

## Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

### Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a Confirmed

- ☐ ☒ The exact sample size ( $n$ ) for each experimental group/condition, given as a discrete number and unit of measurement
- ☐ ☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- ☐ ☒ The statistical test(s) used AND whether they are one- or two-sided  
*Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
- ☒ ☐ A description of all covariates tested
- ☐ ☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- ☐ ☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
- ☐ ☒ For null hypothesis testing, the test statistic (e.g.  $F$ ,  $t$ ,  $r$ ) with confidence intervals, effect sizes, degrees of freedom and  $P$  value noted  
*Give  $P$  values as exact values whenever suitable.*
- ☐ ☒ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- ☒ ☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- ☐ ☒ Estimates of effect sizes (e.g. Cohen's  $d$ , Pearson's  $r$ ), indicating how they were calculated

*Our web collection on [statistics for biologists](#) contains articles on many of the points above.*

### Software and code

Policy information about [availability of computer code](#)

Data collection No software was used for the data collection.

Data analysis INSPIRE (<https://github.com/jiazhao97/INSPIRE>, <https://inspire-tutorial.readthedocs.io/en/latest>), python v3.8.15, pytorch v1.12.1, pandas v1.5.3, numpy v1.24.4 were used for designing and running the algorithm. SpiceMix v1.0.0 (<https://github.com/ma-compbio/SpiceMix>), NSFH v1.0.0 (<https://github.com/willtownes/nsf-paper>), PASTE v1.4.0 (<https://github.com/raphael-group/paste>), PRECAST v1.6.4 (<https://github.com/feiyong/PRECAST>), mofapy2 v0.7.2 (<https://github.com/bioFAM/mofapy2>), GraphST v1.0.0 (<https://github.com/JinmiaoChenLab/GraphST>), Harmony v0.1 (<https://github.com/immunogenomics/harmony>), Seurat v4.3.0 (<https://github.com/satijalab/seurat>), LIGER v1.0.1 (<https://github.com/welch-lab/liger>), STAGATE v1.0.0 (<https://github.com/zhanglabtools/STAGATE>), Banksy v0.1.6 (<https://github.com/prabhakarlab/Banksy>), SpaGCN v1.2.7 (<https://github.com/jianhuupenn/SpaGCN>), SpatialGlue v1.0.0 (<https://github.com/JinmiaoChenLab/SpatialGlue>), BayesSpace v1.5.1 (<https://github.com/edward130603/BayesSpace>), BASS v1.1.0 (<https://github.com/zhengli09/BASS>), SpatialLeiden v0.2.0 (<https://github.com/HiDiHlabs/SpatialLeiden>) were used for the benchmarking study. scanpy v1.8.2, anndata v0.9.2, louvain v0.8.0, umap-learn v0.5.5, matplotlib v3.5.3 were used for preprocessing and post-processing of the spatial transcriptomics data.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

## Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

All data used in this work are publicly available through online sources.

Human dorsolateral prefrontal cortex dataset profiled by Visium platform (<https://research.libd.org/spatialLIBD/>);

Mouse brain sagittal anterior, sagittal posterior, and coronal sections profiled by Visium (<https://www.10xgenomics.com/datasets>);

Mouse brain sections profiled by Slide-seq V2 ([https://singlecell.broadinstitute.org/single\\_cell](https://singlecell.broadinstitute.org/single_cell));

Mouse brain sections profiled by MERFISH (<https://doi.brainimaginglibrary.org/doi/10.35077/act-bag>);

Mouse whole-embryo section profiled by seqFISH (<https://crukci.shinyapps.io/SpatialMouseAtlas/>);

Mouse skin sections during wound healing profiled by the Visium platform (<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE178758>);

Human breast cancer sections profiled by Xenium (<https://www.10xgenomics.com/products/xenium-in-situ/preview-dataset-human-breast>);

Mouse whole-embryo datasets across different developmental time points profiled by Stereo-seq (<https://db.cngb.org/stomics/mosta/>);

Mouse hypothalamic preoptic region sections profiled by MERFISH (<https://doi.org/10.5061/dryad.8t8s248>);

Mouse hippocampus region sections profiled by SRARmap PLUS (<https://doi.org/10.5281/zenodo.7458952>);

Mouse brain sections profiled by the ST platform (<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE147747>).

## Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender

N.A.

Reporting on race, ethnicity, or other socially relevant groupings

N.A.

Population characteristics

N.A.

Recruitment

N.A.

Ethics oversight

N.A.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

## Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

## Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size

We used 11 publicly available data in the manuscript.

Data exclusions

We removed genes, cells, and spots by applying standard preprocessing steps such as removing lowly expressed genes, cells, and spots.

Replication

While we did not generate any data, all code is provided openly to enable others to replicate our results.

Randomization

Randomization does not apply to this work because there is no experimental data collected in this study.

Blinding

Blinding does not apply to this work because there is no experimental data collected in this study.

## Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

## Materials & experimental systems

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input checked="" type="checkbox"/>	<input type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants

## Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

## Plants

Seed stocks	Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.
Novel plant genotypes	Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.
Authentication	Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.