

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                                                                                                                                                                                                                                                                                      |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The exact sample size ( <i>n</i> ) for each experimental group/condition, given as a discrete number and unit of measurement                                                                                                                               |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly                                                                                                                                    |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided<br><i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>                                                               |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A description of all covariates tested                                                                                                                                                                                                                     |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons                                                                                                                                        |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> 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) |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i> ) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted<br><i>Give P values as exact values whenever suitable.</i>                     |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings                                                                                                                                                                      |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes                                                                                                                                                |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i> ), 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 | All analysis in this manuscript is from publicly available data and the data sources are described in the Data Availability section.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Data analysis   | <p>The code for data analysis for this manuscript is detailed in the Code Availability section, specifically on Github at <a href="https://github.com/SydneyBioX/wSIR_2024">https://github.com/SydneyBioX/wSIR_2024</a>. The algorithm software is available online at <a href="https://github.com/SydneyBioX/wSIR">https://github.com/SydneyBioX/wSIR</a></p> <p>We compared wSIR against established dimension reduction methods designed for spatial transcriptomics data, or designed for more general applications. These were SpatialPCA (v 1.3.0), DRSC (v 3.7), PRECAST (v 1.8), STAMP (from scdm v 0.1.0), PCA (from stats v 4.5.1), LDA (from MASS v 7.3.65), pls (v 2.8.5), GraphPCA (from st-graphpca v 0.0.5) and SIR (own own implementation, wSIR v 0.99.3).</p> <p>For performing the method and our analysis, we used the following packages in addition to those above: abind (v 1.4.8), anndata (v 0.8.0), ape (v 5.8.1), aricode (v 1.1.0), bench (v 1.1.4), BiocGenerics (v 0.56.0), BiocParallel (v 1.44.0), bluster (v 1.20.0), clusterProfiler (v 4.18.4), cowplot (1.2.0), DescTools (v 0.99.60), distances (v 0.1.13), doBy (v 4.7.1), dplyr (v 1.2.1), DR.SC (v 3.7), DropletUtils (v 1.30.0), energy (v 1.7.12), FNN (v 1.1.4.1), ggplot2 (v 4.0.3), ggplotify (v 0.1.3), ggpubr (v 0.6.3), ggrepel (v 0.9.8), grid (v 4.5.1), gt (v 1.2.0), magrittr (v 2.0.5), Matrix (v 1.7.5), methods (v 4.5.1), microbenchmark (v 1.5.0), MouseGastrulationData (v 1.24.0), nnet (v 7.3.20), org.Mm.eg.db (v 3.22.0), patchwork (v 1.3.2), pheatmap (v 1.0.13), Rcpp (v 1.1.1.1.1), reticulate (v 1.44.1), Rfast (v 2.1.5.2), rlang (v 1.1.6), rSPDE (v 2.5.2), scatter (v 1.38.1), scan (v 1.38.1), scuttle (v 1.20.1), Seurat (v 5.4.0), SeuratObject (v 5.4.0), SingleCellExperiment (v 1.32.0), SpatialExperiment (v 1.20.0), StabMap (v 1.4.0), stringr (v 1.6.0), SummarizedExperiment (v 1.40.0), tidyverse (v 2.0.0), umap (v 0.2.10.0), vctrs (v 0.7.3), zellkonverter (1.20.0).</p> |

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](#)

This study used publicly available data. The mouse embryo seqFISH data was accessed via Bioconductor (version 3.19) ExperimentHub package MouseGastrulationData (version 1.18.0). The breast cancer 10x Genomics Xenium data was accessed via the 10x Genomics website (<https://www.10xgenomics.com/products/xenium-in-situ/preview-dataset-human-breast>) on 2 February 2024 and processed using MoleculeExperiment (version 1.5.1). The matching Visium data was accessed by the same website on 1 December 2024 and processed using DropletUtils (version 1.24.0). The human thymus and DLPFC data was downloaded from the cellxgene website (<https://cellxgene.cziscience.com/datasets>) on 1 October 2025.

## 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                                        | Gender- and sex-based analyses were not performed.                                            |
| Reporting on race, ethnicity, or other socially relevant groupings | Analyses related to race, ethnicity, or other socially relevant groupings were not performed. |
| Population characteristics                                         | Analyses related to population characteristics were not performed.                            |
| Recruitment                                                        | No participants were recruited.                                                               |
| Ethics oversight                                                   | No ethics oversight was required.                                                             |

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://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     | Sample sizes were already determined from public data sources           |
| Data exclusions | No data were excluded from analyses.                                    |
| Replication     | Findings were not replicated given the algorithmic nature of the study. |
| Randomization   | Samples were already determined from public data sources.               |
| Blinding        | No blinding was performed.                                              |

## 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 &amp; 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.