

WEAVE SOFTWARE FOR SPATIAL MULTI-OMICS DATA INTEGRATION - COMBINING MSI AND SRT TO INVESTIGATE MOLECULAR HETEROGENEITY IN PROSTATE CANCER AND PARKINSON'S DISEASE

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Reading direction

Introduction

We describe a spatial multi-omics dataset integration pipeline, and cloud-based software suite of bioinformatics tools, allowing for combined visualisation and downstream analysis. This pipeline was applied to mass spectrometry imaging (MSI) and spatially resolved transcriptomics (SRT) measurements of human prostate cancer (PCa) and mouse models of Parkinson's disease (PD).

Methods

After co-registration and granularity matching in the Weave platform, the MSI and SRT data were directly linked, obtaining a representative mass spectrum associated with a representative SRT spot, and matched spatial readouts. Detailed pathology annotations were transferred to the shared SRT-MSI spatial coordinates.

Materials

Matched prostate normal and tumour biopsies (8 x normal, 8 x tumour) were collected from PCa patients who had undergone radical prostatectomy, snap frozen, and stored at -80°C. Serial cryosections (10 µm) were used for SRT (Visium assay, 10X Genomics) and MALDI-2 MSI analysis.

MALDI-2 MSI for lipids was performed on an Orbitrap Elite mass spectrometer (Thermo Fisher Scientific) in positive ion mode. The SRT and MSI-measured sections were H&E stained according to recommended protocols and digitised for pathologist annotations^[1].

Non-embedded snap-frozen mouse PD brain tissue was sectioned onto Visium gene expression arrays. It was firstly imaged using a MALDI FTICR instrument (Bruker Daltonics) for neurotransmitters then followed by H&E staining for microscopy and SRT measurement^[2].

Results

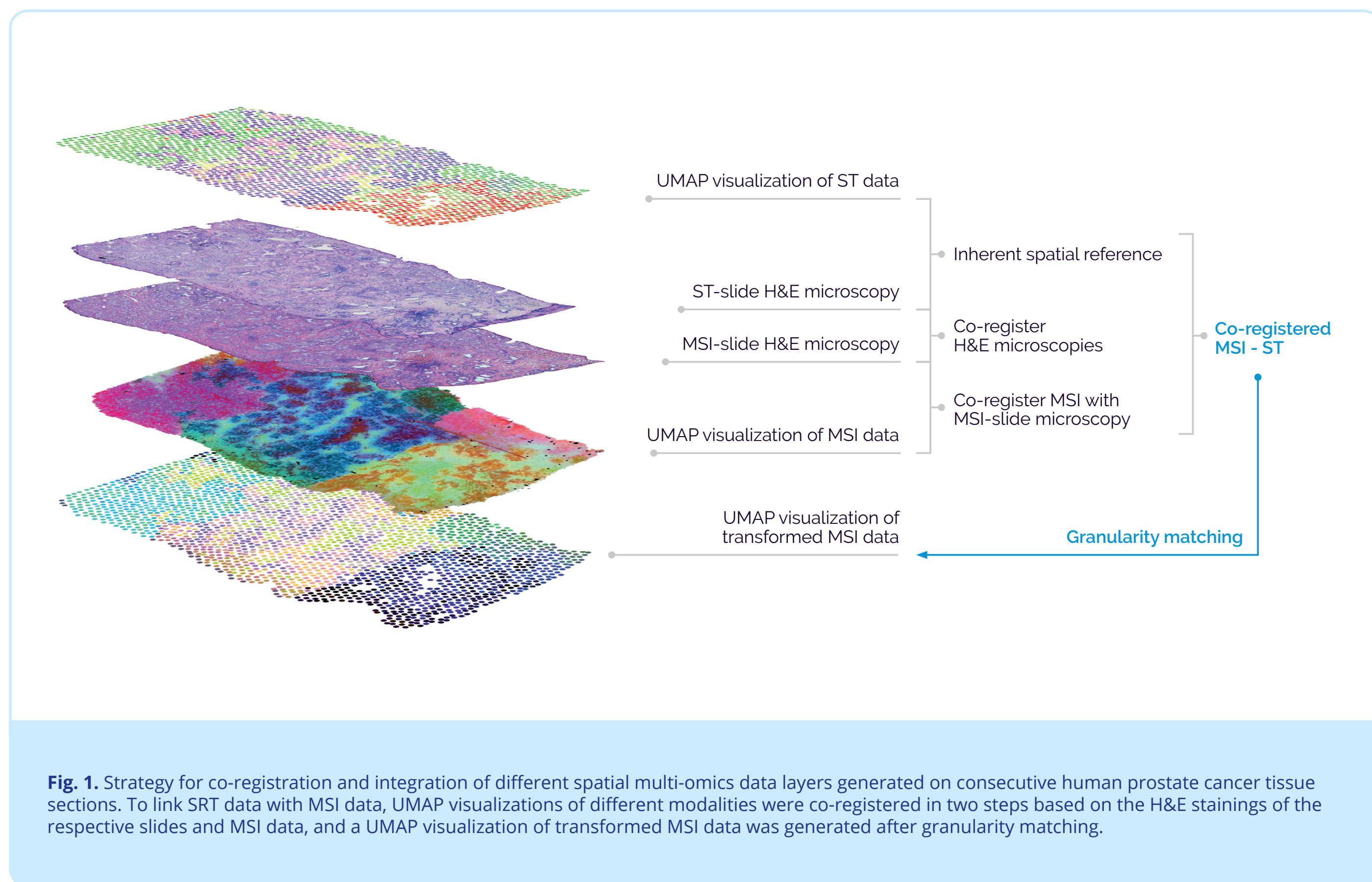
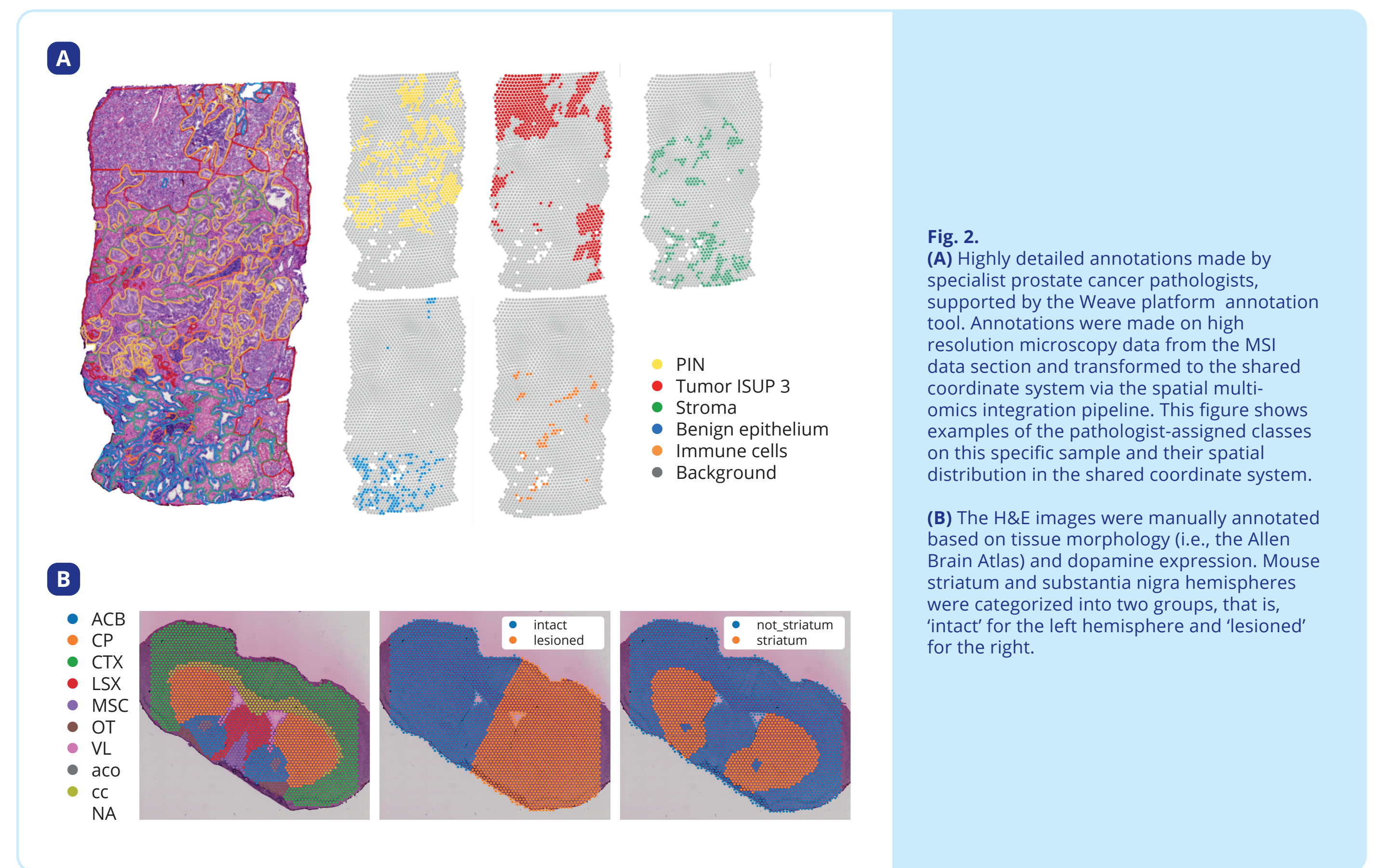
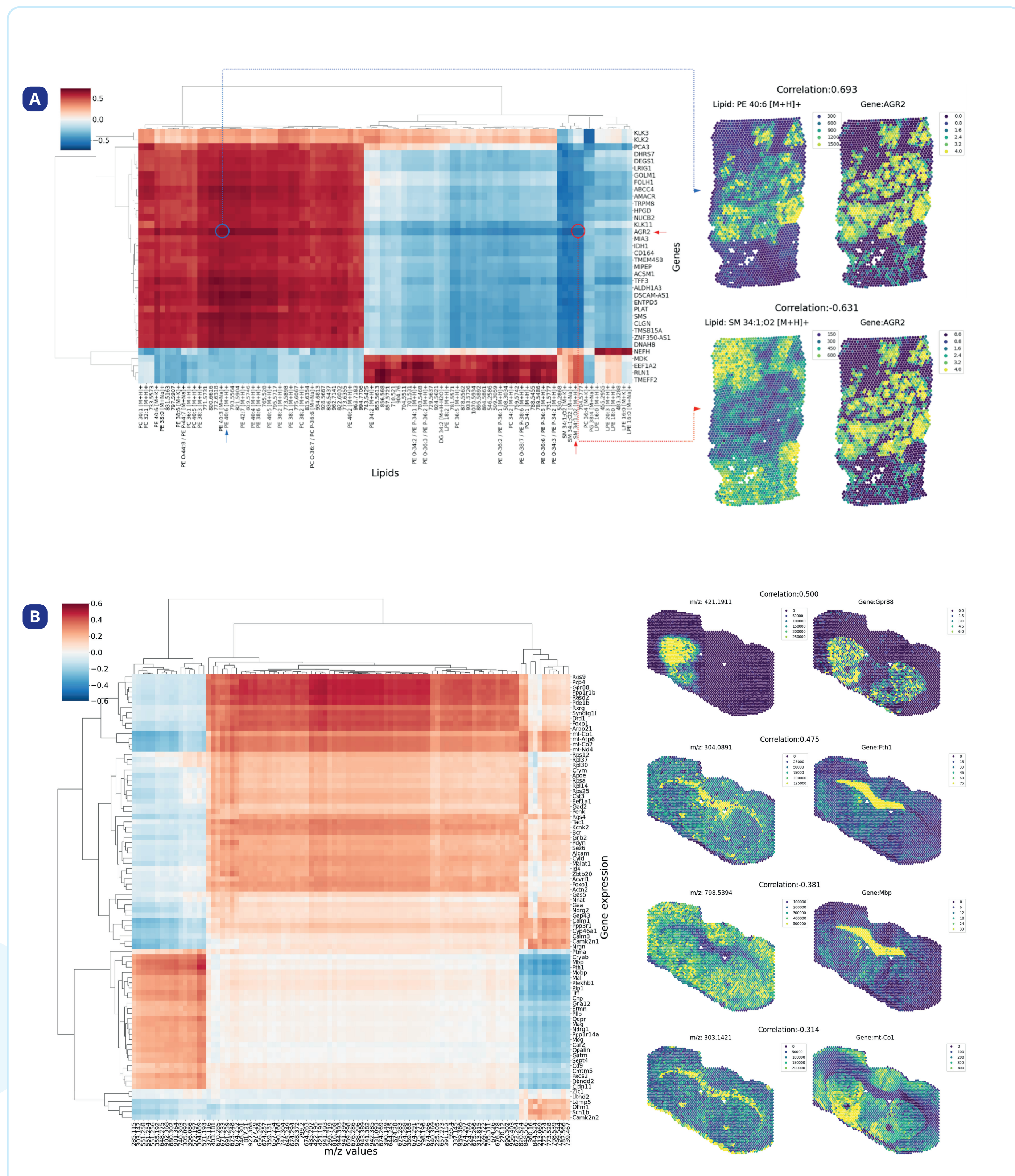


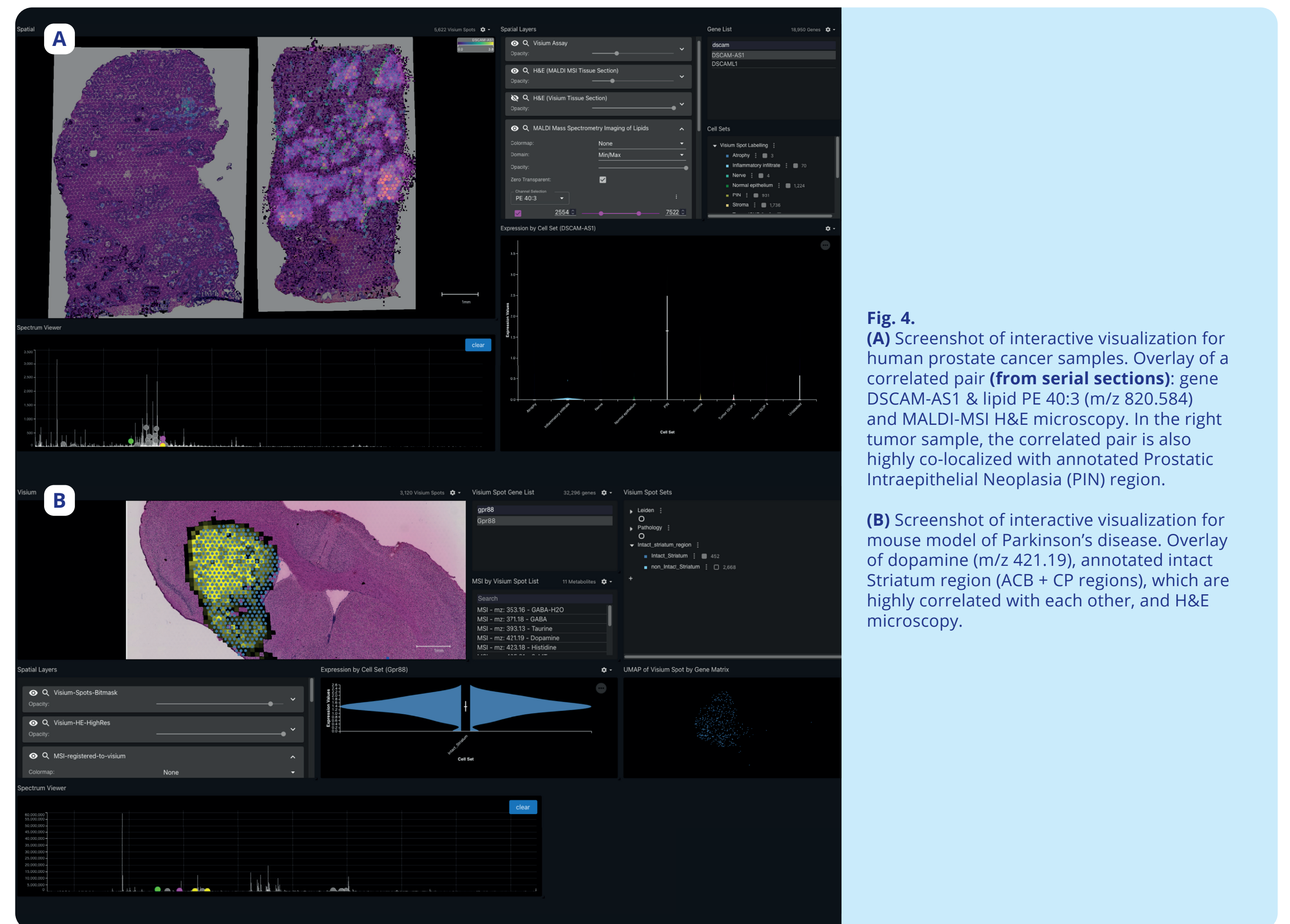
Fig. 1. Strategy for co-registration and integration of different spatial multi-omics data layers generated on consecutive human prostate cancer tissue sections. To link SRT data with MSI data, UMAP visualizations of different modalities were co-registered in two steps based on the H&E stainings of the respective slides and MSI data, and a UMAP visualization of transformed MSI data was generated after granularity matching.



Direct correlation analysis between spatially resolved transcriptomics and mass spectrometry imaging data



Interactive visualizations of spatial multi-omics data via Weave platform



Conclusion

- MSI-SRT data have both shared and complementary biochemical trends, many of which are highly colocalized with specific diseased regions.
- Spatial multi-omics integration pipeline supported via cloud-based Weave platform successfully combines multiple spatial molecular analysis approaches from both same and serial sections. The resulting aligned and matched spatial multi-omics dataset enables the direct comparison and correlation between gene expression and the distribution of lipids or neurotransmitters, providing a more complete picture and understanding of complex diseases such as high-risk prostate cancer and Parkinson's disease.

References:
^[1] Zhang, Wanqiu, et al. "Integration of Multiple Spatial-Omics Modalities Reveals Unique Insights into Molecular Heterogeneity of Prostate Cancer." *bioRxiv* (2023): 2023-08.
^[2] Vicari, Marco, et al. "Spatial multimodal analysis of transcriptomes and metabolomes in tissues." *Nature Biotechnology* (2023): 1-5.