



SpaceNet: Pathology-guided analysis of lesion-associated spatial molecular programs

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Highlights

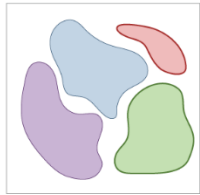
- SpaceNet integrates real pathological spatial information to identify pathology-associated information;
- SpaceNet supports both biomarker-guided and user-defined ROI analyses;
- SpaceNet accommodates multiple sc/snRNA-seq inputs and multiple spatial integration strategies;
- SpaceNet outperforms representative spatial clustering methods.



Introduction

Input of SpaceNet

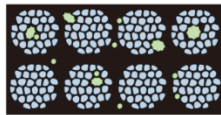
Dataset 1:
Sc/snRNA-seq pathological images



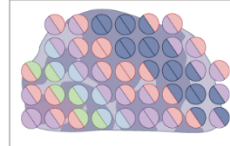
Dataset 2:
SRT



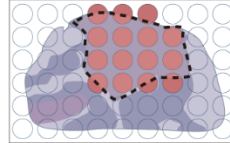
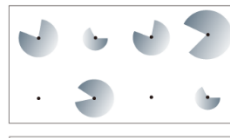
Multiple
pathological images



Mapping or
deconvolution



ROIs selection

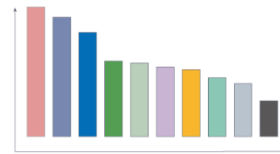


Construction of SpaceNet

Cell type



Gene score



$Score_{cell}$

$Score_{gene}$

PPI calculation



Output of SpaceNet

PPI networks

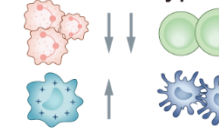
module 1



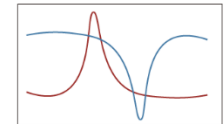
module 2



Cell type



Spatial gene regulation



Analysis of SpaceNet



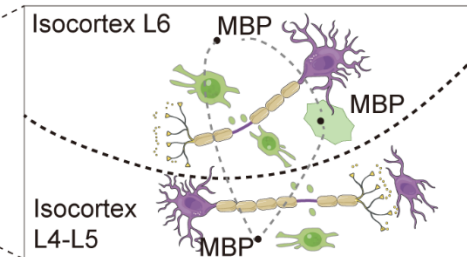
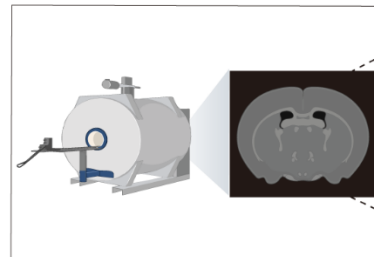
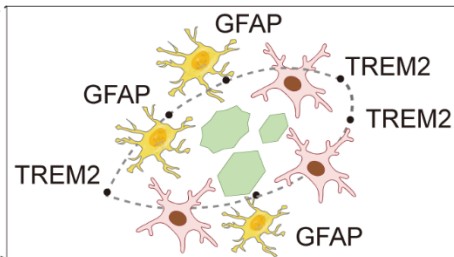
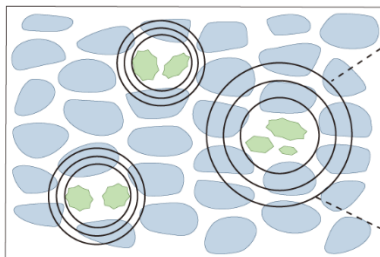
Multi-modal pathological
image information fusion



Spatial network reconstruction



The discovery of
spatial patterns



Overview of SpaceNet workflow

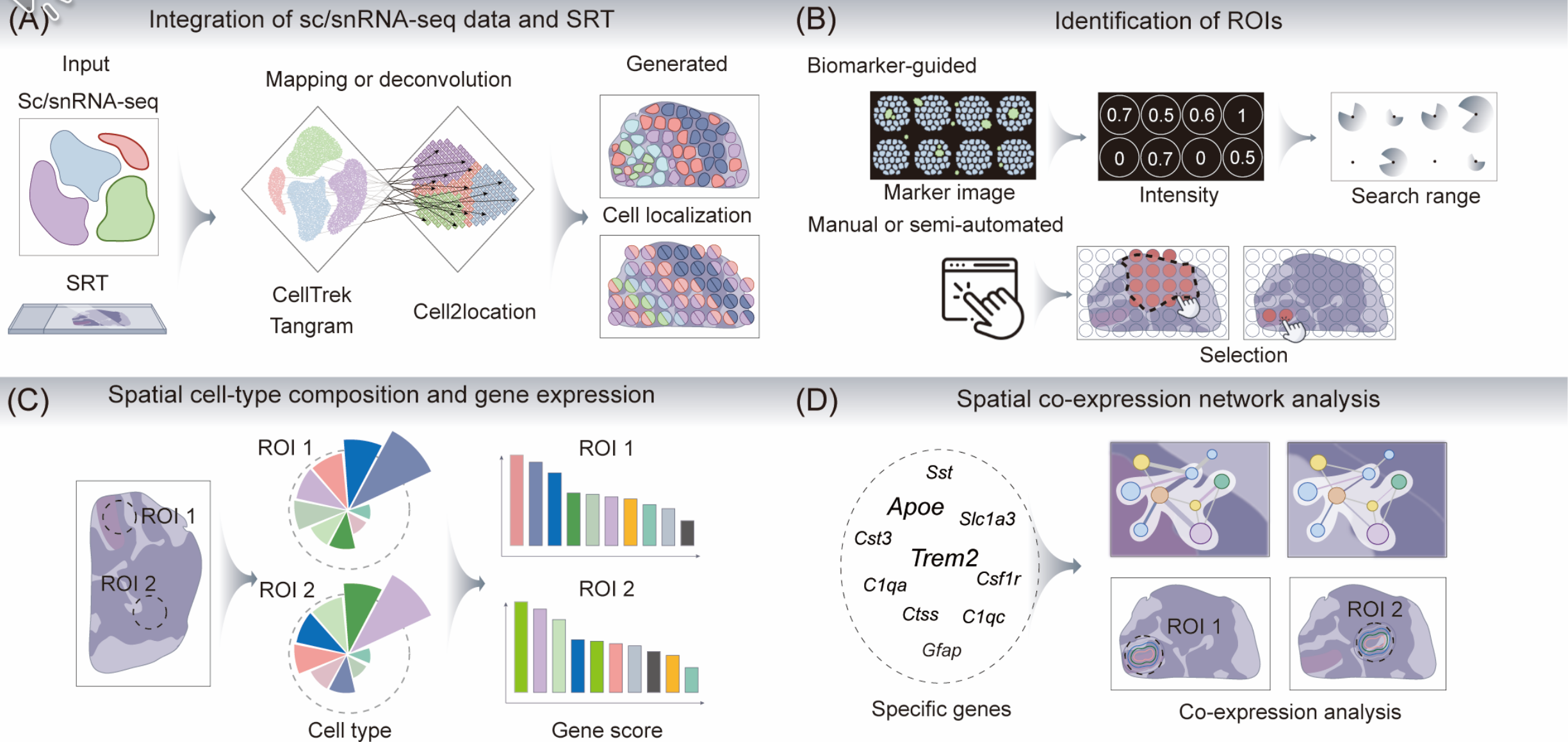


Figure 1. Schematic workflow of SpaceNet.



Benchmark analysis

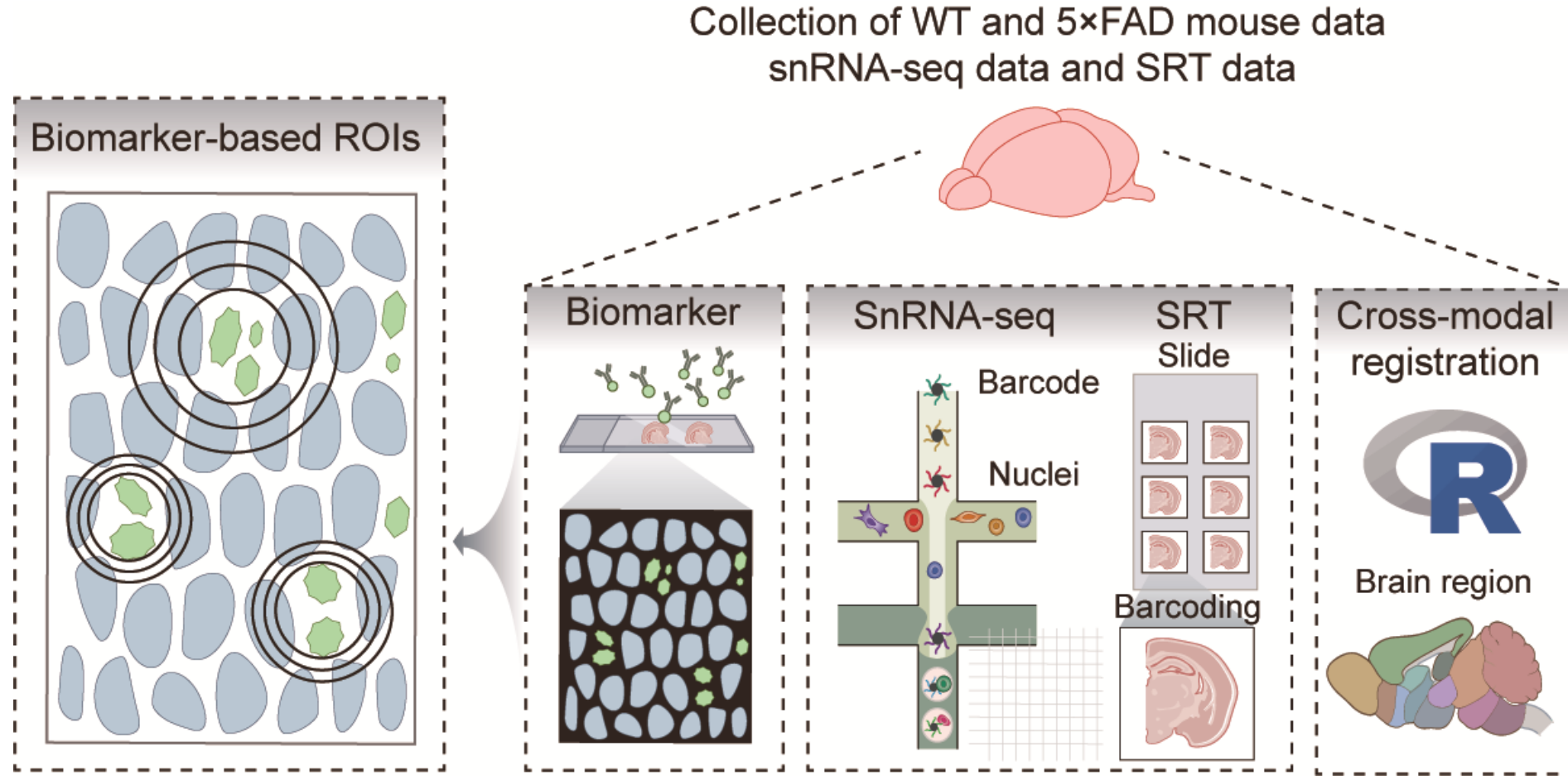
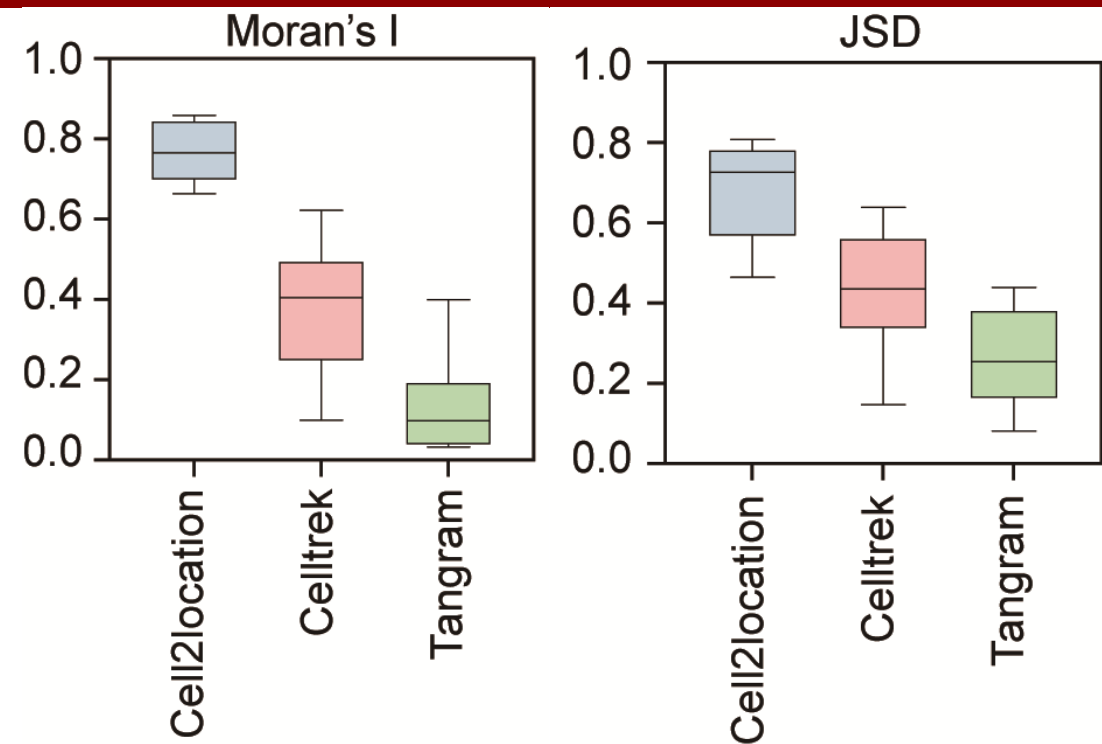
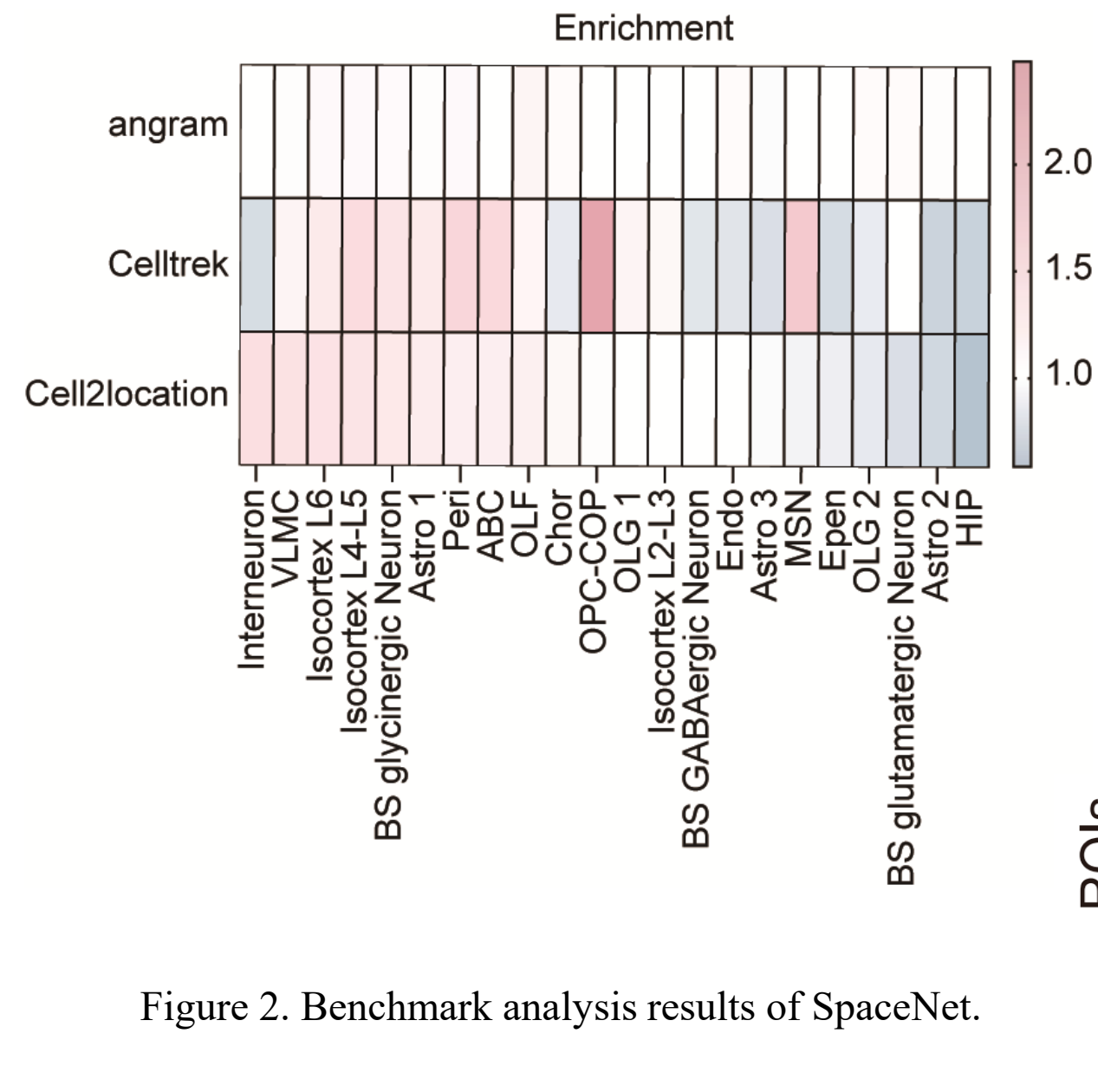


Figure 2. Overview of the multimodal benchmark dataset.

Benchmark analysis



(G)

DAPI|A β |GFAP

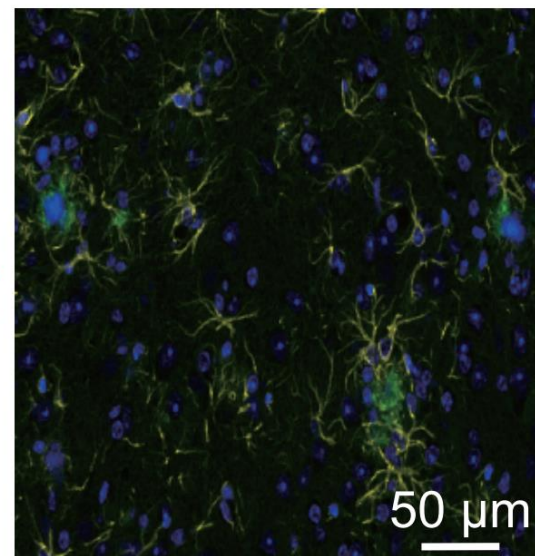


Figure 2. Benchmark analysis results of SpaceNet.



Benchmark analysis

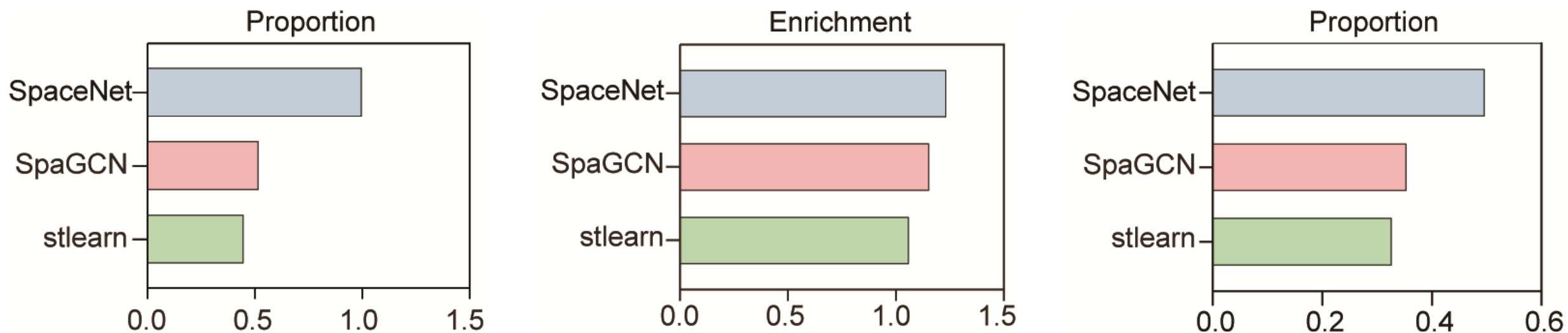
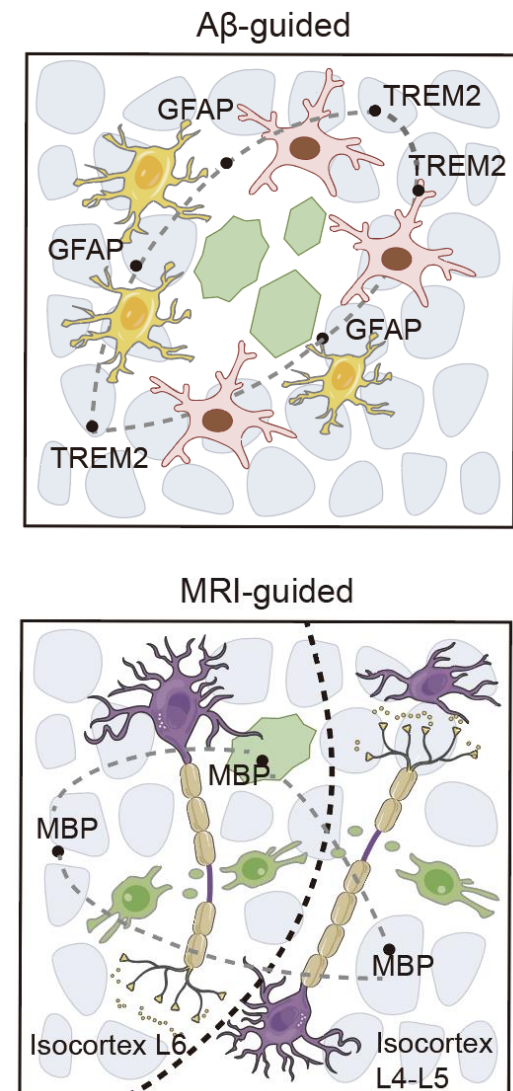
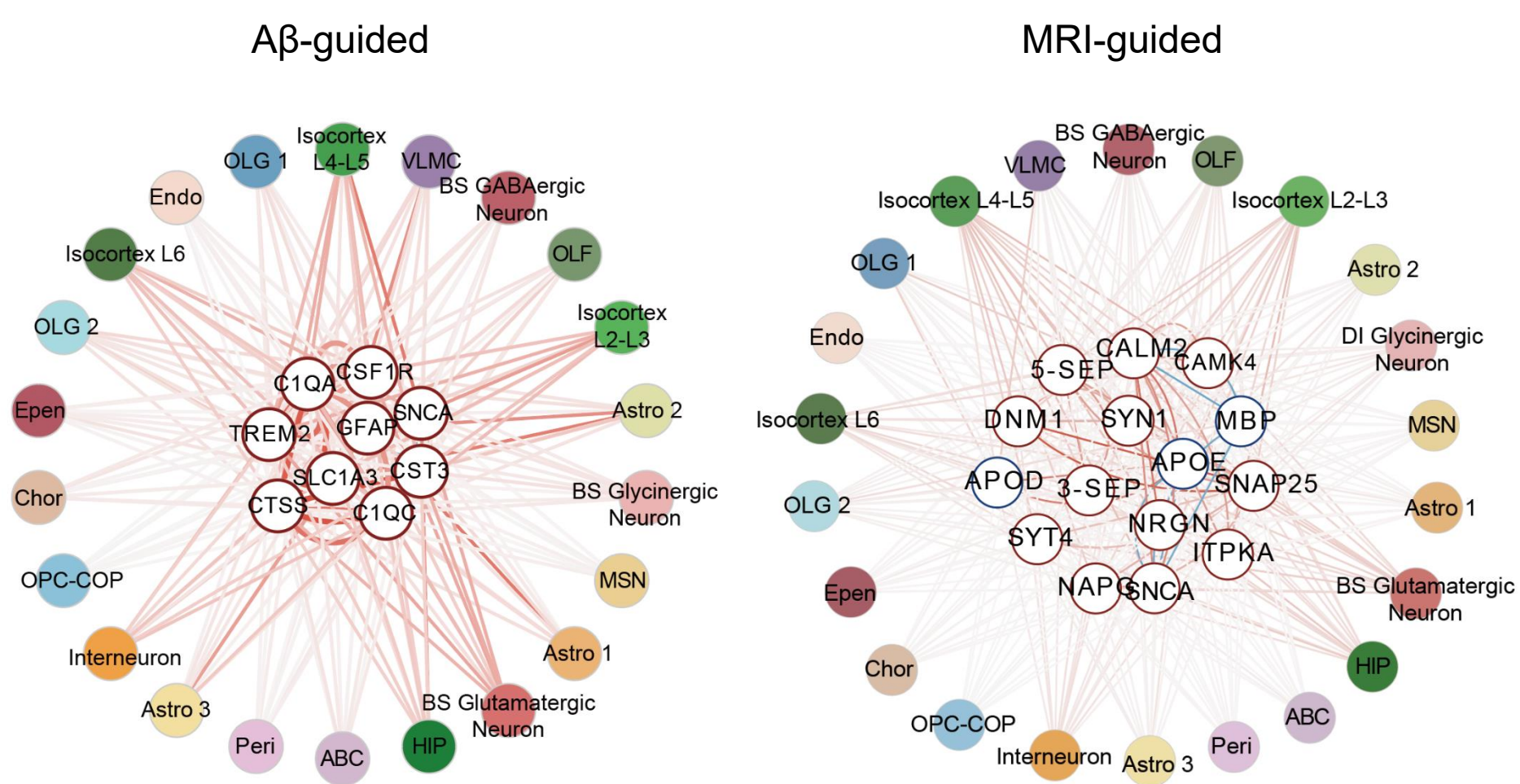


Figure 2. Benchmark analysis results of SpaceNet.



Case Study



Supplementary Figure 3. SpaceNet identifies spatial molecular networks.



User guideline

Quick start

1. Installation of SpaceNet

```
#installation of conda_env, recommended version python3.8.20, consistent with development env
cd SpaceNet-release
conda create -n spacenet python=3.8.20
conda activate spacenet

#installation of requirements
pip install -r requirements.txt
```



2. Accessibility to other softwares/database

choose one to integrate your scRNA-seq data with SRT data

- [CellTrek](#)
- [Cell2location](#)
- [Tangram](#)

visit STRING to obtain the latest complete PPI database, or use [a quick-start version of PPI database](#) (support species: human, mouse, rat)

- [STRING](#) (Optional)

visualize your result with cytoscape

- [Cytoscape](#)

3. Define ROI in your SRT data

use our [tool](#) to select ROI, or save your disease_metric in st_adata.obs

4. Running the SpaceNet pipeline on the [example dataset]

example datasets can be accessed [here](#)

- [biomarker-guided_example](#)
- [user-defined_example](#)

5. Expected output

The output of SpaceNet containing:

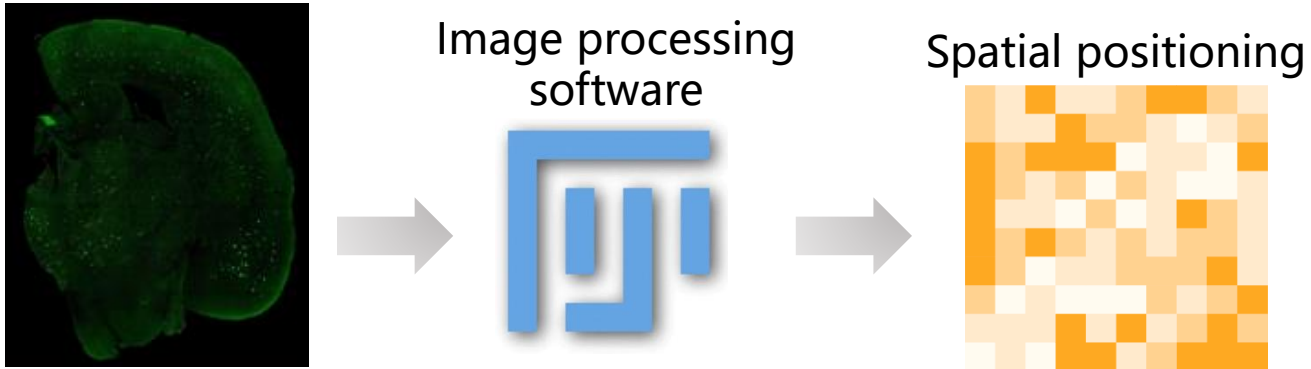
- file 1: A csv file of enriched cell-types and their enrichment score
- file 2: A csv file of enriched genes and their enrichment score
- file 3: A csv file of spatial protein-protein interactions net
- file 4: A csv file of gene-celltype net

<https://github.com/SpaTrek/SpaceNet>



User guideline

- Biomarker-guided ROI



- User-defined ROI (<https://xomics.com.cn/SpaceNet/Home.php>)



Summary



- ❑ In this study, we developed SpaceNet, a pathology-guided analytical framework that integrates imaging, spatial transcriptomics, and sc-/sn-transcriptomics to characterize localized disease-associated cellular and molecular organization.
- ❑ SpaceNet outperformed representative spatial clustering methods and providing flexibility across different pathological contexts.
- ❑ SpaceNet identified distinct pathology-associated molecular modules, including an A β -associated microglial inflammatory module and an MRI/FA-associated myelin module, revealing complementary molecular programs across different pathological contexts.
- ❑ The SpaceNet tutorial : <https://github.com/SpaTrek/SpaceNet>

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