

Quantifying Cellular Microenvironments in Multiplex Images

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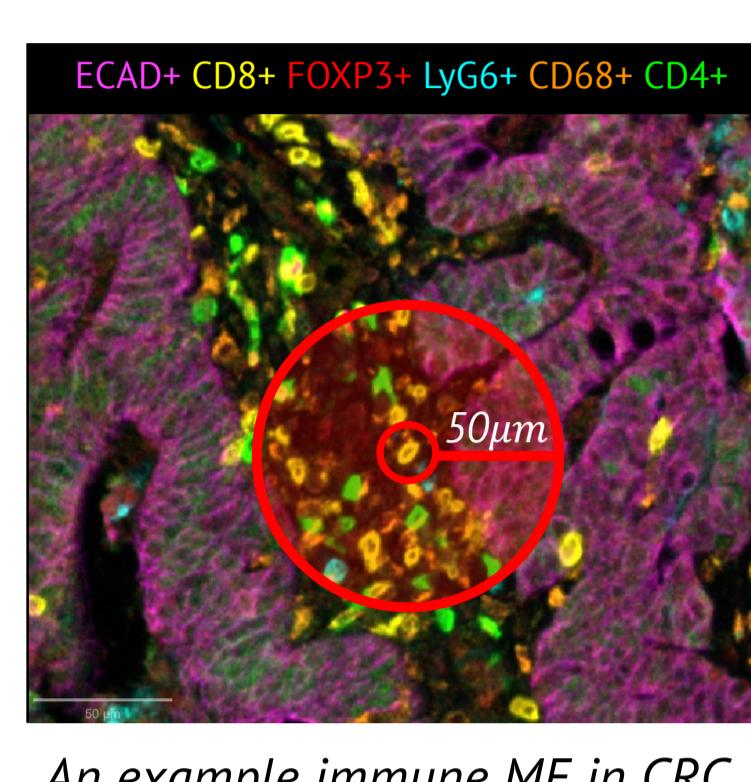
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A ground-up approach to multiplex image analysis

Multiplex imaging allows for the simultaneous visualisation of many biomarkers whilst preserving the spatial structure of the tissue [1]. These methods have provided unprecedented access to the complex spatial distributions of multiple cell-types in local proximity, termed cellular microenvironments (MEs).

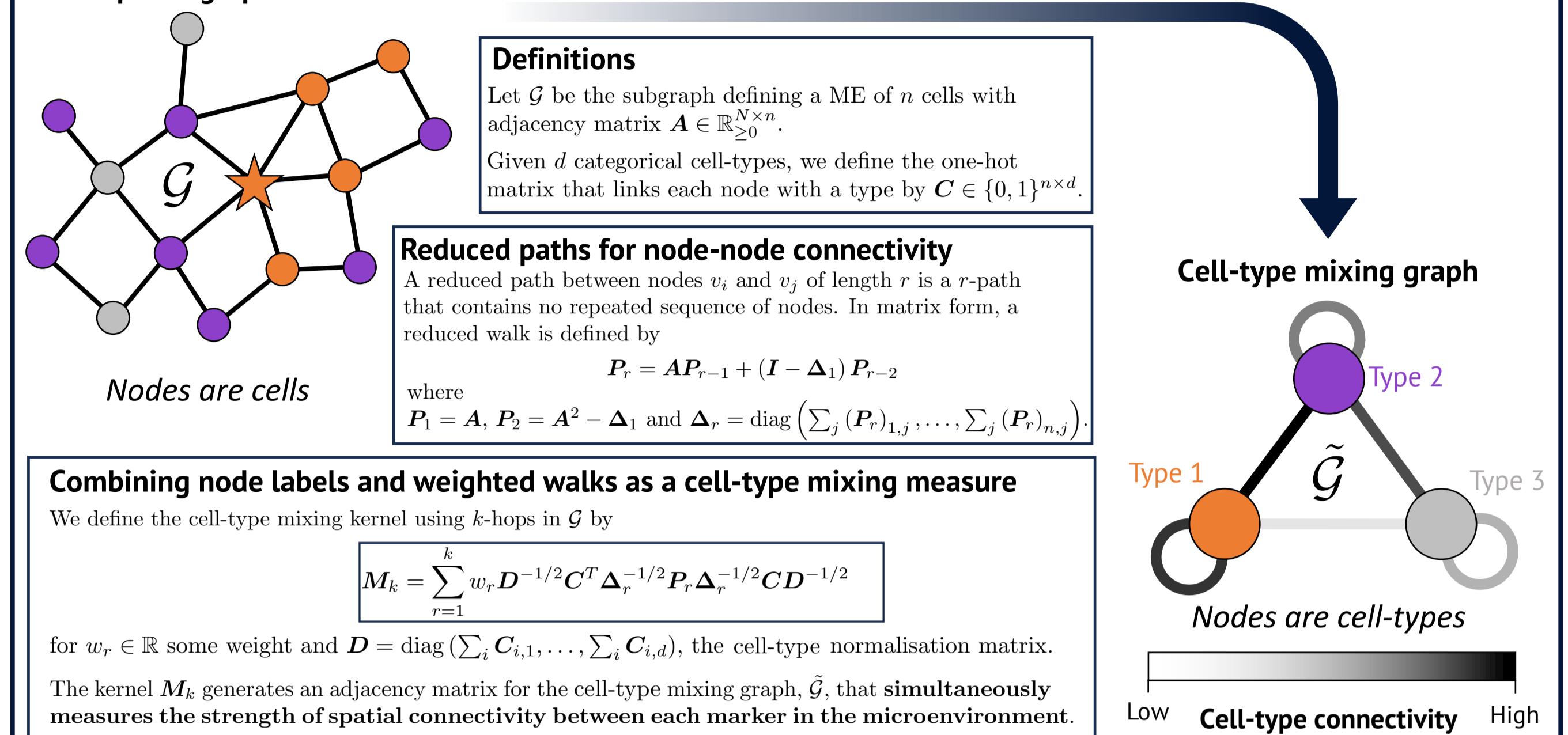


In disease, understanding ME composition at both the local and global spatial scales is crucial for uncovering interaction patterns which can be used to identify biological mechanisms that govern cancer initiation, progression and therapy efficacy [2].

- We seek to design methods for analysing the spatial interactions within MEs derived from multiplex imaging with the following properties:
- Interpretable:** Constructed for biological mechanism exploration
- Scalable:** Capable of simultaneously analysing high-dimensional data from multiplex imaging
- Integrable:** To be used in combination with existing spatial statistical tools

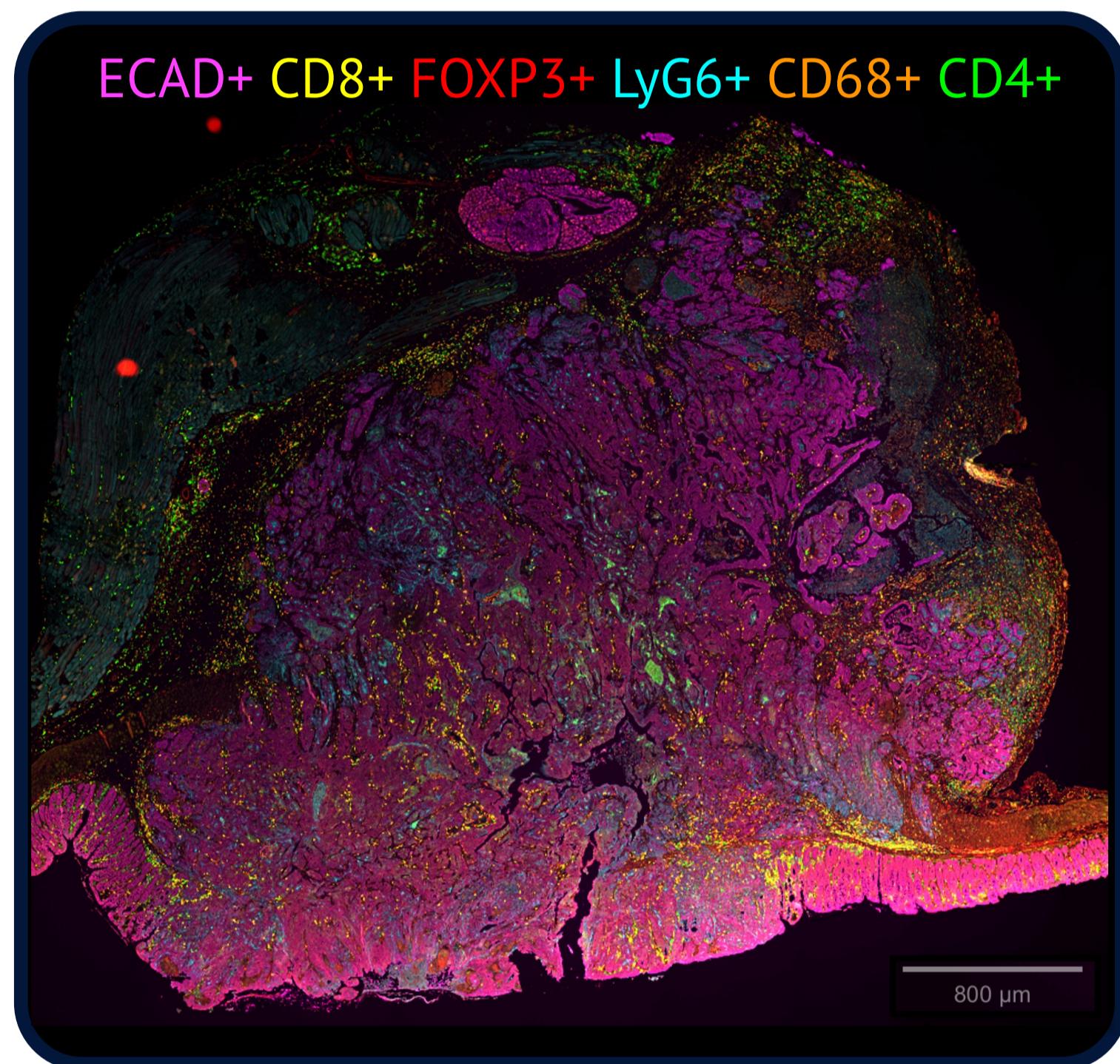
Cell-type mixing kernel for microenvironment characterisation

Local spatial graph about a cell

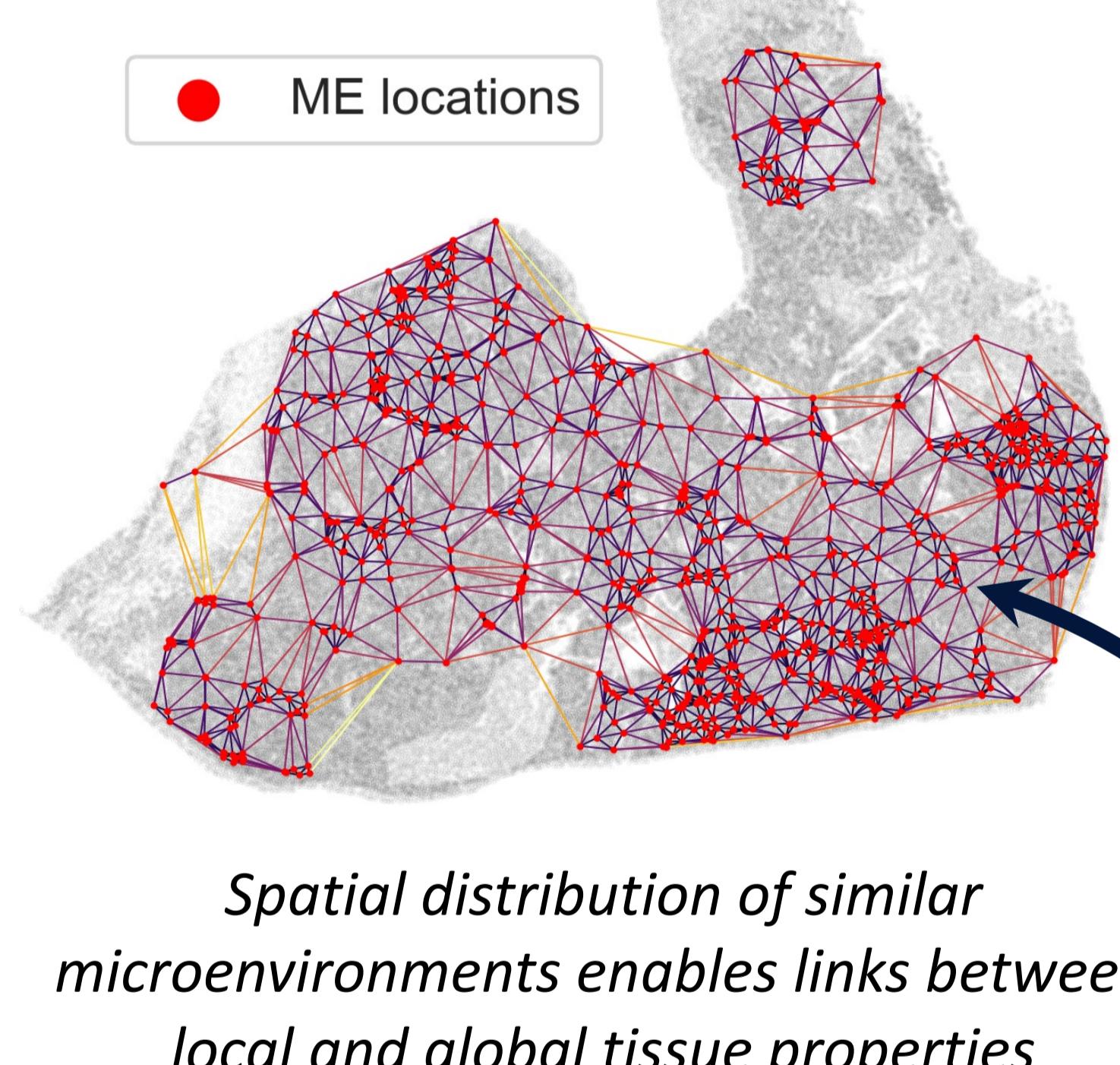


Interpretable workflow for spatially analysing cellular microenvironments

Mouse CRC: Immune panel

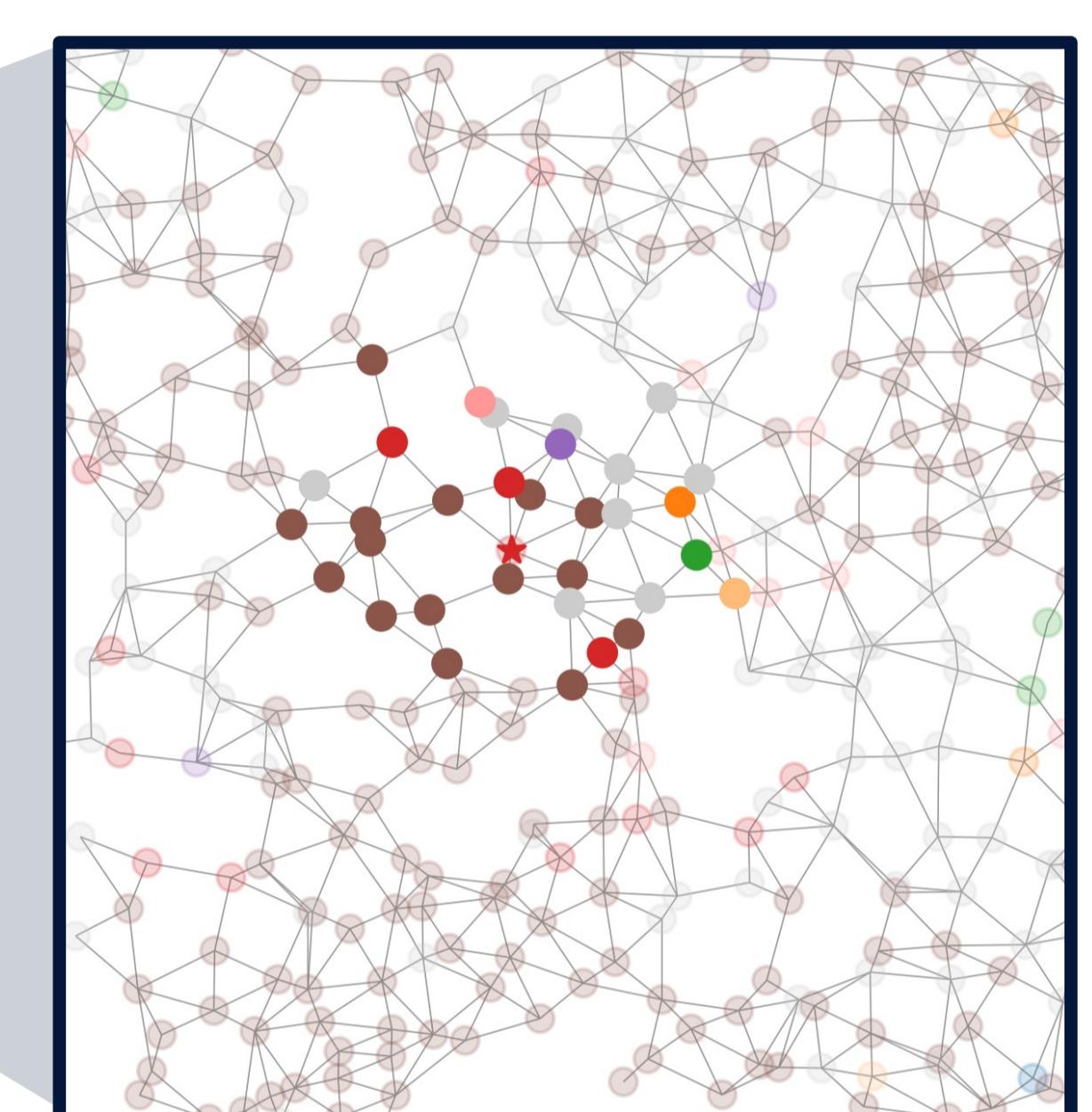


Pointcloud data from segmentation and cell-type classification

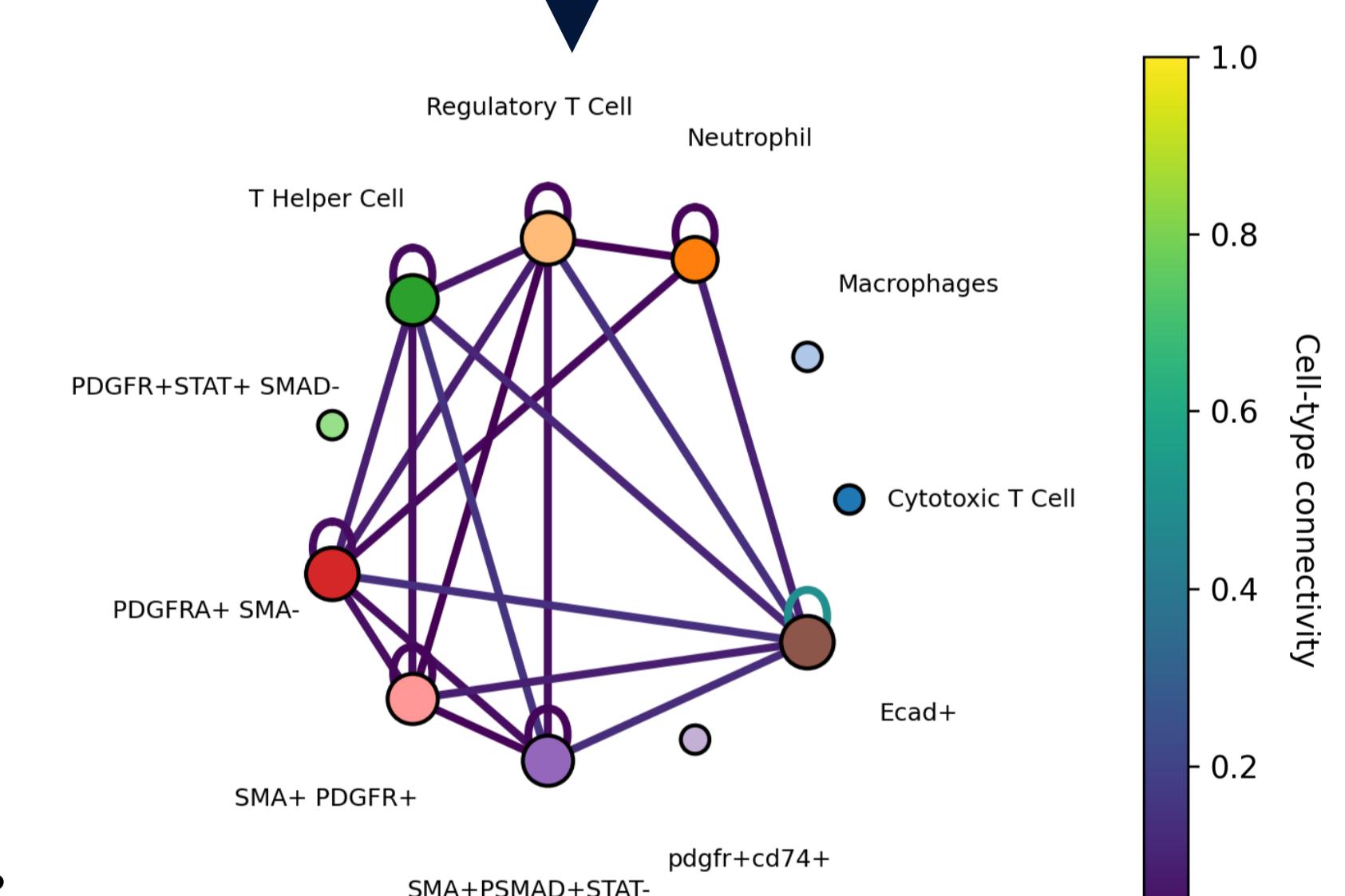


Spatial distribution of similar microenvironments enables links between local and global tissue properties

Local spatial networks about PDGFRA+ SMA- cells



Computing cell-type connectivity

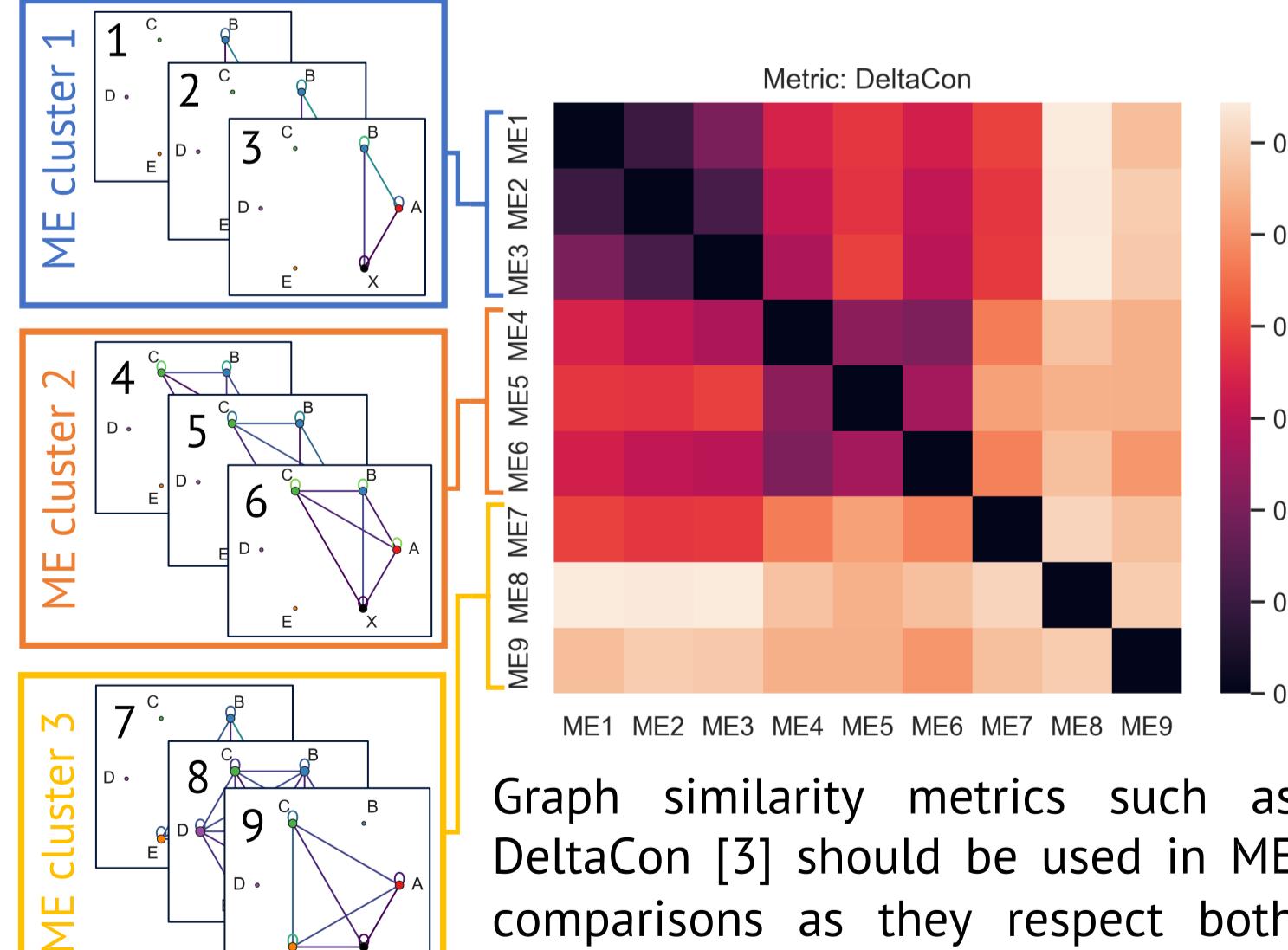


Embedding cell-type connectivity graphs in low-dimensional space

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Measuring changes in cellular microenvironments

The cell-type mixing graphs can simultaneously delineate ME cell-type density, ME shape and ME cell-type composition.

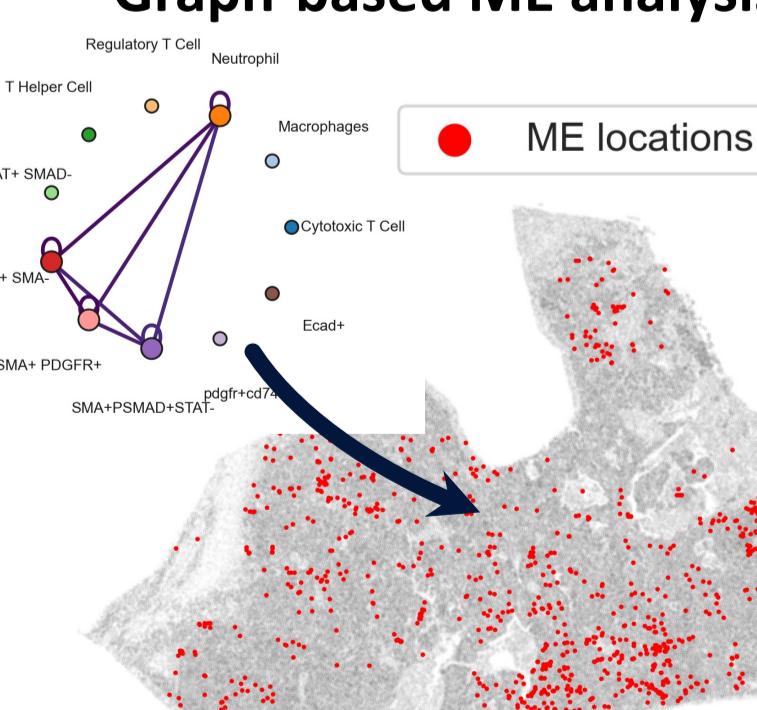


Graph similarity metrics such as DeltaCon [3] should be used in ME comparisons as they respect both cell-type existence and connectivity structure in MEs.

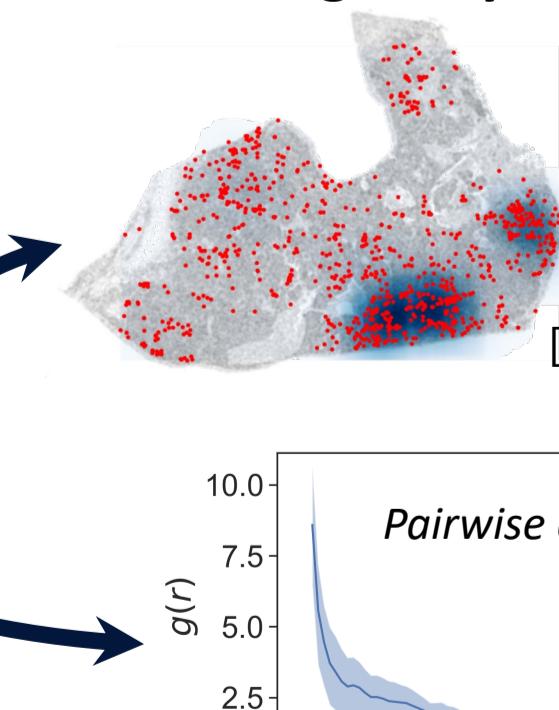
Combining statistics for multiscale microenvironment analysis

We integrate our cellular microenvironment analysis methods within **Multiplex Spatial Analysis (MUSPAN)**, a Python package designed to provide users with a wide range of statistical tools for analysing multiplex images.

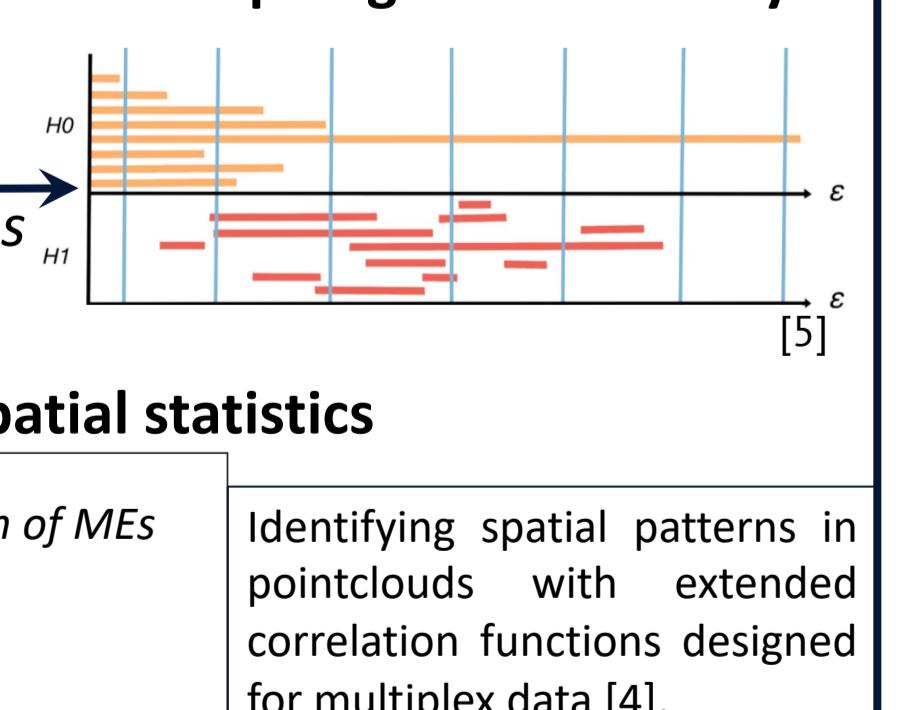
Graph-based ME analysis



Density-based ME clustering analysis



Persistent density features with Topological Data Analysis



Combining our ME metrics with existing methods in spatial data analysis, we aim to explore the rich spatial relationships contained within multiplex images to identify spatial biomarkers related to cancer progression and treatment response.

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