Automated Bioinformatics Analysis via AutoBA

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Abstract—Here we introduce Automated Bioinformatics Analysis (AutoBA), the firsr autonomous AI agent designed explicitly for regular omics data analysis based on large language models. AutoBA simplifies the analytical process by requiring minimal user input while delivering detailed step-by-step plans for various bioinformatics tasks. Through rigorous validation by expert bioinformaticians, AutoBA's robustness and adaptability are affirmed across a diverse range of omics analysis cases, including whole genome/exome sequencing (WGS/WES), chromatin immunoprecipitation assays with sequencing (ChIP-seq), RNA sequencing (RNA-seq), single-cell RNA-seq, spatial transcriptomics and so on. AutoBA's unique capacity to self-design analysis processes based on input data variations further underscores its versatility. Compared with online bioinformatic services, AutoBA offers five LLM backends, with options for both online and local usage, prioritizing data security and user privacy. Moreover, different from the predefined pipeline, AutoBA has adaptability in sync with emerging bioinformatics tools. Overall, AutoBA represents an advanced and convenient tool, offering robustness and adaptability for conventional bioinformatics analysis.

Index Terms—Bioinformatics, Omics analysis, Large language model, Agent.

1 Introduction

Bioinformatics is an interdisciplinary field that encompasses computational, statistical, and biological approaches to analyze, understand and interpret complex biological data [1], [2], [3]. With the rapid growth of gigabyte-sized biological data generated from various high-throughput technologies, bioinformatics has become an essential tool for researchers to make sense of these massive datasets and extract meaningful biological insights. The applications of bioinformatics typically cover diverse fields such as genome analysis [4], [5], [6], structural bioinformatics [7], [8], [9], systems biology [10], data and text mining [11], [12], [13], phylogenetics [14], [15], [16], and population analysis [17], [18], which has further enabled significant advances in personalized medicine [19] and drug discovery [5].

In broad terms, bioinformatics could be categorized into two primary domains: the development of innovative algorithms to address various biological challenges [20], [21], [22], [23], [24], and the application of established tools to analyze extensive biological datasets [25], [26], especially high-throughput sequencing data. Developing new bioinformatics software requires a substantial grasp of biology and programming expertise. Alongside the development of novel computational methods, one of the most prevalent applications of bioinformatics is the investigation of biological data using the existing tools and pipelines [27], [28], which typically involves a sequential, flow-based analysis of omics data, encompassing variety types of datasets like whole genome sequencing (WGS) [29], whole exome sequencing (WES), RNA sequencing (RNA-seq) [30], single-cell RNA-seq (scRNA-Seq) [31], transposase-accessible chromatin with sequencing (ATAC-Seq) [32], ChIP-seq [33], and spatial transcriptomics [34].

For example, the conventional analytical framework for bulk RNA-seq involves a meticulously structured sequence

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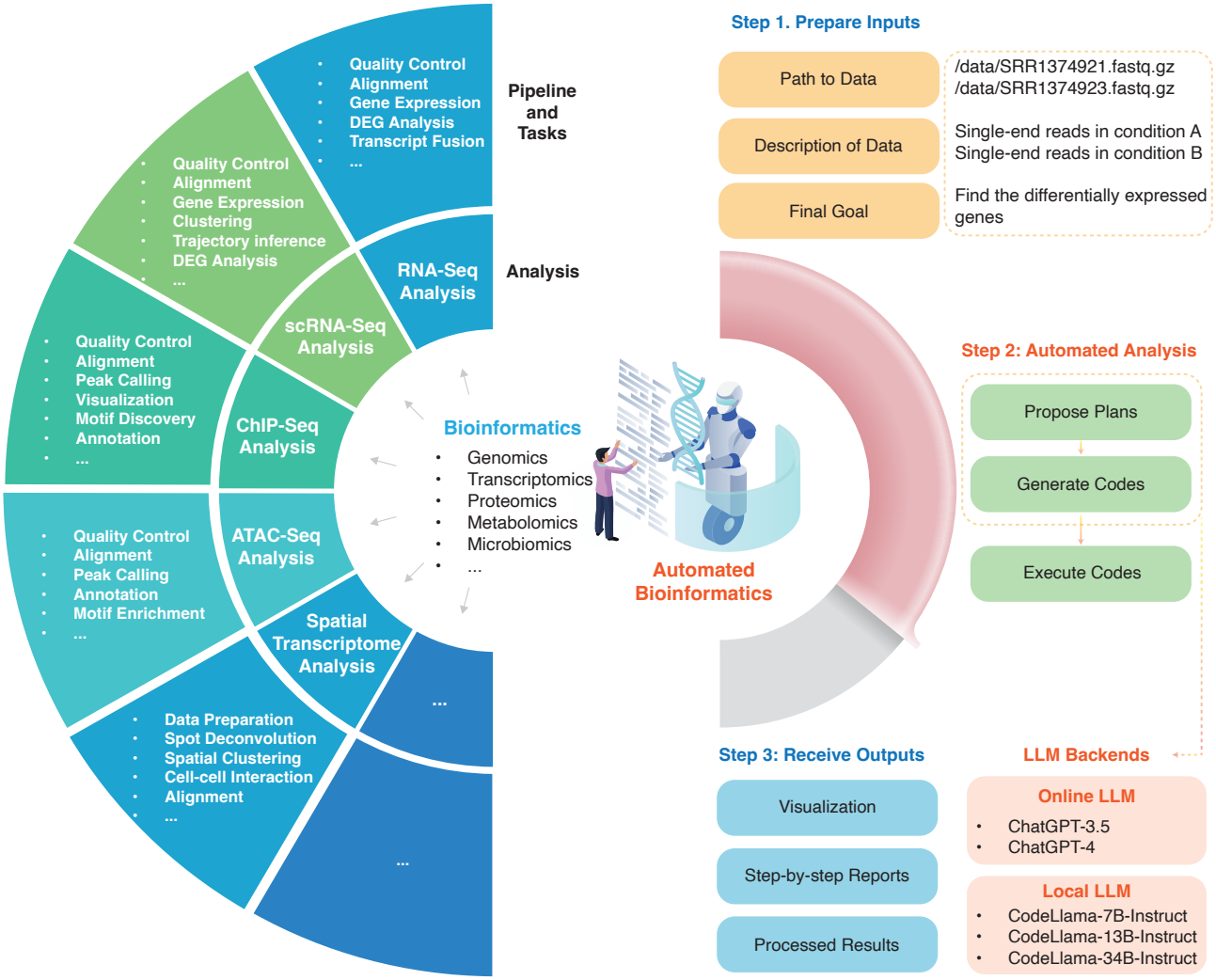

Methods	Easy to Master	Save Time	Rapid Redevelopment	Generalizability	Robustness	Privacy
AutoBA	✓✓✓	✓✓✓	✓✓✓	✓✓✓	✓✓✓	✓✓✓
Conventional Bioinformatics Tools	✓	✓	✓✓	✓	✓✓	✓✓✓
Online Webserver	✓✓	✓✓	✗	✓	✓	✗

Fig. 1. **Design of AutoBA.** AutoBA stands as the first autonomous AI agent meticulously crafted for conventional bioinformatics analysis. Remarkably user-friendly, AutoBA simplifies the analytical process by requiring minimal user input, including data path, data description, and the final objective, while delivering detailed step-by-step plans for various bioinformatics tasks. With these inputs, it autonomously proposes analysis plans, generates code, executes codes, and conducts subsequent data analysis by using our well-designed prompts. AutoBA was implemented as open-source software that offers five LLM backends, with options for both online and local deployment, prioritizing data security and user privacy and offering a streamlined and efficient solution for bioinformatics tasks. Step 1 and Step 3 require human involvement, while Step 2 requires no human involvement.

of computational steps [35]. This intricate pipeline reveals its complexity through a series of carefully orchestrated stages. It begins with quality control [36], progresses to tasks such as adapter trimming [37] and the removal of low-quality reads, and then moves on to critical steps like genome or transcriptome alignment [38]. Furthermore, it extends to some advanced tasks, including the identification of splice junctions [39], quantification through read counting [40], and the rigorous examination of differential gene expression [41]. Moreover, the pipeline delves into the intricate domain

TABLE 1

Summary of AutoBA application scenarios in bioinformatics multi-omics analysis. The table displays a comprehensive list of real-world cases utilized to assess AutoBA, providing information on the class of the cases, the respective task name, and the corresponding case ID.

Bioinformatics Pipelines	Tasks	Types of Omics	Case ID
WGS data analysis	Genome assembly	Genomics	1.1
WGS/WES data analysis	Somatic SNV+indel calling	Genomics	2.1
WGS/WES data analysis	Somatic SNV+indel calling and annotation	Genomics	2.2
WGS/WES data analysis	Structure variation identification with normal	Genomics	2.3
WGS/WES data analysis	Structure variation identification without normal	Genomics	2.4
ChIP-seq data analysis	Peak calling	Genomics	3.1
ChIP-seq data analysis	Motif discovery for binding sites	Genomics	3.2
ChIP-seq data analysis	Functional enrichment of target gene	Genomics	3.3
Bisulfite-Seq data analysis	Identifying DNA methylation	Genomics	4.1
ATAC-seq data analysis	Identifying open chromatin regions	Genomics	5.1
DNase-seq data analysis	Identifying Dnasel hypersensitive site	Genomics	6.1
4C-seq data analysis	Find genomics interactions	Genomics	7.1
Nanopore DNA sequencing data analysis	Genome assembly	Genomics	8.1
Nanopore DNA sequencing data analysis	Tandem repeats variation identification	Genomics	8.2
PacBio DNA sequencing data analysis	Genome assembly	Genomics	9.1
RNA-Seq data analysis	Find Differentially expressed genes	Transcriptomics	10.1
RNA-Seq data analysis	Identify the top5 downregulated genes	Transcriptomics	10.2
RNA-Seq data analysis	Predict Fusion gene with annotation	Transcriptomics	10.3
RNA-Seq data analysis	Isoform expression	Transcriptomics	10.4
RNA-Seq data analysis	Splicing analysis	Transcriptomics	10.5
RNA-Seq data analysis	APA analysis	Transcriptomics	10.6
RNA-Seq data analysis	RNA editing	Transcriptomics	10.7
RNA-Seq data analysis	Circular RNA identification	Transcriptomics	10.8
Small RNA sequencing data analysis	microRNA quantification	Transcriptomics	11.1
Small RNA sequencing data analysis	microRNA prediction	Transcriptomics	11.2
CAGE-seq data analysis	TSS identification	Transcriptomics	12.1
3′ end-seq data analysis	PAS (polyadenylation site) identification	Transcriptomics	13.1
Nanopore RNA sequencing data analysis	Isoform expression	Transcriptomics	14.1
PacBio RNA sequencing data analysis	Isoform expression	Transcriptomics	15.1
CLIP-seq data analysis	Identify protein-RNA crosslink sites	Transcriptomics	16.1
RIP-seq data analysis	Find enriched genes bounded by RBP	Transcriptomics	16.2
Ribo-seq data analysis	Identify translated ORFs	Transcriptomics	17.1
single-cell RNA-seq data analysis	Cell clustering from fastq data	Transcriptomics	18.1
single-cell RNA-seq data analysis	Find differentially expressed genes based on count matrix	Transcriptomics	18.2
single-cell RNA-seq data analysis	Find marker genes based on count matrix	Transcriptomics	18.3
single-cell RNA-seq data analysis	Cell clustering and visualization	Transcriptomics	18.4
Spatial transcriptomics	Neighborhood enrichment analysis	Transcriptomics	19.1
Spatial transcriptomics	Single-cell mapping	Transcriptomics	19.2
Mass spectrometry data analysis	Protein expression quantification	Proteomics	20.1
Mass spectrometry data analysis	Metabolites quantification	Metabolomics	21.1

of alternative splicing [42] and isoform analysis [43]. This progressive journey ultimately ends in downstream tasks like the exploration of functional enrichment [44], providing a comprehensive range of analytical pursuits. Compared to bulk RNA-seq, ChIP-seq involves distinct downstream tasks, such as peak calling [45], motif discovery [46], peak annotation [47] and so on. In summary, the analysis of different types of omics data requires professional skills and an understanding of the corresponding field. Moreover, the methods and pipelines might vary across different bioinformaticians and they even may evolve with the development of more advanced algorithms.

Meanwhile, online bioinformatics analysis platforms are currently in vogue, such as iDEP [48], ICARUS [49] and STellaris [50]. However, they often necessitate the uploading of either raw data or pre-processed statistics by users, which

could potentially give rise to additional privacy concerns and data leakage risks [51].

In the context described above, the bioinformatics community grapples with essential concerns regarding the standardization, portability, and reproducibility of analysis pipelines [52], [53], [54]. Moreover, achieving proficiency in utilizing these pipelines for data analysis demands additional training, posing challenges for many wet lab researchers due to its potential complexity and time-consuming nature. Even dry-lab researchers may find the repetitive process of running and debugging these pipelines to be quite tedious [55]. Consequently, there is a growing anticipation within the community for the development of a more user-friendly, low-code, multi-functional, automated, and natural language-driven intelligent tool tailored for bioinformatics analysis. Such a tool has the potential to generate significant excitement and benefit researchers across the field.

Over the past few months, the rapid advancement of Large Language Models (LLMs) [56] has raised substantial expectations for the enhancement of scientific research, particularly in the field of biology [57], [58], [59]. These advancements hold promise for applications such as disease diagnosis [60], [61], [62], [63], drug discovery [64], and all. In the realm of bioinformatics, LLMs, such as ChatGPT, also demonstrate immense potential in tasks related to bioinformatics education [65] and code generation [66]. While researchers have found ChatGPT to be a valuable tool in facilitating bioinformatics research, such as data analysis, there remains a strong requirement for human involvement in the process. AutoGPT [67], as a recently developed, advanced, and experimental open-source autonomous AI agent, has the capacity to string together LLM-generated "thoughts" to autonomously achieve user-defined objectives. Nevertheless, given the intricate and specialized nature of bioinformatics tasks, the direct application of AutoGPT in this field still presents significant challenges.

In this study, we introduce Automated Bioinformatics Analysis (AutoBA), a groundbreaking autonomous AI agent tailored for comprehensive and conventional bioinformatics analysis. AutoBA simplifies user interactions to just three inputs: data path, data description, and the final objective. This powerful tool autonomously proposes analysis plans, generates code, executes codes, and conducts subsequent data analysis by using our well-designed prompts. We implemented AutoBA as an open-source software that offers five LLM backends, with options for both online and local usage, prioritizing data security and user privacy. To show the reliability of AutoBA, we tested it in a large number of real-world bioinformatics analysis scenarios. In summary, AutoBA represents a pioneering leap in the application of Large Language Models (LLMs) and automated AI agents within the domain of bioinformatics, highlighting their potential to accelerate future research in this field.

2 METHODS

2.1 The overall framework design of AutoBA

AutoBA is the first autonomous AI agent tailor-made for conventional bioinformatics analysis. As illustrated in Fig. 1, conventional bioinformatics typically entails the use of pipelines to analyze diverse data types such as WGS, WES, RNA-seq, single-cell RNA-seq, ChIP-seq, ATAC-seq, spatial transcriptomics, and more, all requiring the utilization of various software tools. Users are traditionally tasked with selecting the appropriate software tools based on their specific analysis needs. In practice, this process involves configuring the environment, installing software, writing code, and addressing code-related issues, which are time-consuming and labor-intensive.

With the advent of AutoBA, this labor-intensive process is revolutionized. Users are relieved from the burden of dealing with multiple software packages and need only provide three key inputs: the data path (e.g., */data/SRR1374921.fasta.gz*), data description (e.g., *single-end reads in condition A*), and the ultimate analysis goal (e.g., *identify differentially expressed genes*). AutoBA takes over by autonomously analyzing the data, generating comprehensive step-by-step plans, composing code for each step, executing the generated code, and conducting in-depth analysis. Depending on the complexity and difficulty of the tasks, users can expect AutoBA to complete the tasks within a

matter of minutes to a few hours, all without the need for additional manual labor (Table 1 and Fig. 2).

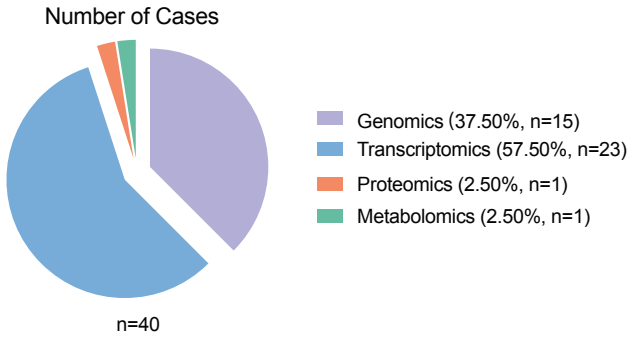

Fig. 2. **Pie chart of all cases used for validating AutoBA.**

2.2 Prompt engineering of AutoBA

To initiate AutoBA, users provide three essential inputs: the data path, data description, and the previously mentioned analysis objective. AutoBA comprises three distinct phases: the planning phase, the code generation phase, and the execution phase as shown in Step 2 of Fig. 1. During the planning phase, AutoBA meticulously outlines a comprehensive step-by-step analysis plan. This plan includes details such as the software name and version to be used at each step, along with guided actions and specific sub-tasks for each stage. Subsequently, in the code generation phase, AutoBA systematically follows the plan and generates codes for sub-tasks, which entails procedures like configuring the environment, installing the necessary software, and writing code. Then, in the execution phase, AutoBA executes the generated code. In light of this workflow, AutoBA incorporates two distinct prompts: one tailored for the planning phase and the other for the code generation phase. Intensive experiments have shown that these two sets of prompts are essential for the proper functioning of AutoBA in automated bioinformatics analysis tasks.

The prompt for the planning phase is displayed as follows:

```
prompt = {
    "role": "Act as a bioinformatician, the
       rules must be strictly followed!",
    "rules": [
        "When acting as a bioinformatician,
           you strictly cannot stop acting
           as a bioinformatician.",
        "All rules must be followed strictly
           .",
        "You should use information in input
            to write a detailed plan to
           finish your goal.",
        f"You should include the software
           name and should not use those
           software: {self.blacklist}.",
        "You should only respond in JSON
           with the required format.",
        "Your JSON should only enclosed in
           double quotes."
    ],
    "input": [
        "You have the following information
           in a list with the format file
           path: file description. I
           provide those files to you, so
           you don't need to prepare the
           data.",
        data_list
    ],
    "goal": self.current_goal,
    "format": {
        "plan": [
        "Your detailed step-by-step sub-
           tasks to finish your goal."
        ]
    }
}
```

The prompt for the code generation phase is displayed as follows:

```
prompt = {
    "role": "Act as a bioinformatician, the
       rules must be strictly followed!",
    "rules": [
        "When acting as a bioinformatician,
           you strictly cannot stop acting
           as a bioinformatician.",
        "All rules must be followed strictly
           .",
        "You are provided a system with
           specified constraints."
        "The history of what you have done
           is provided, you should take the
            name changes of some files into
            account, or use some output
           from previous steps.",
        "You should use all information you
           have to write bash codes to
           finish your current task.",
        "All code requirements must be
           followed strictly when you write
            codes.",
        "You should only respond in JSON
           with the required format.",
        "Your JSON should only enclosed in
           double quotes."
    ],
    "system": [
        "You have a Ubuntu 18.04 system",
        "You have a conda environment named
           abc",
        "You do not have any other software
           installed"
    ],
    "input": [
        "You have the following information
           in a list with the format file
           path: file description. I
           provide those files to you, so
           you don't need to prepare the
           data.",
```

```
        data_list
    ],
    "history": self.history_summary,
    "current task": self.current_goal,
    "code requirement": [
        f"You should not use those software:
            {self.blacklist}.",
        'You should always source activate
            the environment abc first, add
            conda-forge and bioconda to the
            list of channels',
        'You should always install
            dependencies with -y with conda
            or pip.',
        'You should pay attention to the
            number of input files and do not
             miss any.',
        'You should process each file
            independently and can not use
            FOR loop.',
        'You should use the path for all
            files according to input and
            history.',
        'You should use the default values
            for all parameters that are not
            specified.',
        'You should not repeat what you have
             done in history.',
        'You should only use software
            directly you installed with
            conda.',
        'If you use Rscript -e, you should
            make sure all variables exist in
             your command, otherwise you
            need check your history to
            repeat previous steps and
            generate those variables.'
    ],
    "format": {
        "tool": "name of the tool you use",
        "code": "bash code to finish the
            current task"
    }
}
```

In the two aforementioned prompt designs, the term *blacklist* pertains to the user's personalized list of prohibited software. The current default blacklist contains several tools frequently caused errors during our testing processes. Meanwhile, *data list* encompasses the inputs necessary for AutoBA, encompassing data paths and data descriptions. The term *current goal* serves as the final objective during the planning phase and as the sub-goal in the execution phase, while *history summary* encapsulates AutoBA's memory of previous actions and information.

2.3 Memory management of AutoBA

A memory mechanism is incorporated within AutoBA to enable it to generate code more effectively by drawing from past actions, thus avoiding unnecessary repetition of certain steps. AutoBA meticulously logs the outcome of each step in a specific format, and all these historical records become part of the input for the subsequent prompt. In the planning phase, memories are structured as follows: "Firstly, you provided input in the format 'file path: file description' in a list: <data list>. You devised a detailed plan to accomplish your overarching objective. Your overarching goal is <global goal>. Your plan involves <tasks>." In the code generation phase, memories follow this format: "Then, you successfully completed the task: <task> with the corresponding code: <code>."

2.4 Evaluation of AutoBA

The results produced by AutoBA undergo thorough validation by bioinformatics experts. This validation process encompasses a comprehensive review of the proposed plans, generated codes, execution of the code, and confirmation of the results for accuracy and reliability. AutoBA's development and validation are built upon a specific environment and software stack, which includes Ubuntu version 18.04, Python 3.10.0, and openai version 0.27.6. These environment and software specifications form the robust foundation for AutoBA's functionality in the field of bioinformatics, ensuring its reliability and effectiveness.

2.5 Online and local LLM backends of AutoBA

AutoBA offers several versions of LLM backends, including online backends based on ChatGPT-3.5 and ChatGPT-4, and local LLMs, including CodeLlama-7B-Instruct, CodeLlama-13B-Instruct and CodeLlama-34B-Instruct [68].

3 Results

3.1 AutoBA proposes detailed analysis plans for tasks

AutoBA offers a robust capability to generate a highly detailed and customized analysis plan, leveraging the user's input, which encompasses critical elements such as data paths, data descriptions, and objective descriptions.

As an example, in Fig. 3, the user supplied four RNA-Seq samples: two from the LoGlu group (SRR1374921.fastq.gz and SRR1374922.fastq.gz, mouse pancreatic islets cultured at low ambient glucose) and two from the HiGlu group

(SRR1374923.fastq.gz and SRR1374924.fastq.gz, mouse pancreatic islets cultured at high ambient glucose) from Benner et al.'s paper [69]. Additionally, the user also provided the mouse reference genome (mm39.fa) and genome annotation (mm39.ncbiRefSeq.gtf). The primary objective of this case was to identify differentially expressed genes between the two data groups. Using textual inputs only, AutoBA generated a detailed, step-by-step analysis plan during the planning phase, as outlined below:

```
1. First, I will use the "Trimmomatic"
    software to trim the adapters from the
    single-end mouse rna-seq reads. The
    input files for this step will be "./
    examples/case1.1/data/SRR1374921.fastq.
    gz", "./examples/case1.1/data/SRR1374922
    .fastq.gz", "./examples/case1.1/data/
    SRR1374923.fastq.gz", "./examples/case1
    .1/data/SRR1374924.fastq.gz" and the
    adapter file "./examples/case1.1/data/
    TruSeq3-SE.fa".

2. Next, I will use the "Hisat2" software to
     align the trimmed reads to the mouse
    mm39 genome. The input files for this
    step will be the output files from the
    previous step and the genome file "./
    examples/case1.1/data/mm39.fa".

3. Then, I will use the "Samtools" software
    to convert the alignment output files
    from Hisat2 (in SAM format) to BAM
    format.

4. After that, I will use the "HTSeq"
    software to count the number of reads
    mapped to each gene. The input files for
     this step will be the BAM files from
    the previous step and the annotation
    file "./examples/case1.1/data/mm39.
    ncbiRefSeq.gtf".

5. Finally, I will use the "DESeq2" software
     to identify the differentially
    expressed genes. The input files for
    this step will be the count files from
    the previous step.
```

Within each step of the plan outlined above, AutoBA provides precise instructions regarding the required software, including names like Trimmomatic, Hisat2, Samtools, HTSeq, and DESeq2, along with clear sub-tasks for each analytical stage. This level of tailored planning ensures that the analysis process aligns precisely with the user's objectives, promoting both efficiency and accuracy in data processing and results generation.

3.2 AutoBA generates precise codes for sub-tasks

During the code generation phase, AutoBA generates code in bash format for every sub-task of the plan established in the planning phase. These scripts encompass environment setup, software installation, and tailored code for software utilization. Parameters and data paths specific to the software are meticulously incorporated. As exemplified in Fig. 3, the preliminary phase of the differentially expressed genes (DEG) analysis constitutes the essential process of adapter trimming, an indispensable preprocessing step in the context of raw RNA-Seq data. Within this critical step, AutoBA automatically generated code, including activating the conda environment, installing software packages, and calling software to analyze data as shown below:

```
source activate abc
conda config --add channels conda-forge
conda config --add channels bioconda
conda install -y Trimmomatic
Trimmomatic SE -phred33 ./examples/case1.1/
    data/SRR1374921.fastq.gz ./examples/
    case1.1/output/SRR1374921_trimmed.fastq.
    gz ILLUMINACLIP:./examples/case1.1/data/
    TruSeq3-SE.fa:2:30:10
Trimmomatic SE -phred33 ./examples/case1.1/
    data/SRR1374922.fastq.gz ./examples/
    case1.1/output/SRR1374922_trimmed.fastq.
    gz ILLUMINACLIP:./examples/case1.1/data/
    TruSeq3-SE.fa:2:30:10
Trimmomatic SE -phred33 ./examples/case1.1/
    data/SRR1374923.fastq.gz ./examples/
    case1.1/output/SRR1374923_trimmed.fastq.
    gz ILLUMINACLIP:./examples/case1.1/data/
    TruSeq3-SE.fa:2:30:10
Trimmomatic SE -phred33 ./examples/case1.1/
    data/SRR1374924.fastq.gz ./examples/
    case1.1/output/SRR1374924_trimmed.fastq.
    gz ILLUMINACLIP:./examples/case1.1/data/
    TruSeq3-SE.fa:2:30:10
```

The generated code further underwent a meticulous and thorough validation process, which included a manual verification and execution performed by experienced and proficient bioinformaticians, as meticulously documented in Table 2 and Supplementary information. This critical validation step ensures the accuracy and reliability of the code, reaffirming the robustness of AutoBA.

3.3 AutoBA adeptly manages similar tasks with robustness

In practical bioinformatics applications, even when researchers are working with similar data types, such as RNA-Seq, it's noteworthy that analyses often manifest variations

RNA-Seq Analysis **Case 1.1: Find differentially expressed genes**

User's Inputs

Data and Description
SRR1374921.fastq.gz: single-end mouse rna-seq reads, replicate 1 in LoGlu group
SRR1374922.fastq.gz: single-end mouse rna-seq reads, replicate 2 in LoGlu group
SRR1374923.fastq.gz: single-end mouse rna-seq reads, replicate 1 in HiGlu group
SRR1374924.fastq.gz: single-end mouse rna-seq reads, replicate 2 in HiGlu group
TruSeq3-SE.fa: trimming adapter
mm39.fa: mouse mm39 genome fasta
mm39.ncbiRefSeq.gtf: mouse mm39 genome annotation

Goal
Find the differentially expressed genes

Generated Plans by AutoBA

1. First, I will use the 'Trimmomatic' software to trim the adapters from the single-end mouse rna-seq reads. The input files for this step will be './examples/case1.1/data/SRR1374921.fastq.gz', './examples/case1.1/data/SRR1374922.fastq.gz', './examples/case1.1/data/SRR1374923.fastq.gz', './examples/case1.1/data/SRR1374924.fastq.gz' and the adapter file './examples/case1.1/data/TruSeq3-SE.fa'.
2. Next, I will use the 'Hisat2' software to align the trimmed reads to the mouse mm39 genome. The input files for this step will be the output files from the previous step and the genome file './examples/case1.1/data/mm39.fa'.
3. Then, I will use the 'Samtools' software to convert the alignment output files from Hisat2 (in SAM format) to BAM format.
4. After that, I will use the 'HTSeq' software to count the number of reads mapped to each gene. The input files for this step will be the BAM files from the previous step and the annotation file './examples/case1.1/data/mm39.ncbiRefSeq.gtf'.
5. Finally, I will use the 'DESeq2' software to identify the differentially expressed genes. The input files for this step will be the count files from the previous step.

Generated Codes by AutoBA

```
# Step 1
source activate abc
conda config --add channels conda-forge
conda config --add channels bioconda
conda install -y trimmomatic
trimmomatic SE -phred33 ./examples/case1.1/data/SRR1374921.fastq.gz ./examples/case1.1/output/SRR1374921_trimmed.fastq.gz
ILLUMINACLIP:./examples/case1.1/data/TruSeq3-SE.fa:2:30:10
trimmomatic SE -phred33 ./examples/case1.1/data/SRR1374922.fastq.gz ./examples/case1.1/output/SRR1374922_trimmed.fastq.gz
ILLUMINACLIP:./examples/case1.1/data/TruSeq3-SE.fa:2:30:10
trimmomatic SE -phred33 ./examples/case1.1/data/SRR1374923.fastq.gz ./examples/case1.1/output/SRR1374923_trimmed.fastq.gz
ILLUMINACLIP:./examples/case1.1/data/TruSeq3-SE.fa:2:30:10
trimmomatic SE -phred33 ./examples/case1.1/data/SRR1374924.fastq.gz ./examples/case1.1/output/SRR1374924_trimmed.fastq.gz
ILLUMINACLIP:./examples/case1.1/data/TruSeq3-SE.fa:2:30:10

# Step 2
source activate abc
conda config --add channels conda-forge
conda config --add channels bioconda
conda install -y hisat2
hisat2 -x ./examples/case1.1/data/mm39.fa -U ./examples/case1.1/output/SRR1374921_trimmed.fastq.gz -S ./examples/case1.1/output/SRR1374921.sam
hisat2 -x ./examples/case1.1/data/mm39.fa -U ./examples/case1.1/output/SRR1374922_trimmed.fastq.gz -S ./examples/case1.1/output/SRR1374922.sam
hisat2 -x ./examples/case1.1/data/mm39.fa -U ./examples/case1.1/output/SRR1374923_trimmed.fastq.gz -S ./examples/case1.1/output/SRR1374923.sam
hisat2 -x ./examples/case1.1/data/mm39.fa -U ./examples/case1.1/output/SRR1374924_trimmed.fastq.gz -S ./examples/case1.1/output/SRR1374924.sam

# Step 3
source activate abc
conda config --add channels conda-forge
conda config --add channels bioconda
conda install -y samtools
samtools view -S -b ./examples/case1.1/output/SRR1374921.sam > ./examples/case1.1/output/SRR1374921.bam
samtools view -S -b ./examples/case1.1/output/SRR1374922.sam > ./examples/case1.1/output/SRR1374922.bam
samtools view -S -b ./examples/case1.1/output/SRR1374923.sam > ./examples/case1.1/output/SRR1374923.bam
samtools view -S -b ./examples/case1.1/output/SRR1374924.sam > ./examples/case1.1/output/SRR1374924.bam

# Step 4
source activate abc
conda config --add channels conda-forge
conda config --add channels bioconda
conda install -y htseq
htseq-count -f bam -s no ./examples/case1.1/output/SRR1374921.bam ./examples/case1.1/data/mm39.ncbiRefSeq.gtf
> ./examples/case1.1/output/SRR1374921.count
htseq-count -f bam -s no ./examples/case1.1/output/SRR1374922.bam ./examples/case1.1/data/mm39.ncbiRefSeq.gtf
> ./examples/case1.1/output/SRR1374922.count
htseq-count -f bam -s no ./examples/case1.1/output/SRR1374923.bam ./examples/case1.1/data/mm39.ncbiRefSeq.gtf
> ./examples/case1.1/output/SRR1374923.count
htseq-count -f bam -s no ./examples/case1.1/output/SRR1374924.bam ./examples/case1.1/data/mm39.ncbiRefSeq.gtf
> ./examples/case1.1/output/SRR1374924.count

# Step 5
source activate abc
conda install -y bioconductor-deseq2
Rscript -e "library('DESeq2'); countData <- read.table('./examples/case1.1/output/SRR1374921.count', './examples/case1.1/output/SRR1374922.count',
'./examples/case1.1/output/SRR1374923.count', './examples/case1.1/output/SRR1374924.count', header=TRUE, row.names=1); colData <-
DataFrame(condition=factor(c('LoGlu', 'LoGlu', 'HiGlu', 'HiGlu'))); dds <- DESeqDataSetFromMatrix(countData=countData, colData=colData, design=~condition);
dds <- DESeq(dds); res <- results(dds); write.csv(as.data.frame(res), file='./examples/case1.1/output/differential_expression_results.csv')"
```

Fig. 3. **Example of applying AutoBA to find differentially expressed genes with RNA-Seq data.** In this case, the user supplied four RNA-seq datasets, comprising two from the LoGlu group and two from the HiGlu group. The primary objective of this analysis was to identify differentially expressed genes across the two datasets.

stemming from diverse sources. These variations are primarily attributed to disparities in the characteristics of input data and the distinct objectives pursued in the analytical process.

As exemplified in Case 10.1 (find differentially expressed genes), Case 10.2 (identify the top five down-regulated genes in HiGlu group), and Case 10.3 (predict fusion genes), when performing RNA-Seq analysis, users may have distinct final goals, necessitating adjustments in software and parameter selection during the actual execution. In comparison to case 10.1, AutoBA introduces a 6th step in case 10.2, tailored for screening the top five differentially expressed genes to fulfill the user's specific requirements as shown in the code below:

```
Rscript -e "library('pheatmap'); library('
    DESeq2'); res <- read.csv('./examples/
    case1.2/output/
    differential_expression_results.csv',
    row.names=1); res_ordered <- res[order(
    res$log2FoldChange),];
    top5_downregulated <- head(res_ordered,
    5);
```

3.4 AutoBA adjusts analysis based on task and input data variations

Alignment is an essential step for bioinformatic analysis, for which multiple tools have been developed for distinct tasks. For instance, tools including STAR [70] and HISAT2 [71] designed for RNA-seq data analysis are splicing aware, which is efficient in identifying junction reads that map to two distal positions in the reference genome. Besides, long-read sequencing data from Pacific Bioscience (PacBio) and Oxford Nanopore Technology (ONT) also require specialized tools for the alignment, for which Minimap2 [72] is the most widely used method. Moreover, each read from single-cell sequencing data contains barcodes for UMI and cell labels, which needs to be integrated with the alignment. CellRanger is a popular software with this capacity. Therefore, bioinformatic analysis should use appropriate tools for the alignment based on the types of tasks. Interestingly, we found that AutoBA has learned this knowledge and can correctly employ the tool for the alignment (Fig. 4a).

For many bioinformatic analysis, multiple tools are available but require different conditions of inputs. For instance, to identify structural variations from tumor WGS/WES data, the method "manta" [73] can handle the analysis against the matched normal. On the other hand, tools like "Pindel" [74] that relies on the detection of breakpoints with the reference genome, only conduct analysis on the tumor samples. We found that AutoBA can automatically select "manta" when the matched normal samples were provided and correctly utilized the parameters "–normalBam" and "–tumorBam". However, if only the tumor samples were provided in the input data, AutoBA will select "Pindel" for the analysis (Fig. 4b). These results suggest that AutoBA learned the requirements of different bioinformatic tools and is capable of selecting appropriate tools based on different conditions of the input data.

```
manta --normalBam ../output/case2.3/
    SRR23015874.recalibrated.bam --tumorBam
    ../output/case2.3/SRR23015876.
    recalibrated.bam --referenceFasta ./
    examples/case5.1/hg38.fa --runDir ../
    output/case2.3/manta_SRR23015874
```

3.5 Apply AutoBA to a variety of conventional bioinformatics analysis scenarios

To evaluate the robustness of AutoBA, we conducted assessments involving a total of 40 cases spanning four distinct types of omics data: genomics, transcriptomics, proteomics, and metabolomics as shown in Table 1 and Supplementary information.

All cases underwent an independent analysis process conducted by AutoBA and were subsequently subjected to validation by experienced bioinformatics experts. The collective results underscore the versatility and robustness of AutoBA across a spectrum of multi-omics analysis procedures in the field of bioinformatics as shown in Table 2. AutoBA demonstrates its capability to autonomously devise novel analysis processes based on varying input data, showcasing its adaptability to diverse input data and analysis objectives with a success rate of 90% (36 out of 40) for proposing plans, 82.5% (33 out of 40) for generating codes, and 65% (26 out of 40) for automated end-to-end analysis.

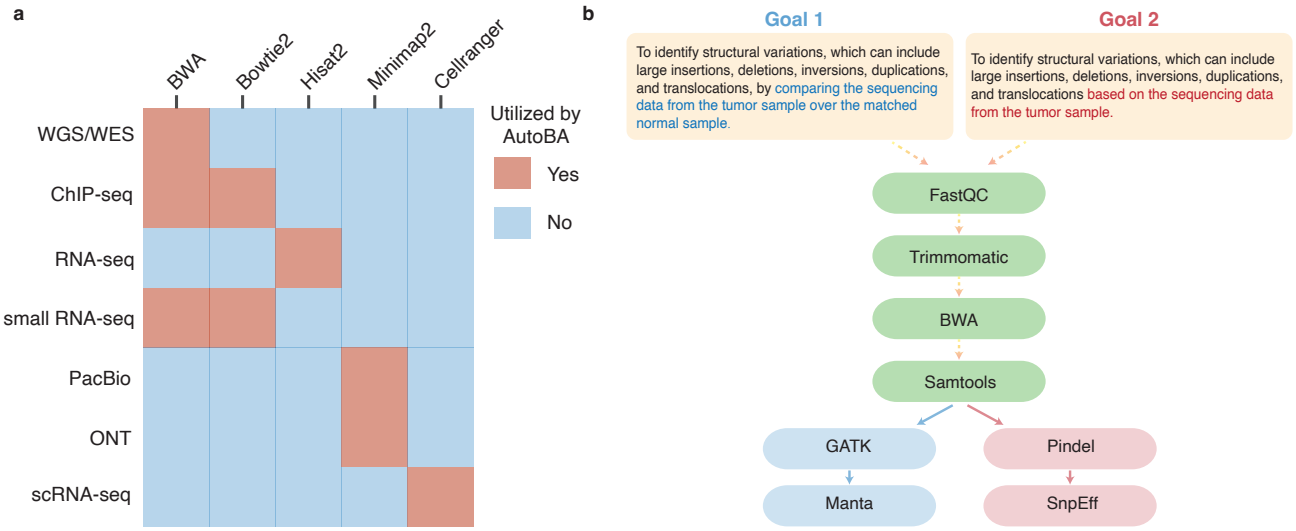

Fig. 4. **AutoBA adjusts analysis based on task and input data variations a** Heatmap illustrating options of utilizing different alignment tools for multiple tasks planned by AutoBA. **b** AutoBA utilizes the tools for identifying structure variations in tumor samples with or without the matched normal samples. The highlight shows the difference between Goal 1 and Goal 2.

4 Discussion

To our knowledge, AutoBA is the first and a pioneering autonomous AI agent tailored explicitly for conventional bioinformatics analysis for omics data. AutoBA streamlines the analytical process, requiring minimal user input while providing detailed step-by-step plans for various bioinformatics tasks. The results of our investigation reveal that AutoBA excels in accurately handling a diverse array of omics analysis tasks, such as RNA-seq, scRNA-seq, ChIP-seq, spatial transcriptomics, and so on. One of the key strengths of AutoBA is its adaptability to variations in analysis objectives. As demonstrated in the cases presented, even with similar data types, such as RNA-Seq, users often have distinct goals, necessitating modifications in software and parameter selection during execution. AutoBA effectively accommodates these variations, allowing users to tailor their analyses to specific research needs without compromising accuracy. Furthermore, AutoBA's versatility is highlighted by its ability to self-design new analysis processes based on differing input data. This autonomous adaptability makes AutoBA a valuable tool for bioinformaticians working on novel or unconventional research questions, as it can adjust its approach to the unique characteristics of the data.

Online bioinformatics analysis platforms are currently in vogue, but they often necessitate the uploading of either raw data or pre-processed statistics by users, which could potentially give rise to privacy concerns and data leakage risks. In contrast, AutoBA offers a local solution that effectively addresses these privacy issues. Moreover, AutoBA showcases its adaptability in sync with emerging bioinformatics tools, with LLM seamlessly incorporating these latest tools into the database. Furthermore, AutoBA is inclined towards selecting the most popular analytical frameworks or widely applicable tools in the planning phase, underscoring its robustness. Another distinguishing feature is AutoBA's transparent and interpretable execution process. This transparency allows professional bioinformaticians to easily modify and customize AutoBA's outputs, leveraging AutoBA to expedite the data analysis process.

Given that classical bioinformatic analysis encompasses a far broader spectrum of tasks and challenges than the 40 cases studied in this work (Table 1 and 2), it is essential to conduct more real-world applications by our potential users to further comprehensively validate the robustness of AutoBA. We found that a large proportion (36%, 5 out of 14) of failed cases in executing code is due to the tools in conda being problematic, not in a regular form (end with .sh, .pl et al), or requiring an edited config file, suggesting a demand for more standard bioinformatics tools. Furthermore, taking into account the timeliness of the training data used for

TABLE 2

Summary of AutoBA generated results evaluated by bioinformatics experts. The table presents an assessment conducted by bioinformatics experts on the analysis plan proposed by AutoBA, along with the generated codes and the code execution. If the evaluation passes, it is displayed as success, while instances of failure are accompanied by detailed explanations of the specific reasons for the failure. Additionally, we provide a summary of the software tools automatically chosen by AutoBA for each case, as well as the total time taken to generate the corresponding code.

Case ID	Propose Plans	Generate Codes	Execute Codes	Tools Used	Time Cost (without Excuting Codes) in Minutes
1.1	Success	Success	Success	FastQC, Trimmomatic, SPAdes, QUAST	3
2.1	Success	Success	Success	FastQC, Trimmomatic, BWA, Samtools, GATK	8
2.2	Success	Success	Success	FastQC, Trimmomatic, BWA, Samtools, GATK, ensembl-vep	8
2.3	Success	Success	Success	FastQC, Trimmomatic, BWA, Samtools, GATK, manta	18
2.4	Success	Success	Failed: pindel it requires configuration file	FastQC, Trimmomatic, BWA, Samtools, pindel, SnpEff	6
3.1	Success	Success	Success	FastQC, Trim Galore, Bowtie 2, Samtools, MACS2,BEDTools, IGV	6
3.2	Success	Success	Success	FastQC, Trim Galore, Bowtie2, MACS2, HOMER, MEME	4
3.3	Failed: DESeq2 is not suitable for peaks identified by MACS2	-	-	FastQC, BWA, MACS, BEDTools, DESeq2, g:Profiler, R	6
4.1	Success	Success	Success	Trim Galore, Bismark, IGV	9
5.1	Success	Success	Failed: (wrongly usedBEDTools)	Trim Galore, BWA, Samtools, MACS2, BEDTools	8
6.1	Success	Success	Success	FastQC, Cutadapt, BWA, MACS2, IGV, GREAT	5
7.1	Success	Success	Success	FastQC,BEDTools, Samtools, Bowtie 2, R	6
8.1	Success	Success	Failed: racon medaka wrongly used the parameters	canu, Minimap2, Racon, Flye, Medaka, Bandage	7
8.2	Failed: cannot find a correct pipeline	-	-	Minimap2, Samtools, trf	7
9.1	Success	Failed: install the wrong tool, pb-falcon rather than falcon	-	Canu, FALCON, Quiver, MUMmer,	7
10.1	Success	Success	Success	FASTQC, Trimmomatic, HISAT2, htseq, DESeq2	5
10.2	Success	Success	Success	FASTQC, Trimmomatic, HISAT2, htseq, DESeq2, gprofileR	5
10.3	Success	Success	Success	gunzip, HISAT2, fusioncatcher, gffcompare	6
10.4	Success	Success	Success	Trim Galore, HISAT2, Samtools, StringTie	5
10.5	Success	Success	Success	Trimmomatic, HISAT2, Samtools, StringTie, featureCounts, rMATs	6
10.6	Success	Failed: DaPars (not available in conda)	-	Trim Galore, HISAT2, StringTie, DaPars	7
10.7	Failed: cannot find a correct pipeline	-	-	FastQC, Trimmomatic, HISAT2, Samtools, StringTie, ballgowan, GATK	7
10.8	Success	Failed: CIRI2 (not available in conda)	-	Trim Galore, HISAT2, CIRI2, CIRIQuant	5
11.1	Success	Success	Success	Fastqc, Cutadapt, Bowtie, Samtools, subread/featureCounts, DESeq2, edgeR	11
11.2	Success	Success	Failed: conda of miRDeep2 is problematic	Fastqc, Cutadapt, Bowtie, Samtools, featureCounts, miRDeep2, DESeq2, edgeR	11
12.1	Success	Success	Success	Fastqc, Trimmomatic, HISAT2, HTSeq/htseq-count, CAGEr	6
13.1	Failed: cannot find a correct pipeline	-	-	Trim Galore, HISAT2, StringTie, DaPars	5
14.1	Success	Success	Failed: prepDE.py no need to run with 'python prepDE.py'	Minimap2, Samtools, StringTie, DESeq2	9
15.1	Success	Success	Success	Minimap2, Samtools, StringTie, cufflinks	5
16.1	Success	Success	Failed: conda of Piranha is problematic	FastQC,Cutadapt, Bowtie2, Samtools,BEDTools,Piranha	6
16.2	Success	Success	Success	FastQC, Trim Galore, HISAT2, htseq, DESeq2	4
17.1	Success	Success	Failed: not regular conda of ribotaper	FastQC, Trim Galore, HISAT2, Samtools, StringTie, RiboTaper	7
18.1	Success	Success	Success	Cell Ranger, Seurat	5
18.2	Success	Success	Success	Scanpy	8
18.3	Success	Success	Success	Scanpy	6
18.4	Success	Success	Success	Scanpy	5
19.1	Success	Success	Success	Squidpy, AnnData	5
19.2	Success	Success	Success	AnnData, Scanpy, Tangram	3
20.1	Success	Success	Success	proteowizard, OpenMS	15
21.1	Success	Success	Success	pymzml, pandas, numpy, scipy	13

large language models, it's important to note that some of the most recently proposed methods in bioinformatics may still pose challenges in automatically generating code by AutoBA. Therefore, a future endeavor to train an up-to-date large language model explicitly tailored for bioinformatics can significantly enhance AutoBA's ability to maintain up-to-date code generation capabilities. Nevertheless, AutoBA represents a significant advancement in the field of bioin-

formatics, offering a user-friendly, efficient, and adaptable solution for a wide range of omics analysis tasks. Its capacity to handle diverse data types and analysis goals, coupled with its robustness and adaptability, positions AutoBA as a valuable asset in the pursuit of accelerating bioinformatics research. We anticipate that AutoBA will find extensive utility in the scientific community, supporting researchers in their quest to extract meaningful insights from complex biological data.

5 Data availability

The RNA-seq dataset could be downloaded from Sequence Read Archive (SRA) with IDs: SRR1374921, SRR1374922, SRR1374923, and SRR1374924. The dataset for case 1.3 could be downloaded from https://github.com/STAR-Fusion/STAR-Fusion-Tutorial/wiki. The scRNA-seq dataset could be downloaded from http://cf.10xgenomics.com/samples/cell-exp/1.1.0/pbmc3k/pbmc3k_filtered_gene_bc_matrices.tar.gz. The ChIP-seq dataset could be downloaded with IDs: SRR620204, SRR620205, SRR620206, and SRR620208. The Spatial Transcriptomics dataset could be downloaded from https://doi.org/10.5281/zenodo.6334774. The CAGE-seq dataset could be downloaded from SRA with IDs: SRR11351697, SRR11351698, SRR11351700, and SRR11351701. The 3'end-seq dataset could be downloaded from SRA with IDs: SRR17422754, SRR17422755, SRR17422756, and SRR17422757. The CLIP-seq dataset could be downloaded from ENCODE (https://www.encodeproject.org) with IDs: ENCLB742AYH and ENCLB770EDJ. The Ribo-seq data could be downloaded from SRA with IDs: RR12354645 and RR12354646. The raw single-cell RNA sequencing data could be downloaded from 10X genomics. The PacBio long-read sequencing data could be downloaded from SRA with IDs: SRR19552218 and SRR19785215. The small RNA-seq data could be downloaded from the previous study [75].

6 Code availability

The AutoBA software is publicly available at https://github.com/JoshuaChou2018/AutoBA.

7 Credit author statement

Conceptualization: J.Z. and X.G. Design: J.Z., B.Z. and X.G. Code implementation: J.Z. Application: J.Z., B.Z., X.C., H.L. Drafting of the manuscript: J.Z. and B.Z. Critical revision of the manuscript for important intellectual content: J.Z., B.Z., X.X., S.C., X.G. Supervision: J.Z. and X.G. Funding acquisition: X.G.

8 Acknowledgements

Juexiao Zhou, Bin Zhang, Xiuying Chen, Haoyang Li, Xiaopeng Xu, Siyuan Chen and Xin Gao were supported in part by grants from the Office of Research Administration (ORA) at King Abdullah University of Science and Technology (KAUST) under award number FCC/1/1976-44-01, FCC/1/1976-45-01, REI/1/5202-01-01, REI/1/5234-01-01, REI/1/4940-01-01, RGC/3/4816-01-01, and REI/1/0018-01-01.

9 Competing Interests

The authors have declared no competing interests.

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