | **23** | **3** | **3** | **16** | **2** |
| **mi\_me** | **9** | **3** | **2** | **24** | **11** | **2** | **3** | **17** | **13** | **32** | **18** | **23** | **17** | **15** | **4** | **2** | **14** | **7** |
| **mi\_cnv** | **9** | **14** | **6** | **15** | **11** | **10** | **2** | **14** | **6** | **7** | **4** | **4** | **15** | **17** | **6** | **2** | **25** | **4** |
| **me\_cnv** | **4** | **2** | **2** | **13** | **3** | **4** | **5** | **30** | **3** | **2** | **4** | **4** | **16** | **19** | **6** | **2** | **24** | **5** |
| **m\_mi\_me** | **8** | **2** | **2** | **2** | **2** | **3** | **2** | **4** | **3** | **2** | **7** | **2** | **4** | **3** | **3** | **2** | **2** | **9** |
| **m\_mi\_cnv** | **8** | **2** | **3** | **9** | **2** | **2** | **2** | **2** | **2** | **2** | **3** | **2** | **4** | **7** | **2** | **2** | **3** | **2** |
| **m\_me\_cnv** | **4** | **2** | **2** | **7** | **8** | **3** | **3** | **5** | **3** | **3** | **3** | **2** | **4** | **3** | **3** | **2** | **2** | **2** |
| **mi\_me\_cnv** | **7** | **2** | **2** | **4** | **3** | **2** | **3** | **3** | **4** | **2** | **3** | **2** | **5** | **3** | **2** | **3** | **2** | **2** |
| **m\_mi\_me\_cnv** | **8** | **5** | **4** | **4** | **5** | **3** | **4** | **7** | **3** | **5** | **7** | **2** | **2** | **5** | **3** | **3** | **2** | **2** |
| **NEMO** | **m\_mi** | **7** | **2** | **6** | **7** | **4** | **6** | **8** | **8** | **7** | **5** | **2** | **7** | **7** | **3** | **5** | **3** | **8** | **2** |
| **m\_me** | **3** | **2** | **4** | **4** | **4** | **4** | **3** | **8** | **3** | **3** | **2** | **3** | **4** | **3** | **7** | **3** | **5** | **2** |
| **m\_cnv** | **3** | **2** | **4** | **6** | **2** | **3** | **8** | **3** | **5** | **3** | **2** | **3** | **4** | **2** | **6** | **7** | **6** | **7** |
| **mi\_me** | **2** | **3** | **5** | **5** | **6** | **2** | **3** | **4** | **3** | **3** | **3** | **5** | **5** | **3** | **4** | **8** | **8** | **2** |
| **mi\_cnv** | **7** | **2** | **6** | **5** | **2** | **6** | **7** | **7** | **5** | **3** | **3** | **4** | **5** | **2** | **8** | **7** | **3** | **6** |
| **me\_cnv** | **3** | **7** | **6** | **6** | **5** | **6** | **2** | **4** | **3** | **3** | **3** | **5** | **6** | **2** | **8** | **8** | **4** | **6** |
| **m\_mi\_me** | **3** | **3** | **7** | **4** | **2** | **4** | **8** | **8** | **3** | **3** | **3** | **4** | **5** | **2** | **2** | **2** | **2** | **2** |
| **m\_mi\_cnv** | **3** | **3** | **4** | **4** | **2** | **6** | **4** | **6** | **7** | **3** | **3** | **3** | **4** | **2** | **6** | **3** | **4** | **3** |
| **m\_me\_cnv** | **3** | **3** | **5** | **2** | **2** | **4** | **2** | **3** | **4** | **3** | **2** | **4** | **5** | **4** | **4** | **6** | **3** | **3** |
| **mi\_me\_cnv** | **3** | **2** | **6** | **4** | **3** | **3** | **2** | **3** | **3** | **3** | **2** | **5** | **5** | **3** | **8** | **7** | **3** | **6** |
| **m\_mi\_me\_cnv** | **3** | **3** | **3** | **4** | **5** | **4** | **3** | **6** | **3** | **3** | **3** | **5** | **5** | **2** | **4** | **7** | **6** | **3** |
| **moCluster** | **m\_mi** | **4** | **2** | **4** | **4** | **3** | **2** | **6** | **4** | **7** | **2** | **3** | **7** | **2** | **2** | **3** | **2** | **2** | **4** |
| **m\_me** | **6** | **3** | **2** | **7** | **2** | **8** | **2** | **2** | **3** | **2** | **6** | **3** | **2** | **2** | **8** | **2** | **2** | **2** |
| **m\_cnv** | **2** | **4** | **7** | **2** | **2** | **6** | **2** | **4** | **8** | **2** | **2** | **4** | **2** | **4** | **5** | **3** | **3** | **8** |
| **mi\_me** | **2** | **2** | **5** | **2** | **2** | **7** | **2** | **2** | **NA** | **3** | **2** | **8** | **3** | **4** | **6** | **2** | **2** | **2** |
| **mi\_cnv** | **2** | **2** | **2** | **3** | **2** | **7** | **2** | **2** | **7** | **2** | **4** | **4** | **2** | **2** | **2** | **2** | **2** | **2** |
| **me\_cnv** | **4** | **3** | **8** | **2** | **3** | **3** | **3** | **4** | **7** | **2** | **5** | **2** | **2** | **2** | **3** | **8** | **2** | **7** |
| **m\_mi\_me** | **2** | **4** | **8** | **3** | **6** | **8** | **2** | **2** | **7** | **7** | **4** | **4** | **3** | **3** | **3** | **2** | **8** | **2** |
| **m\_mi\_cnv** | **3** | **6** | **8** | **2** | **2** | **3** | **8** | **2** | **6** | **2** | **2** | **2** | **2** | **4** | **2** | **2** | **3** | **2** |
| **m\_me\_cnv** | **4** | **7** | **7** | **2** | **2** | **4** | **8** | **8** | **2** | **7** | **2** | **4** | **3** | **4** | **5** | **3** | **2** | **NA** |
| **mi\_me\_cnv** | **3** | **2** | **4** | **2** | **3** | **6** | **7** | **2** | **8** | **2** | **2** | **2** | **2** | **4** | **2** | **2** | **2** | **3** |
| **m\_mi\_me\_cnv** | **2** | **2** | **3** | **2** | **6** | **NA** | **4** | **7** | **8** | **3** | **2** | **2** | **2** | **3** | **2** | **2** | **3** | **2** |
| **CIMLR** | **m\_mi** | **3** | **4** | **6** | **8** | **7** | **2** | **6** | **8** | **8** | **7** | **3** | **6** | **3** | **8** | **8** | **3** | **8** | **7** |
| **m\_me** | **3** | **4** | **2** | **2** | **8** | **5** | **7** | **2** | **4** | **3** | **3** | **3** | **5** | **5** | **6** | **5** | **2** | **7** |
| **m\_cnv** | **6** | **2** | **2** | **5** | **4** | **5** | **8** | **6** | **7** | **5** | **3** | **3** | **5** | **2** | **8** | **7** | **5** | **4** |
| **mi\_me** | **2** | **2** | **3** | **8** | **2** | **8** | **2** | **6** | **6** | **3** | **4** | **6** | **6** | **2** | **7** | **7** | **4** | **7** |
| **mi\_cnv** | **2** | **3** | **3** | **2** | **4** | **2** | **3** | **8** | **7** | **4** | **3** | **5** | **6** | **2** | **8** | **7** | **4** | **3** |
| **me\_cnv** | **8** | **2** | **2** | **3** | **4** | **3** | **2** | **3** | **3** | **8** | **3** | **2** | **2** | **6** | **8** | **8** | **4** | **3** |
| **m\_mi\_me** | **3** | **4** | **6** | **5** | **7** | **5** | **4** | **8** | **8** | **7** | **3** | **6** | **3** | **2** | **8** | **3** | **2** | **3** |
| **m\_mi\_cnv** | **3** | **3** | **3** | **5** | **4** | **2** | **6** | **8** | **7** | **3** | **3** | **8** | **5** | **8** | **8** | **5** | **8** | **8** |
| **m\_me\_cnv** | **3** | **4** | **4** | **6** | **3** | **5** | **7** | **7** | **7** | **8** | **3** | **2** | **5** | **3** | **2** | **8** | **3** | **8** |
| **mi\_me\_cnv** | **3** | **3** | **4** | **8** | **2** | **3** | **3** | **6** | **3** | **8** | **3** | **5** | **8** | **2** | **7** | **7** | **6** | **3** |
| **m\_mi\_me\_cnv** | **3** | **3** | **3** | **5** | **8** | **7** | **6** | **2** | **3** | **3** | **3** | **2** | **3** | **2** | **5** | **3** | **2** | **8** |

Table S1. Recommended k of each method. Notations: B-BRCA, C-COAD, KC-KIRC, LA-LUAD, LS-LUSC, A-ACC, KP-KIRP, LI-LIHC, T-THYM. m-mRNA expression, mi-miRNA expression, me-DNA methylation, cnv-copy number variation.

**2. Evaluation and Comparison based on recommended k**

We also evaluated and compared the performance of these methods based on their recommended k. Figure S1 shows the results.

图表

描述已自动生成

Figure S1. Comparison of the performance based on recommended k. (A) Clinical-based performance comparison. The upper plot shows the cumulative transformed p-value of different cancer types, and the lower plot shows the cumulative number of clinical-significant subtyping results. NEMO and PINS have the best performance on complete and significant datasets, respectively, while moCluster performed the worst on both datasets. (B) Clustering-based performance comparison. The upper and lower plots show the silhouette coefficients of complete and significant datasets, respectively. CIMLR had the highest silhouette coefficients in all the tests, while NEMO performed the worst in half of the tests.