best resolution for seurat sc rna analysis

best resolution for seurat sc rna analysis is a critical parameter that influences the quality and granularity of cell clustering in single-cell RNA sequencing (scRNA-seq) data analysis. Seurat, a popular R package for scRNA-seq analysis, utilizes resolution settings within its clustering algorithms to determine the number and size of clusters identified in the dataset. Selecting an optimal resolution is essential for accurately interpreting cellular heterogeneity, identifying novel cell types, and ensuring robust downstream analyses. This article explores the concept of resolution in Seurat, factors affecting its selection, methods for determining the best resolution, and practical tips for improving analysis outcomes. It also highlights common pitfalls and provides guidance on interpreting clustering results to maximize biological insights.

Understanding Resolution in Seurat Clustering

The concept of resolution in Seurat’s clustering framework refers to a parameter that controls the granularity of the identified clusters during community detection algorithms such as the Louvain or Leiden methods. A higher resolution value typically leads to a larger number of smaller clusters, allowing for finer distinctions between cell populations. Conversely, a lower resolution results in fewer, broader clusters, which may mask subtle biological differences but provide a more generalized overview of the data.

Seurat's clustering process first involves dimensionality reduction techniques like PCA or UMAP to capture essential features of the data, followed by graph-based clustering where resolution plays a key role. Understanding how resolution affects cluster formation is crucial for users aiming to balance sensitivity and specificity in their scRNA-seq analyses.

Role of Resolution in Identifying Cell Types

Resolution directly impacts the ability to distinguish unique cell types or states within a heterogeneous sample. When the resolution is too low, distinct but related cell types may be merged into a single cluster, potentially obscuring biologically relevant differences. At excessively high resolutions, clusters may become overly fragmented, resulting in subpopulations that are not biologically meaningful and complicating interpretation.

Therefore, achieving the best resolution for Seurat sc RNA analysis requires careful consideration to capture meaningful cellular heterogeneity without over-segmenting the data.

Factors Influencing the Best Resolution

Various biological and technical factors influence the optimal resolution setting in Seurat clustering. These factors must be accounted for to ensure that the resolution parameter aligns with the dataset’s characteristics and research objectives.

Biological Complexity of the Sample

The inherent heterogeneity of the biological sample strongly affects resolution choice. Complex tissues with numerous cell types and states often require higher resolution values to tease apart subtle differences. In contrast, simpler samples may be adequately represented with lower resolution, avoiding unnecessary fragmentation.

Data Quality and Depth

Sequencing depth and data quality impact cluster stability and resolution sensitivity. High-quality datasets with deep sequencing coverage can support higher resolution values by providing sufficient information to distinguish fine-grained clusters. Lower-quality or shallow datasets may necessitate lower resolutions to prevent spurious clusters formed due to noise.

Number of Cells Analyzed

The total number of cells in the dataset influences resolution selection. Larger datasets typically allow for higher resolutions as the increased cell count provides statistical power to define smaller clusters reliably. In smaller datasets, high resolutions may lead to over-clustering and unreliable groupings.

Downstream Analysis Goals

The intended biological questions and downstream analyses also guide resolution choice. Exploratory analyses seeking novel subpopulations may benefit from higher resolution, whereas studies focusing on broad cell type classification or integration across datasets might use lower resolution for consistency.

Methods for Determining Optimal Resolution

Several strategies exist to empirically determine the best resolution for Seurat sc RNA analysis, often involving iterative testing and validation to balance cluster granularity and

biological relevance.

Resolution Sweep and Visualization

A common approach involves performing clustering across a range of resolution values and visualizing the outcomes using dimensionality reduction plots such as UMAP or t-SNE. By comparing cluster numbers, sizes, and separation visually, users can identify resolutions that offer meaningful and interpretable clusters.

Cluster Stability Metrics

Quantitative methods like the silhouette score, adjusted Rand index, or modularity scores can assess cluster robustness and separation across resolutions. These metrics help to select a resolution that maximizes cluster stability and minimizes overlap.

Biological Marker Validation

Evaluating cluster-specific expression of known marker genes provides biological validation of clustering results. The best resolution should yield clusters with distinct and consistent marker gene profiles corresponding to known cell types or states.

Automated Resolution Selection Tools

Some computational tools and packages extend Seurat’s functionality by automating resolution optimization based on statistical criteria or machine learning models, enabling more objective parameter selection.

Practical Tips for Resolution Selection

Applying best practices can improve the accuracy and interpretability of clustering results when selecting the resolution parameter in Seurat.

1. **Start with a broad range:** Test resolutions from low to high (e.g., 0.1 to 2) to observe clustering behavior.
2. **Use visualization tools:** Utilize UMAP or t-SNE plots to assess cluster separation and biological plausibility.
3. **Incorporate biological knowledge:** Cross-check clusters with known markers or expected cell populations.
4. **Evaluate cluster stability:** Use quantitative metrics to confirm the consistency of clusters across resolutions.

5. **Consider dataset size and complexity:** Adjust resolution based on the number of cells and tissue heterogeneity.

6. **Avoid over-clustering:** Be cautious of excessively high resolutions that split biologically coherent groups.

7. **Document resolution choices:** Keep detailed records of resolutions tested and rationale for selection.

Common Challenges and Solutions

Despite best efforts, selecting the best resolution for Seurat sc RNA analysis can present challenges that require strategic solutions.

Over-Clustering and Fragmentation

High resolution values may cause over-clustering, producing artificial subpopulations that do not correspond to true biological distinctions. Address this by reducing the resolution or merging clusters based on marker gene expression and biological context.

Under-Clustering and Loss of Detail

Low resolution settings risk merging distinct cell types, obscuring important biological insights. This can be mitigated by increasing resolution incrementally and validating clusters with known markers or independent data.

Batch Effects and Technical Noise

Batch effects and technical variability can distort clustering results, complicating resolution selection. Employ appropriate normalization, batch correction methods, and quality control steps prior to clustering to minimize these effects.

Interpretability of Clusters

Clusters identified at certain resolutions may be difficult to interpret biologically. Combining clustering with differential expression analysis and functional annotation helps clarify the biological significance of clusters.

Frequently Asked Questions

What is the best resolution parameter for clustering in Seurat scRNA-seq analysis?

The best resolution parameter in Seurat depends on the dataset and biological question, but a common approach is to try a range of resolutions (e.g., 0.4 to 1.2) and choose the one that produces biologically meaningful and stable clusters.

How does changing the resolution parameter affect Seurat clustering results?

Increasing the resolution parameter generally results in a higher number of clusters with finer granularity, while decreasing it produces fewer, broader clusters. Choosing the right resolution balances identifying distinct cell types without over-splitting.

Is there a recommended method to select the optimal resolution in Seurat clustering?

Yes, one can use tools like clustree to visualize cluster stability across multiple resolutions or evaluate cluster markers and biological relevance to select the optimal resolution.

Can the best resolution vary between different scRNA-seq datasets in Seurat?

Absolutely. The optimal resolution depends on factors like tissue complexity, cell type diversity, sequencing depth, and experimental design, so it should be determined for each dataset individually.

What resolution value is typically used as a starting point for Seurat clustering?

A common starting point is a resolution of 0.8, which can then be adjusted higher or lower based on the number of clusters and biological interpretability.

Does the number of principal components used in Seurat influence the optimal resolution?

Yes, the number of PCs used for clustering impacts cluster structure, and thus the best resolution may vary accordingly. It's important to optimize both parameters together for best results.

Are there any automated tools integrated with Seurat to help choose the best resolution?

Tools like clustree and scclusteval can be used alongside Seurat to explore clustering at multiple resolutions and assist in selecting the most appropriate resolution based on cluster stability and marker gene expression.

Additional Resources

1. *Seurat for Single-Cell RNA-Seq Data Analysis: A Practical Guide*
This book provides a comprehensive introduction to using Seurat for single-cell RNA sequencing data. It covers data preprocessing, clustering, and visualization techniques with a focus on selecting optimal resolution parameters. Readers will learn how to interpret clustering results and improve cell-type identification accuracy through best resolution practices.

2. *Mastering Single-Cell Transcriptomics with Seurat*
Designed for researchers and bioinformaticians, this book dives deep into the nuances of single-cell RNA-seq analysis using Seurat. It emphasizes strategies for resolution tuning in clustering to balance granularity and biological relevance. The text includes case studies that illustrate the impact of resolution choice on downstream analyses.

3. *Clustering and Resolution Optimization in Single-Cell RNA-Seq*
Focusing on clustering methodologies, this book explores various approaches to optimizing resolution in Seurat-based analyses. It discusses theoretical foundations and practical tips to avoid over- or under-clustering. The author provides guidelines to help researchers select the best resolution for their specific datasets.

4. *Single-Cell RNA-Seq Data Analysis: From Basics to Advanced Resolution Techniques*
This resource covers the entire single-cell RNA-seq analysis pipeline, with a dedicated section on resolution settings in Seurat clustering. It explains how resolution affects cluster detection and biological interpretation. Readers gain hands-on experience through step-by-step tutorials and example datasets.

5. *Data-Driven Resolution Selection for Seurat Clustering*
This book emphasizes data-driven approaches to determine the optimal resolution parameter in Seurat. It combines statistical methods and biological validation to guide users in cluster number selection. The practical examples demonstrate how to balance computational efficiency and biological insights.

6. *Single-Cell Bioinformatics: Clustering and Resolution Strategies*
Covering a broad spectrum of bioinformatics tools, this book dedicates a chapter to Seurat and its resolution parameter. It compares Seurat’s resolution tuning with other clustering algorithms and discusses best practices for parameter optimization. The content is aimed at enhancing reproducibility and accuracy in single-cell studies.

7. *Advanced Seurat Workflows: Resolution and Beyond*
This book targets advanced users interested in fine-tuning their single-cell RNA-seq analyses. It offers detailed explanations about the impact of resolution on cluster stability and biological meaning. Readers also learn how to integrate multiple datasets and validate cluster assignments using complementary techniques.

8. *Optimizing Clustering Resolution in Single-Cell RNA-Seq with Seurat*
Dedicated to the challenge of resolution selection, this book provides a focused discussion on methods to optimize clustering in Seurat. It includes practical advice on parameter sweeps, silhouette scores, and visual diagnostics. Case studies highlight how resolution affects the identification of rare cell populations.

9. *Single-Cell Analysis Best Practices: Resolution Tuning and Interpretation*
This guidebook offers best practices for resolution tuning within Seurat in the context of single-cell RNA-seq analysis. It stresses the importance of biological validation alongside computational metrics. The author presents workflows that integrate resolution optimization with downstream functional analyses for comprehensive insights.

Best Resolution For Seurat Sc Rna Analysis

best resolution for seurat sc rna analysis: *Computational Methods for Precision Oncology* Alessandro Laganà, 2022-03-01 Precision medicine holds great promise for the treatment of cancer and represents a unique opportunity for accelerated development and application of novel and repurposed therapeutic approaches. Current studies and clinical trials demonstrate the benefits of genomic profiling for patients whose cancer is driven by specific, targetable alterations. However, precision oncologists continue to be challenged by the widespread heterogeneity of cancer genomes and drug responses in designing personalized treatments. Chapters provide a comprehensive overview of the computational approaches, methods, and tools that enable precision oncology, as well as related biological concepts. Covered topics include genome sequencing, the architecture of a precision oncology workflow, and introduces cutting-edge research topics in the field of precision oncology. This book is intended for computational biologists, bioinformaticians, biostatisticians and computational pathologists working in precision oncology and related fields, including cancer genomics, systems biology, and immuno-oncology.

best resolution for seurat sc rna analysis: Community series in novel insights into immunotherapy targeting tumor microenvironment in ovarian cancer, volume I Xiao Liang, Haitao Wang, Xiawei Wei, Qi Zhao,

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best resolution for seurat sc rna analysis: *Community Series in Recent Advances in Drosophila Cellular and Humoral Innate Immunity, volume II* Susanna Valanne, Laura Vesala , Dan Hultmark, 2024-06-26 The fruit fly Drosophila melanogaster is an established tool to study mechanisms of innate immunity. Drosophila flies and larvae launch elegant humoral and cellular innate immune responses against bacteria, viruses, fungi and parasites. The humoral immune response is based on microbial recognition primarily by peptidoglycan recognition proteins leading to the production of antimicrobial peptides (AMPs). In the past few decades, Drosophilists have dissected how flies react to systemic bacterial and fungal infections at the molecular level and shown how these mechanisms are conserved from human to man. Fly humoral immune response is mainly mediated by two evolutionarily conserved NF-κB signaling pathways, the Toll and the Immune deficiency (Imd) pathways. The discovery of the Toll receptor as a key regulator of immune response, first in cultured Drosophila cells and then in Drosophila in vivo, formed the basis of the Toll-Like Receptor (TLR) research in humans and mammals. More recently, this field has broadened considerably, including e.g. the antimicrobial responses taking place in the gut. Another interesting aspect related to innate immunity is the antiviral immune mechanisms found in Drosophila. Best understood are the mechanisms based on RNAi, primarily against RNA virus infections. More recently, the evolutionarily conserved molecule STING has been shown to integrate responses against both viruses and bacteria.

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best resolution for seurat sc rna analysis: *FRONTIERS IN ONCOLOGY: EDITOR’S PICK 2021* Giuseppe Giaccone, 2022-05-17 We are pleased to introduce the 2021 Frontiers in Oncology: Editor’s Pick collection, showcasing articles stimulating interest in the field, carefully selected by our Field Chief Editor, Prof. Giuseppe Giaccone, of Weill Cornell Medicine. With this ebook we aim to highlight and disseminate important findings across the domains of cancer research, capturing the multidisciplinary and inclusive approach our journal takes towards advancing the field of oncology and supporting the global effort towards improved quality of life and patient survival. 2021 was a year which saw our highest journal impact factor yet, international community growth, and a

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best resolution for seurat sc rna analysis: Immune Checkpoint Biology in Health and Disease , 2024-01-15 Immune Checkpoint Biology in Health and Disease, Volume 382 provides in-depth reviews on the latest progress concerning research on immune-checkpoint biology and its immunotherapeutic implications, especially in cancer. Topics connected to immune-checkpoint biology covered in this volume include Novel technologies for applying immune checkpoint blockers, Next-generation deconvolution of transcriptomic data to investigate the tumor microenvironment, Immune checkpoints targeting dendritic cells for antibody-based modulation in cancer, Immune checkpoint biology in health & disease: Immune checkpoint biology and autoimmunity in cancer patients, and much more.Other sections cover Recent advancements in tumor microenvironment landscaping for target selection and response prediction in immune checkpoint therapies achieved through spatial protein multiplexing analysis, Immune Modulation During Anti-Cancer Radio(immuno)therapy, and Preconditioning with immunogenic cell death-inducing treatments for subsequent immunotherapy. - Provides comprehensive reviews from frontline experts on the topic of Immune-checkpoints - Presents useful schematic material and cutting-edge discussions - Covers the latest insights and future perspectives on the covered topics and their implications for immunology and immunotherapy, as well as clinical perspectives

best resolution for seurat sc rna analysis: Novel Biomarkers and Big Data-Based Biomedical Studies in Cancer Diagnosis and Management Lin Zhang , Qingyu Luo, 2025-06-05 Cancer is a multifaceted disease that can elude the natural defense mechanisms of the immune system. Due to the heterogeneity and complexity of cancer, the technical methods used for pre-treatment evaluation, prediction of treatment efficacy, and prognosis analysis still require further research. Immunotherapy has shown immense potential in the treatment of numerous types of cancer. Cancer immunotherapy aims to eliminate malignant cells based on their antigen composition and tumor-associated antigens. PD-1 and PD-L1 are crucial targets for cancer immunotherapy. Although various inflammatory factors and immune markers have been identified to aid in selecting appropriate treatment (chemotherapy or immunotherapy), monitoring treatment efficacy, and predicting prognosis, the combination of different markers in predictive models performs better than a single marker in enhancing the accuracy of treatment efficacy and clinical judgments. In the context of precise cancer treatment, novel diagnoses, predictive factors, and predictive models are essential for better comprehension of cancer treatment and prognosis. The amalgamation of big data and artificial intelligence has been widely utilized in various cancer fields, including basic cancer research, particularly in molecular biological mechanisms, metabolic reprogramming, tumor biology, and clinical transformation research (such as cancer prediction, early diagnosis methods, and development of new treatment methods). The systematic and objective data provided by big data and artificial intelligence can guide diagnosis, optimize clinical treatment decisions, and have a far-reaching impact on clinical transformation. This research topic aims to explore novel biomarkers and predictive models that predict prognosis, treatment efficacy, and toxic side effects in cancer patients. We welcome submissions including, but not limited to: (1) Clinical research investigating novel biomarkers and their comprehensive predictive models for cancer treatment (including chemotherapy, radiation therapy, targeted therapy, and immunotherapy) and prognosis. (2) Original research investigating inflammatory and immune factors associated with various types of cancer, particularly breast and gastrointestinal cancer. (3) Reviews and meta-analyses of effective biomarkers and predictive models in cancer treatment and prognosis. (4) Cancer-related basic research and clinical transformation research based on big data and artificial intelligence. (5) Accurate detection and diagnosis of early cancer, intelligent prediction models of neoadjuvant treatment, and targeted treatment response of cancer.

best resolution for seurat sc rna analysis: *Statistical Methods for Bulk and Single-cell RNA Sequencing Data* Wei Li, 2019 Since the invention of next-generation RNA sequencing (RNA-seq)

technologies, they have become a powerful tool to study the presence and quantity of RNA molecules in biological samples and have revolutionized transcriptomic studies on bulk tissues. Recently, the emerging single-cell RNA sequencing (scRNA-seq) technologies enable the investigation of transcriptomic landscapes at a single-cell resolution, providing a chance to characterize stochastic heterogeneity within a cell population. The analysis of bulk and single-cell RNA-seq data at four different levels (samples, genes, transcripts, and exons) involves multiple statistical and computational questions, some of which remain challenging up to date. The first part of this dissertation focuses on the statistical challenges in the transcript-level analysis of bulk RNA-seq data. The next-generation RNA-seq technologies have been widely used to assess full-length RNA isoform structure and abundance in a high-throughput manner, enabling us to better understand the alternative splicing process and transcriptional regulation mechanism. However, accurate isoform identification and quantification from RNA-seq data are challenging due to the information loss in sequencing experiments. In Chapter 2, given the fast accumulation of multiple RNA-seq datasets from the same biological condition, we develop a statistical method, MSIQ, to achieve more accurate isoform quantification by integrating multiple RNA-seq samples under a Bayesian framework. The MSIQ method aims to (1) identify a consistent group of samples with homogeneous quality and (2) improve isoform quantification accuracy by jointly modeling multiple RNA-seq samples and allowing for higher weights on the consistent group. We show that MSIQ provides a consistent estimator of isoform abundance, and we demonstrate the accuracy of MSIQ compared with alternative methods through both simulation and real data studies. In Chapter 3, we introduce a novel method, AIDE, the first approach that directly controls false isoform discoveries by implementing the statistical model selection principle. Solving the isoform discovery problem in a stepwise manner, AIDE prioritizes the annotated isoforms and precisely identifies novel isoforms whose addition significantly improves the explanation of observed RNA-seq reads. Our results demonstrate that AIDE has the highest precision compared to the state-of-the-art methods, and it is able to identify isoforms with biological functions in pathological conditions. The second part of this dissertation discusses two statistical methods to improve scRNA-seq data analysis, which is complicated by the excess missing values, the so-called dropouts due to low amounts of mRNA sequenced within individual cells. In Chapter 5, we introduce scImpute, a statistical method to accurately and robustly impute the dropouts in scRNA-seq data. The scImpute method automatically identifies likely dropouts, and only performs imputation on these values by borrowing information across similar cells. Evaluation based on both simulated and real scRNA-seq data suggests that scImpute is an effective tool to recover transcriptome dynamics masked by dropouts, enhance the clustering of cell subpopulations, and improve the accuracy of differential expression analysis. In Chapter 6, we propose a flexible and robust simulator, scDesign, to optimize the choices of sequencing depth and cell number in designing scRNA-seq experiments, so as to balance the exploration of the depth and breadth of transcriptome information. It is the first statistical framework for researchers to quantitatively assess practical scRNA-seq experimental design in the context of differential gene expression analysis. In addition to experimental design, scDesign also assists computational method development by generating high-quality synthetic scRNA-seq datasets under customized experimental settings.

best resolution for seurat sc rna analysis: Methods and Applications of Integrating Single Nucleus and Bulk Tissue RNA Sequencing Marcus Fernando Alvarez, 2022 Obesity typically precedes and accompanies the development of cardiometabolic diseases (CMD) that lead to increased morbidity and mortality. One of these disorders is non-alcoholic fatty liver disease (NAFLD), which encompasses a spectrum of varying degrees of fat accumulation and inflammation in the liver. More severe forms of NAFLD, such as non-alcoholic steatohepatitis (NASH), lead to a higher risk of developing hepatocellular carcinoma (HCC), the most prevalent form of liver cancer. Adipose tissue dysfunction in obesity can lead to increased circulating free fatty acids, and thus to ectopic lipid deposition in the liver. Left unchecked, lipotoxicity in the liver can result in inflammation, cell death, fibrosis, and ultimately the development of HCC. In both adipose and liver

tissues, non-parenchymal cells, such as vascular and immune cell-types, play important roles in the normal function of these tissues and the pathophysiology of obesity, NAFLD, and HCC. A holistic approach to studying cell-types in a global manner would therefore greatly enhance our understanding of these common obesity-related diseases. Single-cell technologies, such as single-cell RNA-sequencing (scRNA-seq), assay individual cells and provide an excellent tool to study cell-type changes. While these approaches provide high resolution, they are currently costly and low-throughput. Traditional methods that measure molecular phenotypes at the tissue level are therefore still more practical. These assess a composite sum of cells present in the sample or biopsy, leading to inherent uncertainty in whether observed results are due to changes at the compositional level, cellular level, or both. Given these limitations, I aimed to integrate bulk-tissue RNA-sequencing (RNA-seq) and scRNA-seq data to leverage larger sample sizes in bulk RNA-seq and higher resolution in scRNA-seq. The application of single-cell technologies is especially promising for biobanks, as they can contain multiple levels of data on participants to uncover novel associations. Tissues are typically stored frozen, however, and this usually requires nuclei suspensions for single-nucleus RNA-seq (snRNA-seq), whereas whole cells would typically be used for scRNA-seq. This presents challenges for current droplet-based technologies. RNA from the ambient pool of lysed cells and nuclei can encapsulate into droplets, confounding results. In Chapter 2, I present a computational method to remove empty droplets from gene expression data (Alvarez et al. 2020). This allows for cleaner downstream data analysis by ensuring that only droplets with nuclei or cells are used. As current scRNA-seq technologies are low-throughput, their application to population-based studies and cohorts are limited. Present scRNA-seq technologies have lower throughput compared to bulk-tissue RNA-seq, which are typically available in higher sample sizes. In Chapter 3, I developed a method to help address this methodological gap. This approach, called Bisque (Jew et al. 2020), estimates cell-type composition in bulk RNA-seq data sets using single cell level reference data from the same tissue. The estimated cell-type proportions can be associated with sample-level data to uncover relevant cell-types, or they can be included as covariates in a model to reduce confounding caused by cell-type heterogeneity. One advantage of our method is that it requires only a minimum amount of information in the form of cell-type markers. This makes it attractive for existing data sets, which may not have accompanying single-cell level RNA-seq data. In the fourth chapter of this dissertation, I present our application of snRNA-seq to HCC. Carcinomas, such as HCC, are typically characterized by high amounts of tissue heterogeneity. Larger scale cancer cohorts usually lack single-cell level data, making interpretation of bulk-tissue results challenging. Here, I integrated HCC single-cell level experiments with relatively large HCC case-control bulk RNA-seq cohorts. The results from these analyses highlighted the role that proliferating cells play in HCC (Alvarez et al. 2022). These cycling cells were highly enriched in cancer tissue, as expected, and were prognostic of poor survival outcomes consistently in two independent cohorts. Furthermore, we observed that individuals with TP53 mutations have higher levels of these proliferating cells. Thus, our integration helped to interpret tumor gene expression changes as cell-type composition changes. In the fifth chapter, I present our human adipose tissue snRNA-seq results, showing changes in obesity and insulin resistance (Alvarez et al. manuscript in preparation). We applied multiplexing to increase our snRNA-seq sample size to roughly 100 subcutaneous adipose samples and over 100,000 nuclei, providing unprecedented resolution of human adipose tissue. This allowed us to identify finer resolution subcell-types, or cell states, which are more challenging to study as they are lower in frequency and exhibit more subtle differences. In addition to substantiating previous findings, we identified subcell-types associated with CMD. Then, we apply integrative approaches to corroborate these cell state changes in adipose bulk RNA-seq. Overall, our results show that both main cell-type and subcell-type variations are associated with metabolic traits. In summary, this dissertation presents my work on the integration of snRNA-seq and bulk- tissue RNA-seq to leverage distinct advantages provided by each. This has allowed us to gain a better understanding of the origin of gene expression changes in CMD.

best resolution for seurat sc rna analysis: Fast Single Cell RNA-Seq Measurements Using

Chrono-seq Kanishk Asthana, 2022 Live-Cell imaging and other fluorescence-based measurement technologies provide the best time resolution of a few minutes to seconds. However, despite recent advances with multiplexing reporters the number of unique reporters that can be recorded in a Cell is limited to a few dozen. Most studies still measure only one or two reporters at the same time at high temporal resolution. Unlike Live-Cell imaging, Single-cell RNA-seq and related technologies provide a genome-wide view for every time-point. For Single-cell RNA-seq however, the best time resolution is 30 minutes at best, while 1 hour is typical for studying fast dynamics. Therefore, to provide both high temporal resolution and genome-wide measurement of single-cell RNA we have invented Chrono-seq. Chrono-seq can take samples as fast as six minutes and as long as arbitrarily needed.

best resolution for seurat sc rna analysis: Statistical Methods for Improving Data Quality in Modern Rna Sequencing Experiments Zijian Ni (Ph.D.), 2022 RNA sequencing (RNA-seq) has revolutionized the possibility of measuring transcriptome-wide gene expression in the last two decades. Modern RNA sequencing techniques such as single-cell RNA sequencing (scRNA-seq) and spatial transcriptomics (ST) have been developed in recent years, allowing researchers to quantify gene expression in single-cell resolution or to profile gene activity patterns in 2-dimensional space across tissue. While useful, data collected from these techniques always come with noise, and appropriate filtering and cleaning are required for reliable downstream analyses. In this dissertation, I investigate multiple quality-related issues in scRNA-seq and ST experiments, and I develop, implement, evaluate and apply statistical methods to adjust for them. A unifying theme of this work is that all these methods aim at improving data quality and allowing for better power and precision in downstream analyses. For scRNA-seq data, the quality issue we discuss in this dissertation is distinguishing barcodes associated with real cells from those binding background noise. In droplet-based scRNA-seq experiments, raw data contains both cell barcodes that should be retained for downstream analysis as well as background barcodes that are uninformative and should be filtered out. Due to ambient RNAs presenting in all the barcodes, cell barcodes are not easily distinghished from background barcodes. Both misclassified background barcodes and cell barcodes induce misleading results in downstream analyses. Existing filtering methods test barcodes individually and consequently do not leverage the strong cell-to-cell correlation present in most datasets. To improve cell detection, we introduce CB2, a cluster-based approach for distinguishing real cells from background barcodes. As demonstrated in simulated and case study datasets, CB2 has increased power for identifying real cells which allows for the identification of novel subpopulations and improves downstream differential expression analyses. We then present a benchmark study to evaluate the performance of cell detection methods, including CB2, on public scRNA-seq datasets covering a variety of experiment protocols. In recent years, variants of scRNA-seq techniques have been developed for specialized biological tasks. While the data structures remain the same as the standard scRNA-seq experiment, the underlying data properties can alter a lot. Here, we propose the first benchmark study to provide a thorough comparison across existing cell detection methods in scRNA-seq data, and to guide users to choose the appropriate methods for their experiments. Evaluation metrics include power, precision, computational efficiency, robustness, and accessibility. In addition, we provide investigation and guidance on appropriately choosing filtering parameters in order to improve data quality. For ST data, we uncover, for the first time, a novel quality issue that genes expressed at one tissue region bleed out and contaminate nearby tissue regions. ST is a powerful and widely-used approach for profiling transcriptome-wide gene expression across a tissue with emerging applications in molecular medicine and tumor diagnostics. Recent ST experiments utilize slides containing thousands of spots with spot-specific barcodes that bind RNAs. Ideally, unique molecular identifiers at a spot measure spot-specific expression, but this is often not the case owing to bleed from nearby spots, an artifact we refer to as spot swapping. We design a creative human-mouse chimeric ST experiment to validate the existence of spot swapping. Spot swapping hinders inferences of region-specific gene activities and tissue annotations. In order to decontaminate ST data, we

propose SpotClean, a probabilistic model that measures the spot swapping effect and estimates gene expression using EM algorithm. SpotClean is shown to provide a more accurate estimation of the underlying gene expression, increase the specificity of marker gene signals, and, more importantly, allow for improved tumor diagnostics.

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