Workshop: Spatial Multi-Omics for Cancer Systems Biology 02/12/2024

This pdf presentation contains screenshots instead of the originally presented videos.
For interest in the video material please reach out to the speaker.

Visual Analytics for Imaging-Based Spatial Profiling

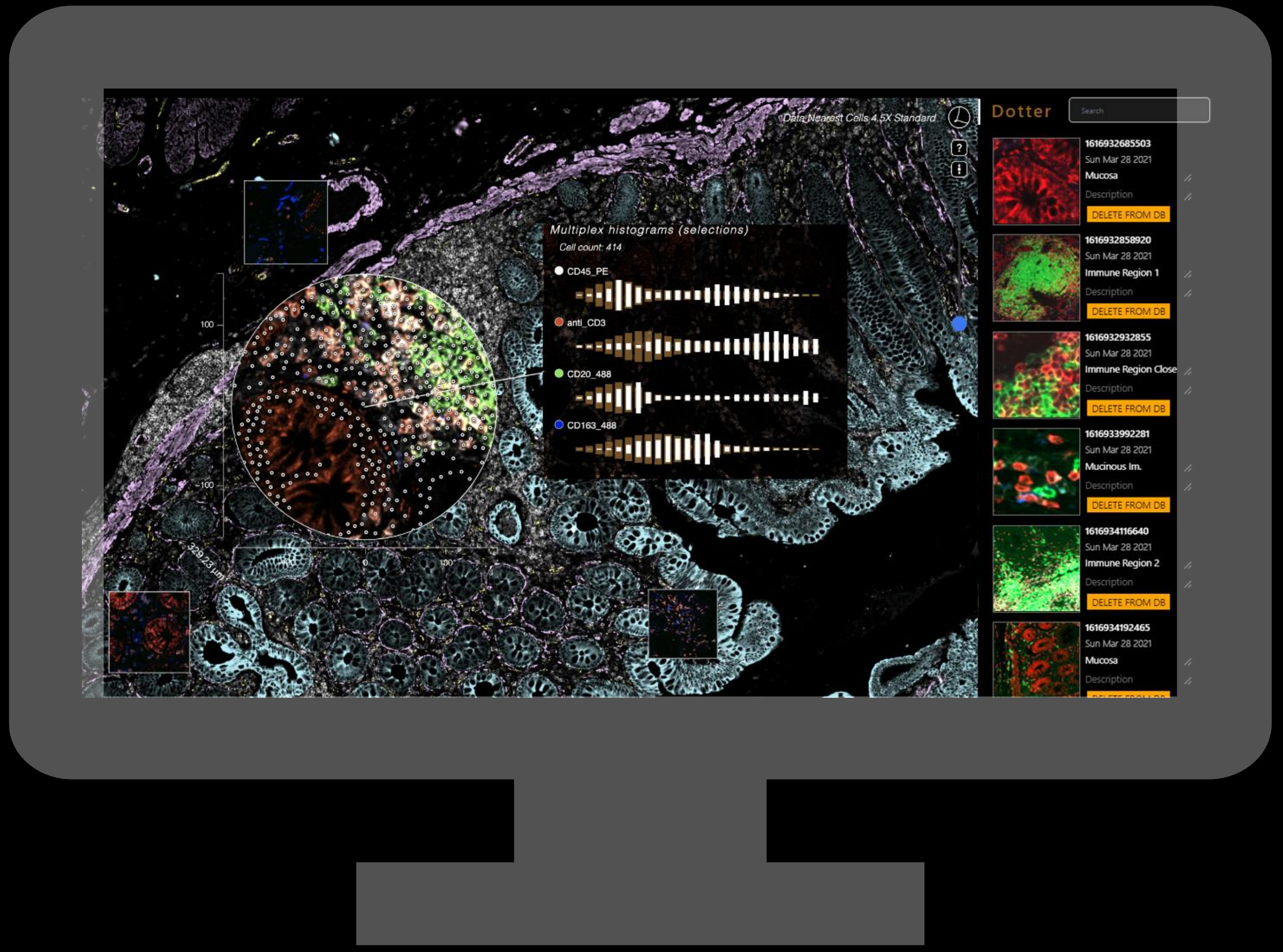
Robert Krueger, Ph.D.

NYU TANDON SCHOOL OF ENGINEERING

Visual Computing Group @ Harvard School of Engineering and Applied Sciences

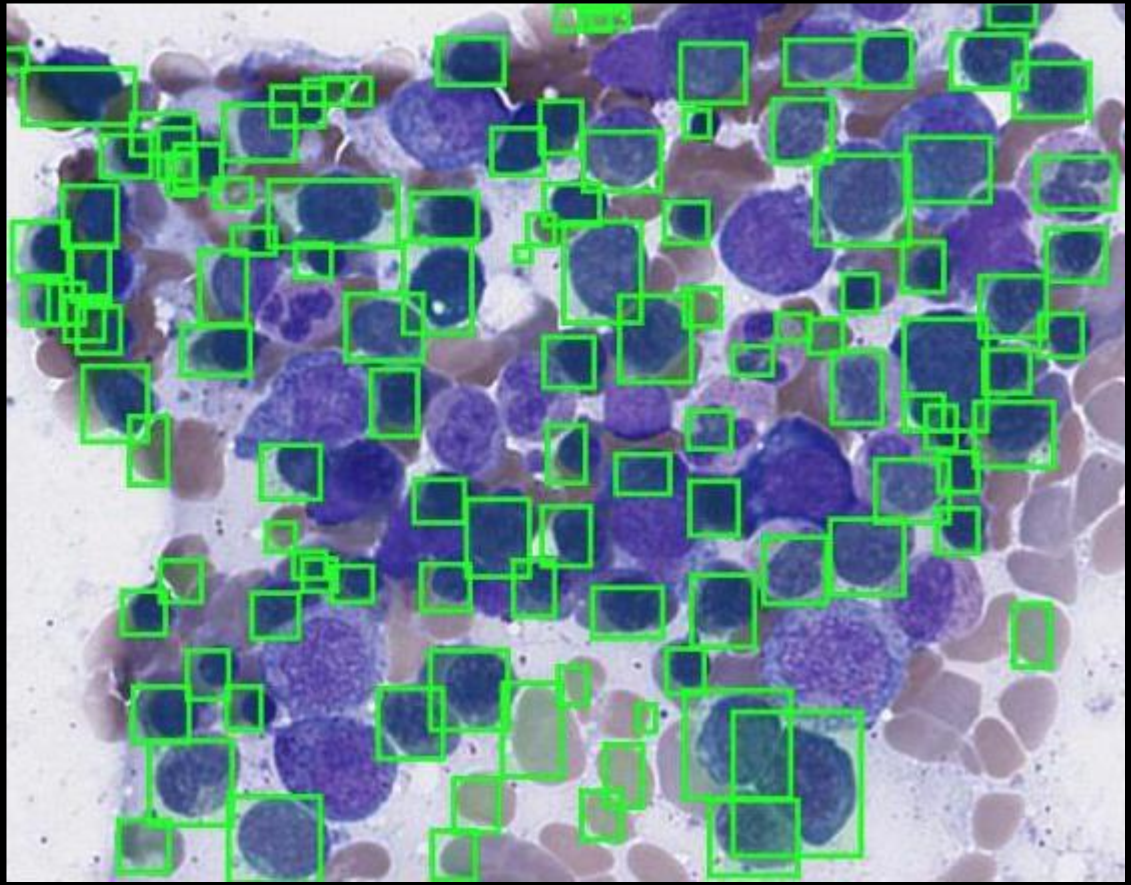
Laboratory of Systems Pharmacology @Harvard Medical School

Digital Pathology

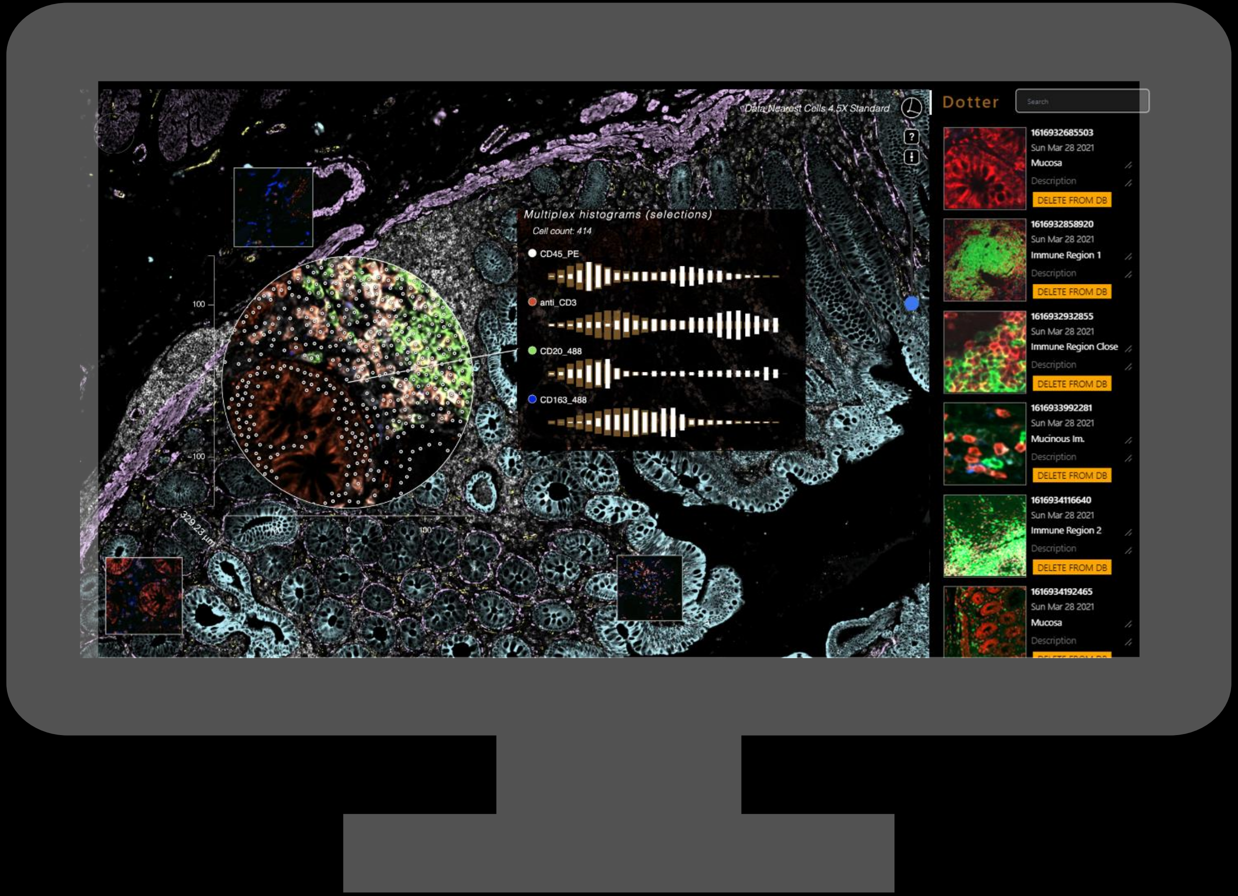


Semi-Automated Workflows

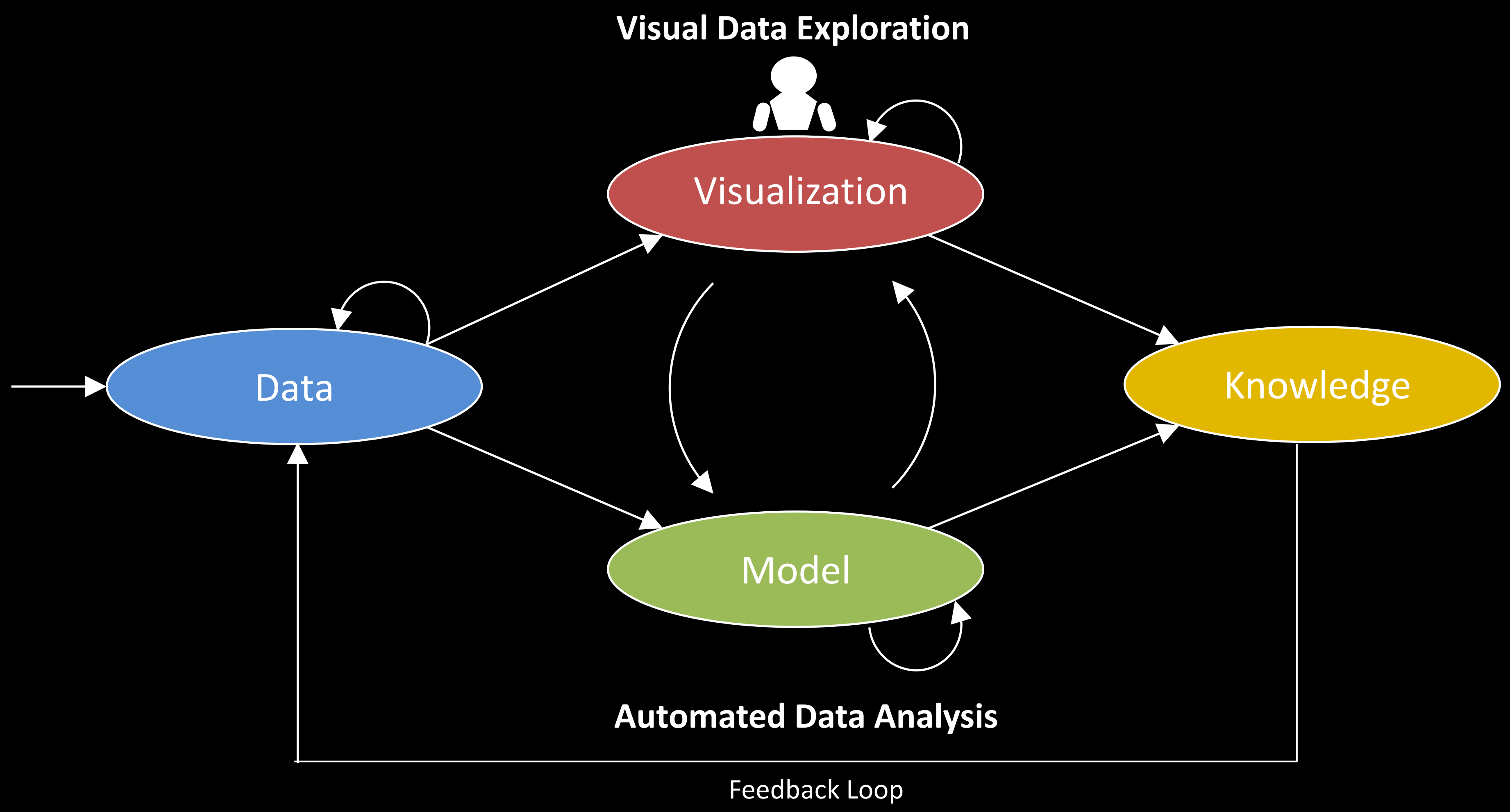
Machine Learning



Expert-in-the-Loop

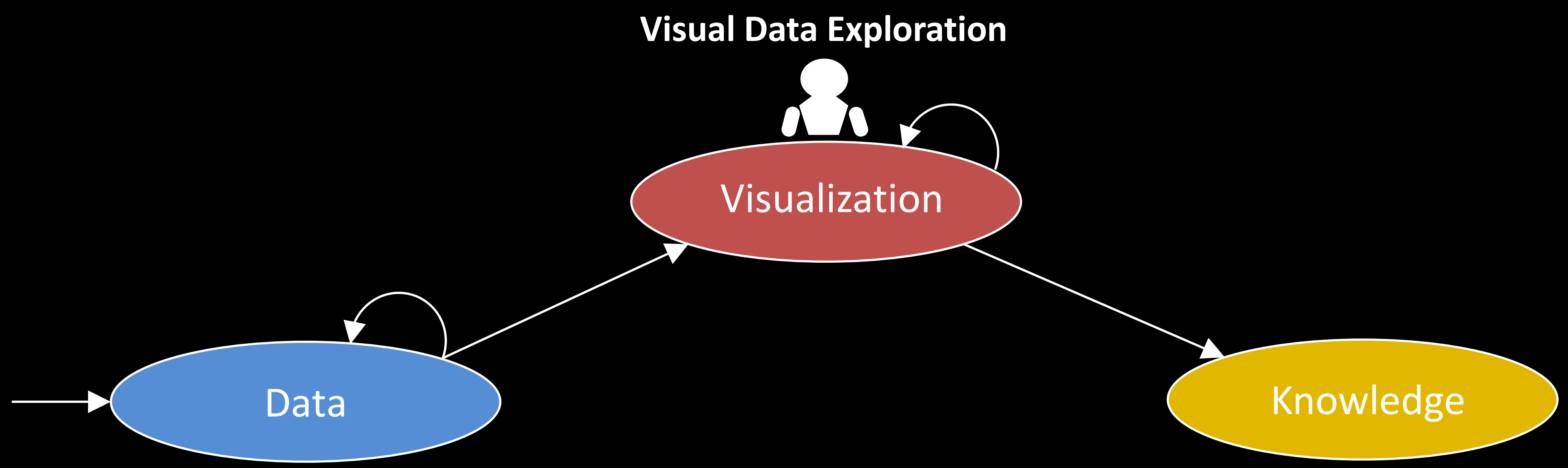


Visual Analytics



D. Keim, G. Andrienko, J.-D. Fekete, C. Görg, J. Kohlhammer, and G. Melançon. Visual analytics: Definition, process, and challenges. In A. Kerren, J. Stasko, J.-D. Fekete, and C. North, editors, *Information Visualization*, volume 4950 of *Lecture Notes in Computer Science*, pages 154–175. Springer Berlin Heidelberg, 2008.

Visual Analytics



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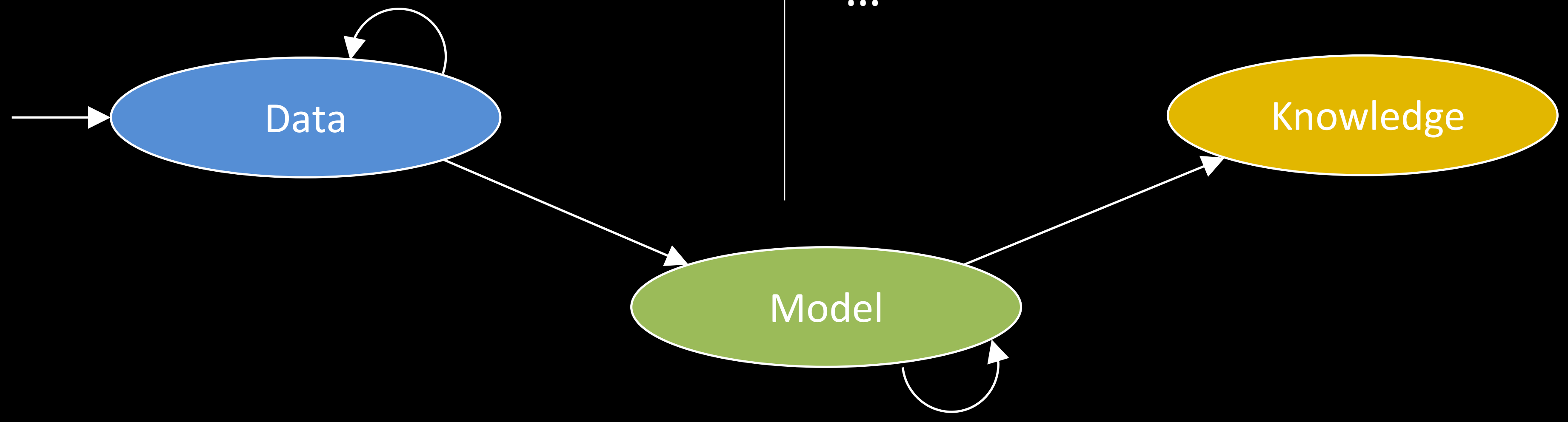
Visual Analytics

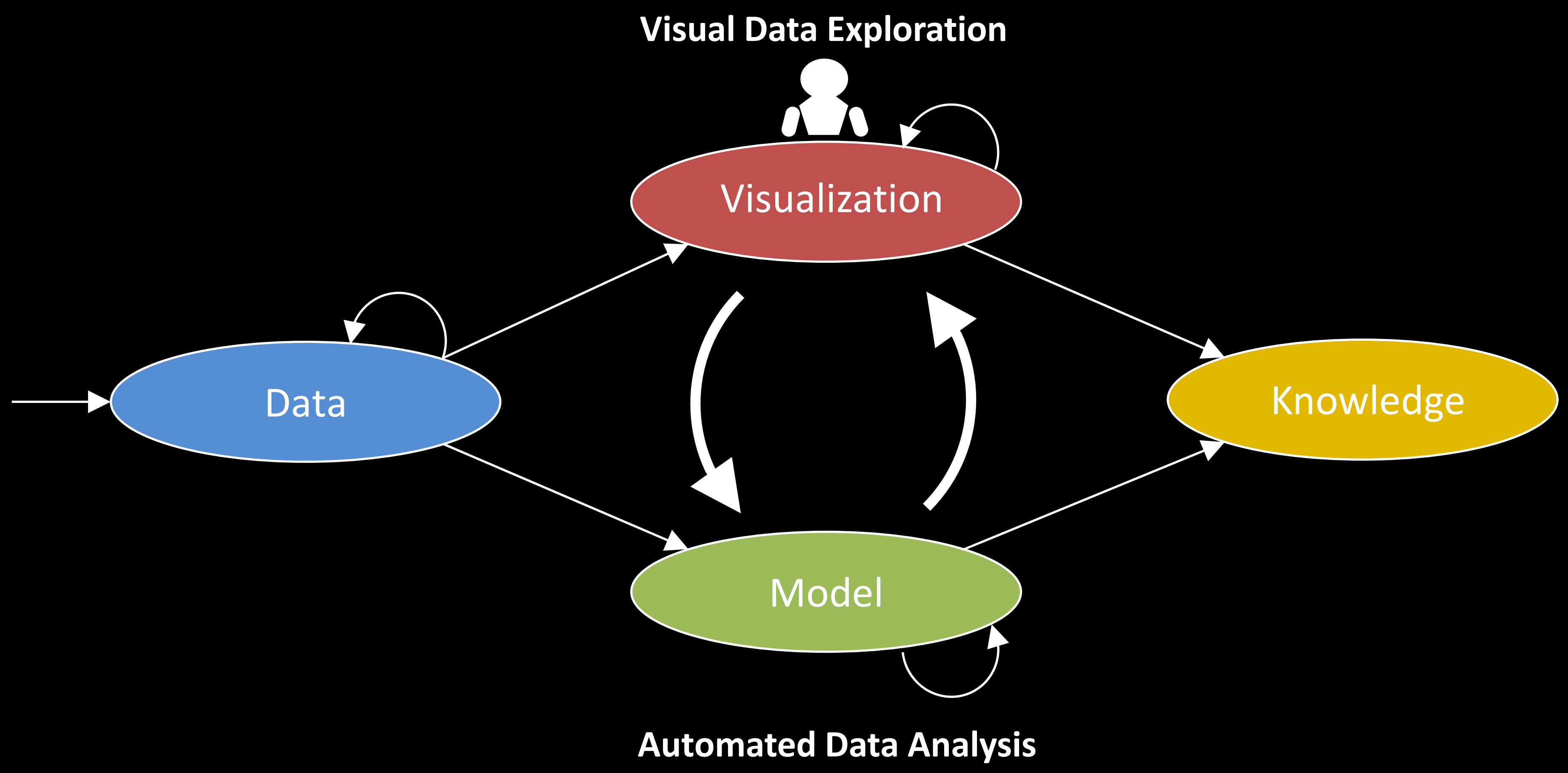
Clustering
Classification
Outlier Detection
Dimensional Reduction
…



Automated Data Analysis

D. Keim, G. Andrienko, J.-D. Fekete, C. Görg, J. Kohlhammer, and G. Melançon. Visual analytics: Definition, process, and challenges. In A. Kerren, J. Stasko, J.-D. Fekete, and C. North, editors, *Information Visualization*, volume 4950 of *Lecture Notes in Computer Science*, pages 154–175. Springer Berlin Heidelberg, 2008.

Visual Analytics



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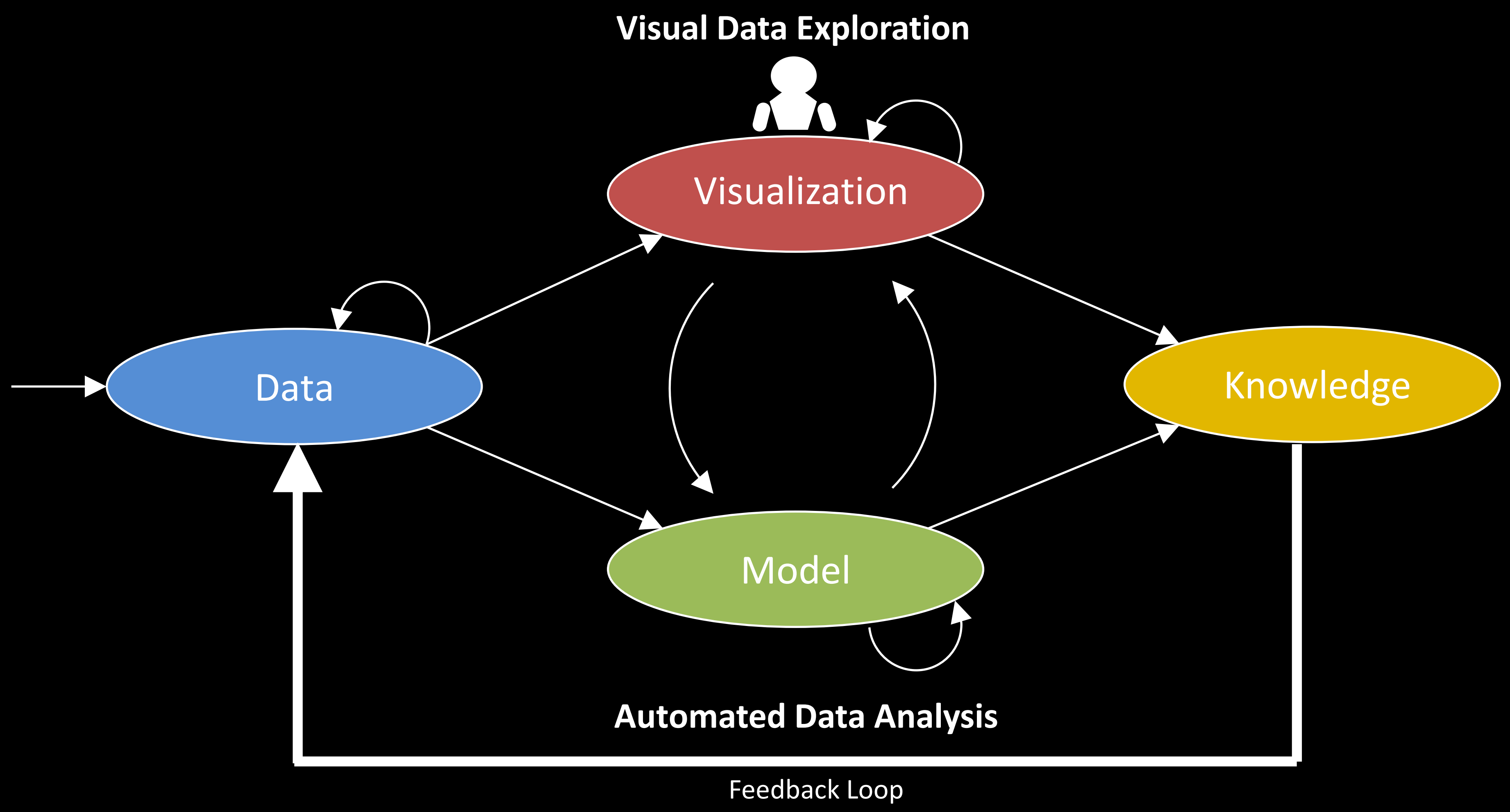
Visual Analytics



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About Me

Assistant Professor of Computer Science
@ New York University | Tandon School of Engineering

>> Research: Data Visualization and Visual Analytics

>> Application Field: Biomedical Data Analysis

>> Previously at Harvard – LSP / VCG

NYU TANDON SCHOOL OF ENGINEERING

Visual Computing Group @ Harvard School of Engineering and Applied Sciences

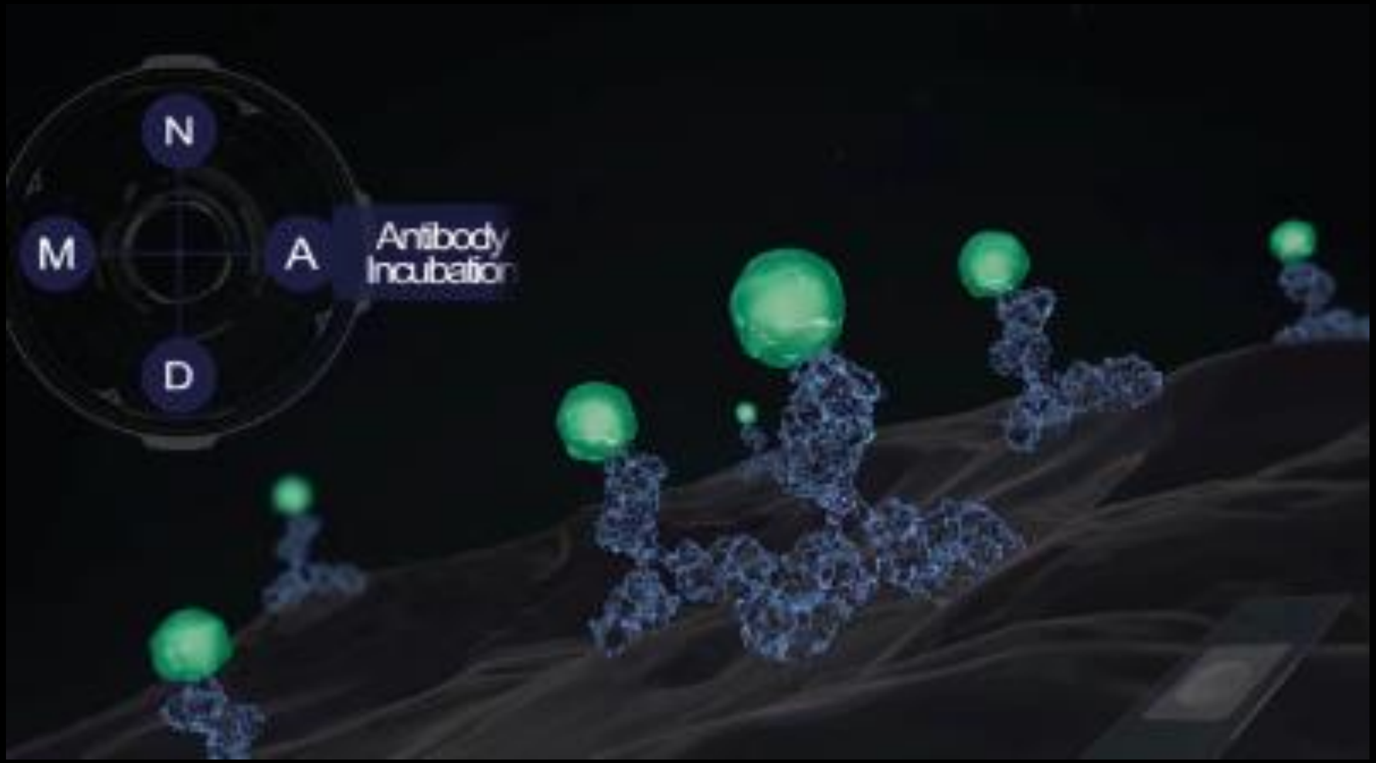
Laboratory of Systems Pharmacology @Harvard Medical School

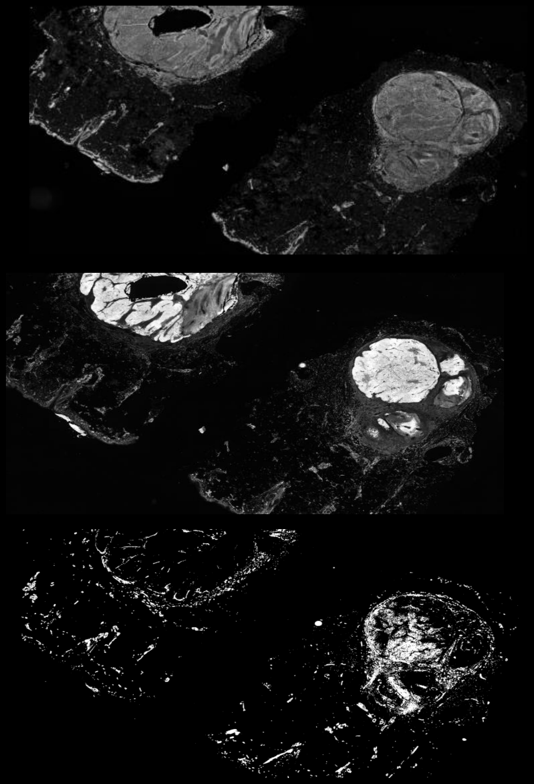
Multiplexed Tissue Imaging

- Making proteins visible (give cells their identity)
- Understand and target tumor microenvironment
- High throughput imaging methods
  e. g., CyCIF - Cyclic Immunofluorescence Imaging

CyCIF - Cyclic Immunofluorescence Imaging

Lin, J.R., et al., 2018. Highly multiplexed immunofluorescence imaging of human tissues and tumors using t-CyCIF and conventional optical microscopes. *Elife*, *7*.





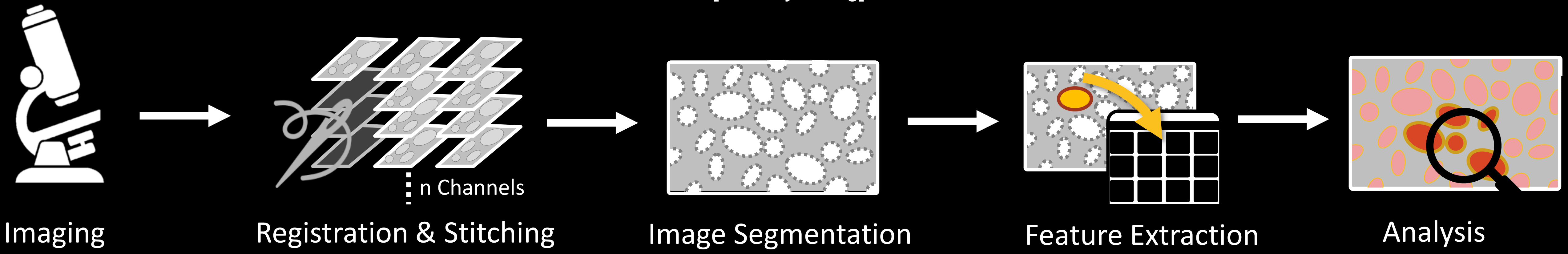
Dataset

60 image channels

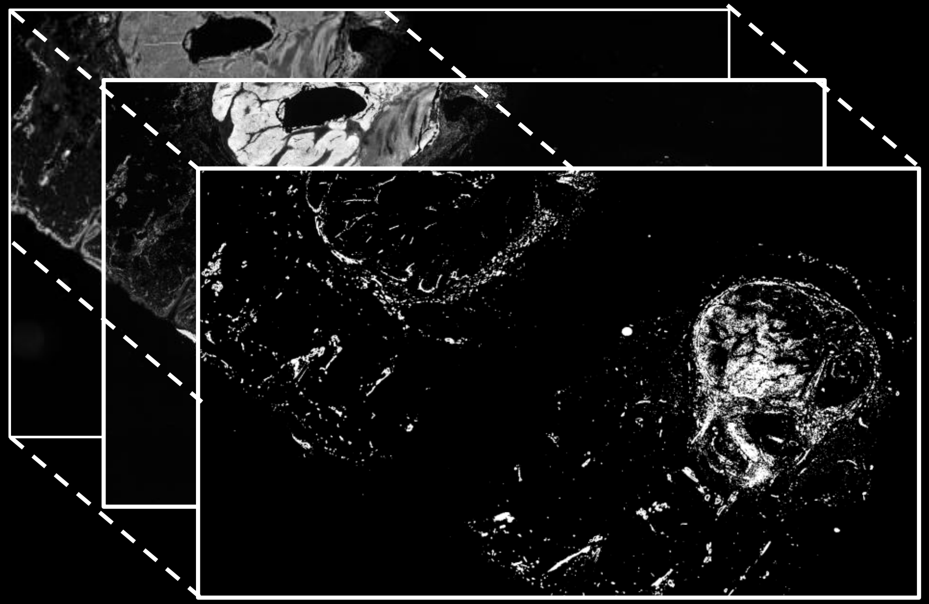
Res: up to 60k x 60k px, 200nm per pixel

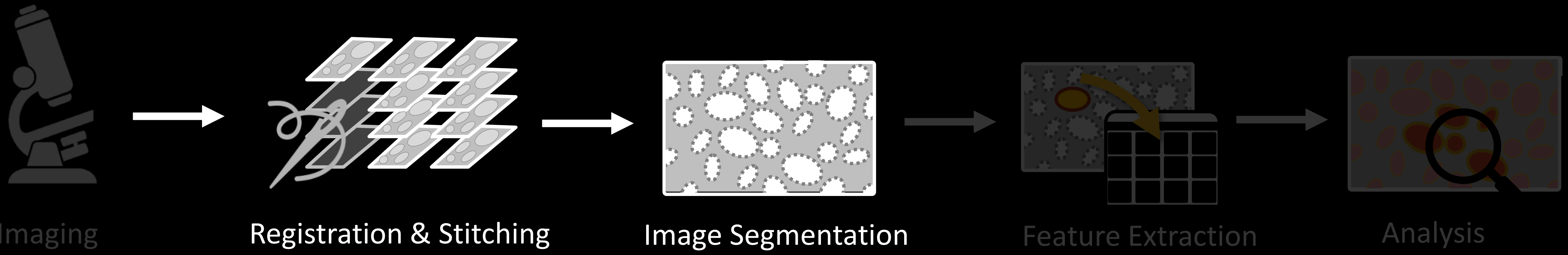
Size: often > 1TB
> 1 million cells

[www.cycif.org]

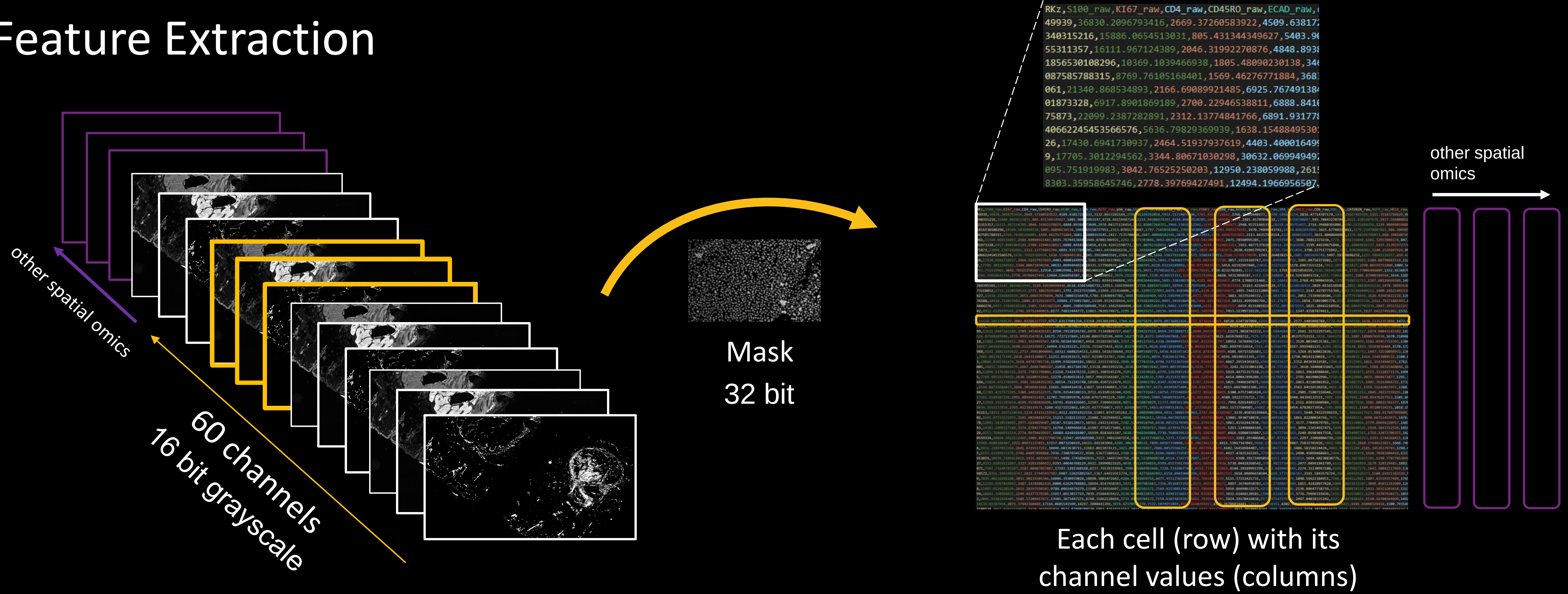


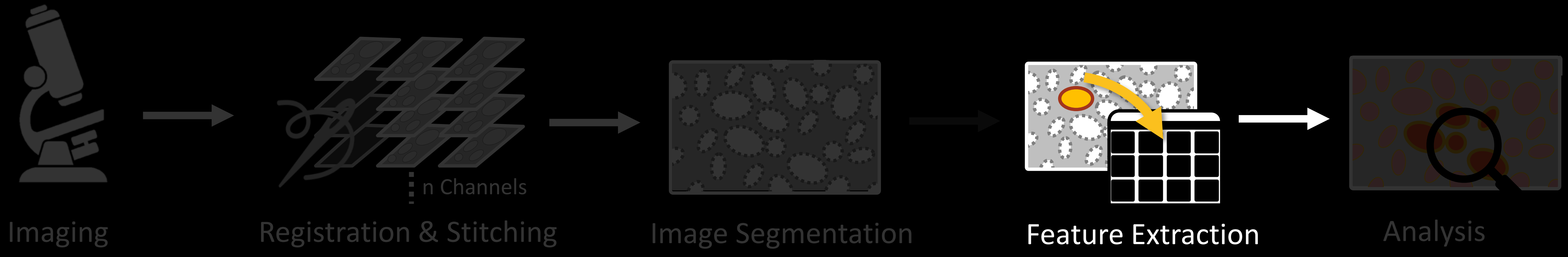
Registration, Segmentation



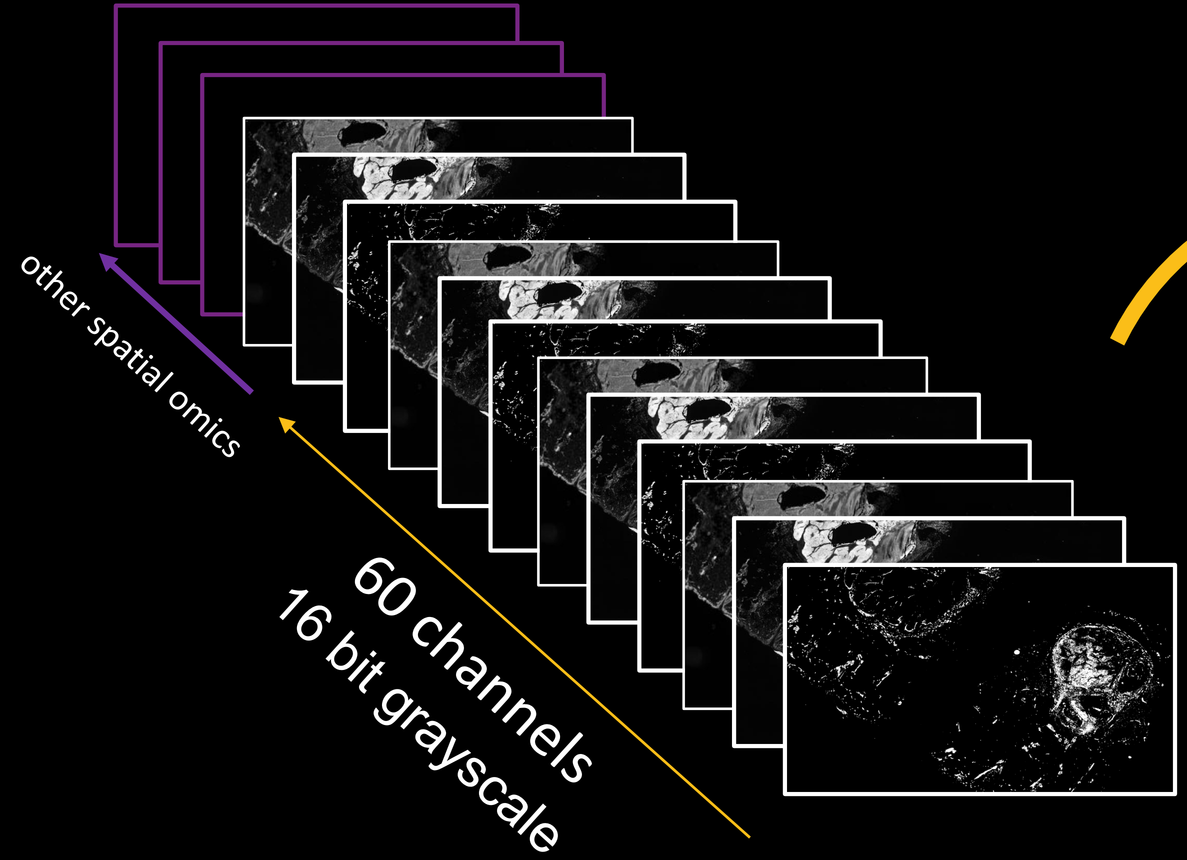


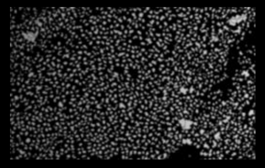
Feature Extraction



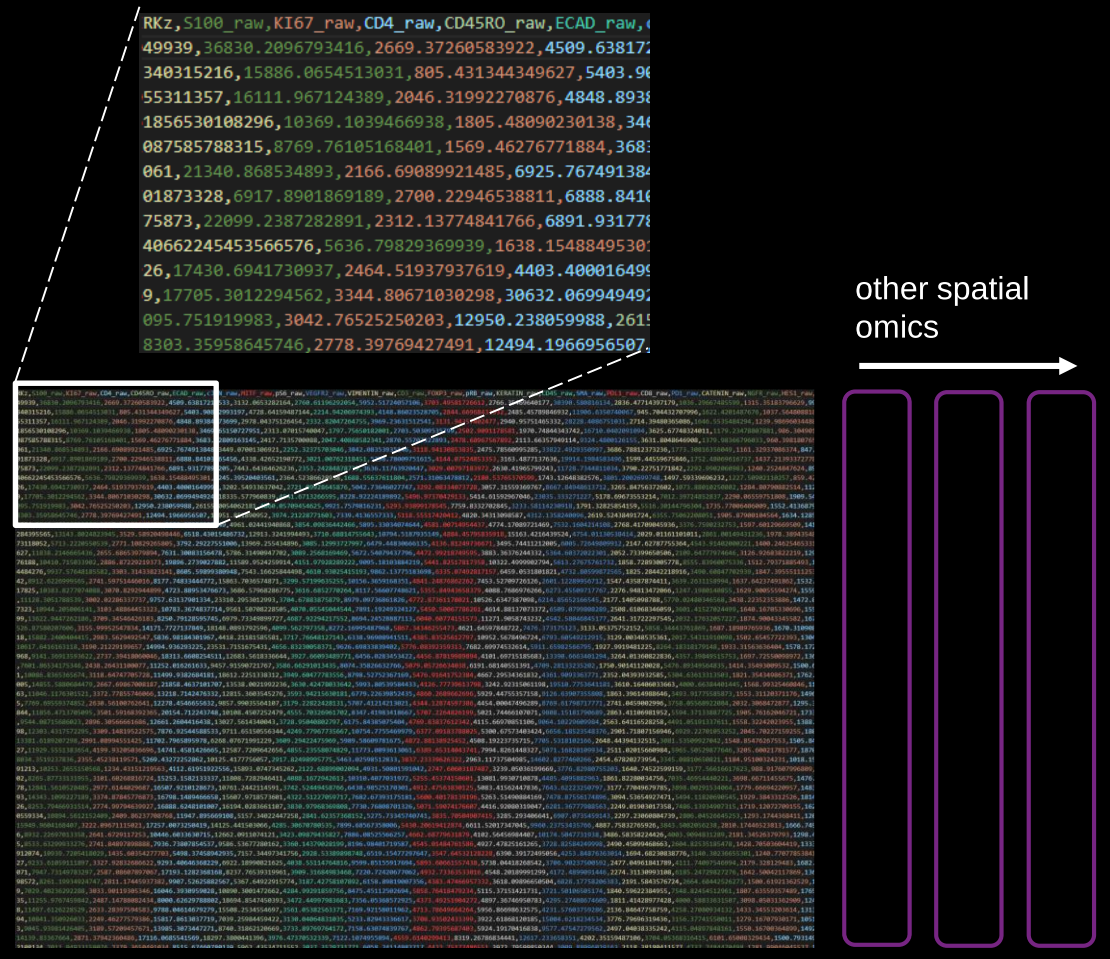


Feature Extraction

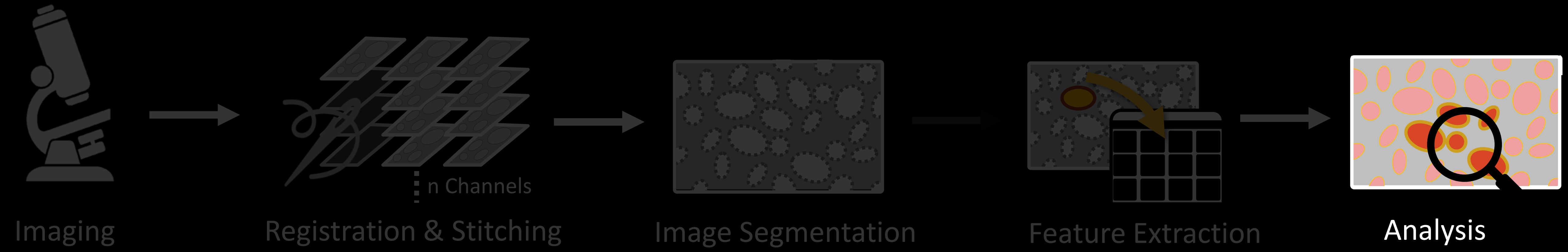




Mask
32 bit



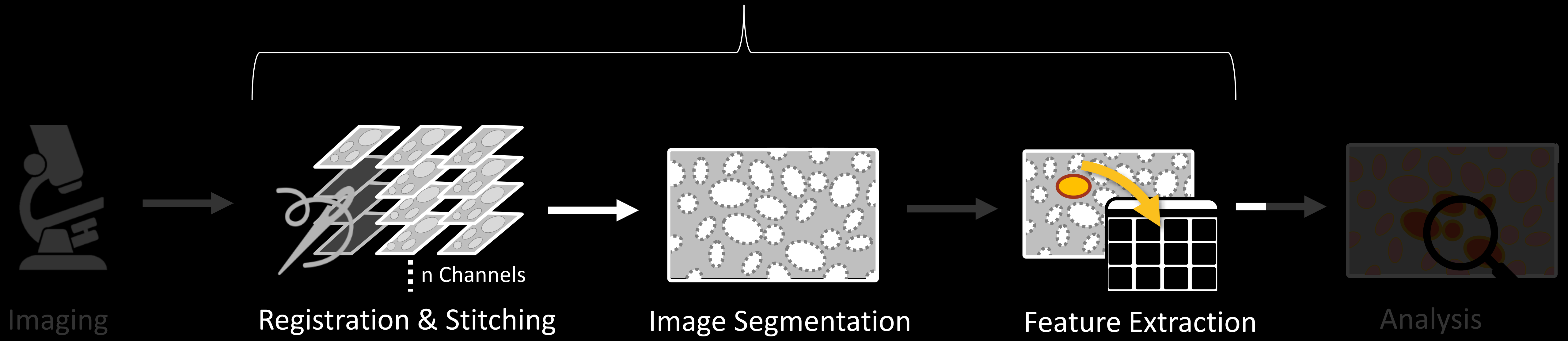
Each cell (row) with its channel values (columns)

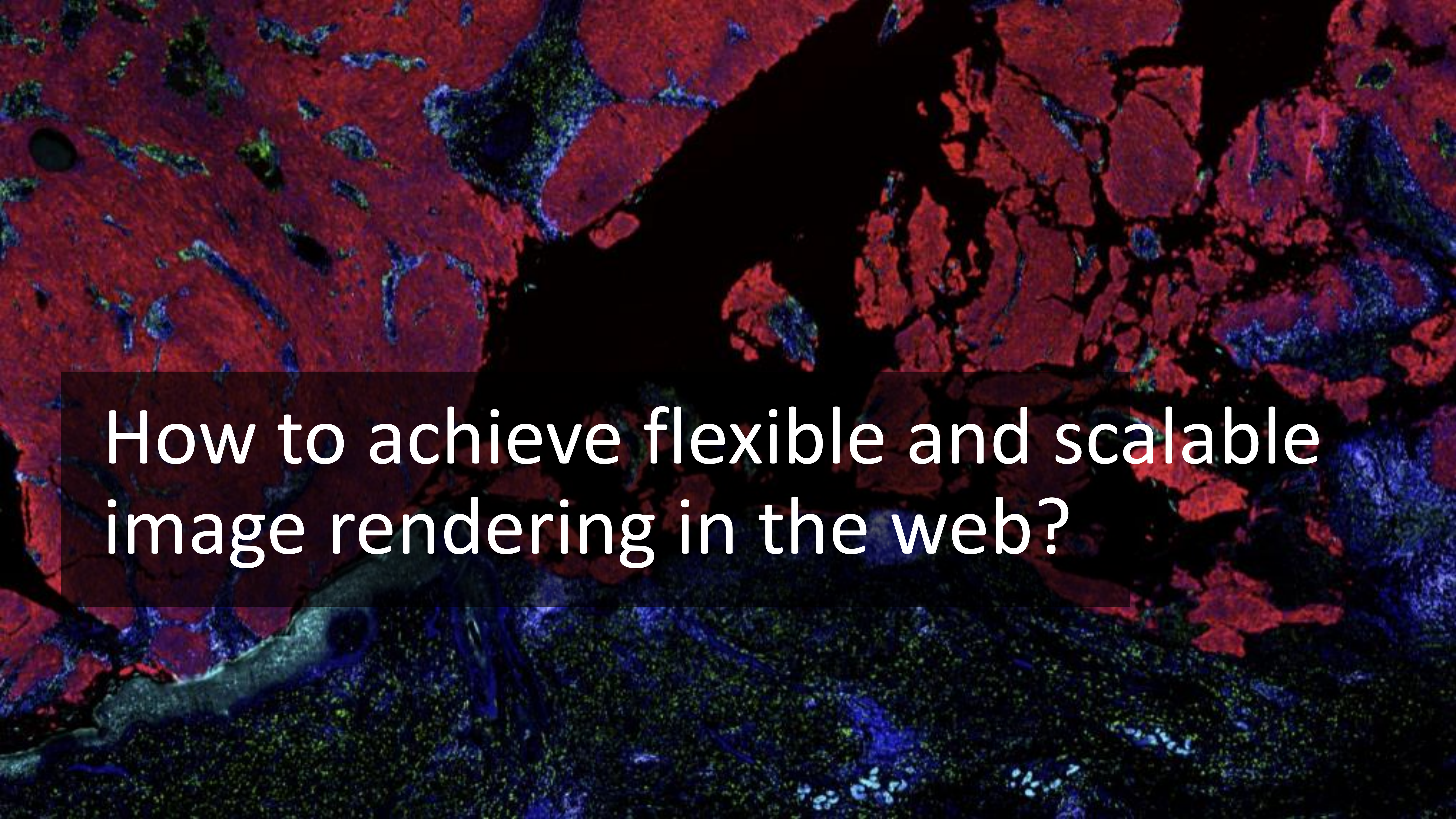


MCMICRO

https://mcmicro.org

Schapiro et al. 2022. MCMICRO: a scalable, modular image-processing pipeline for multiplexed tissue imaging. *Nature methods*

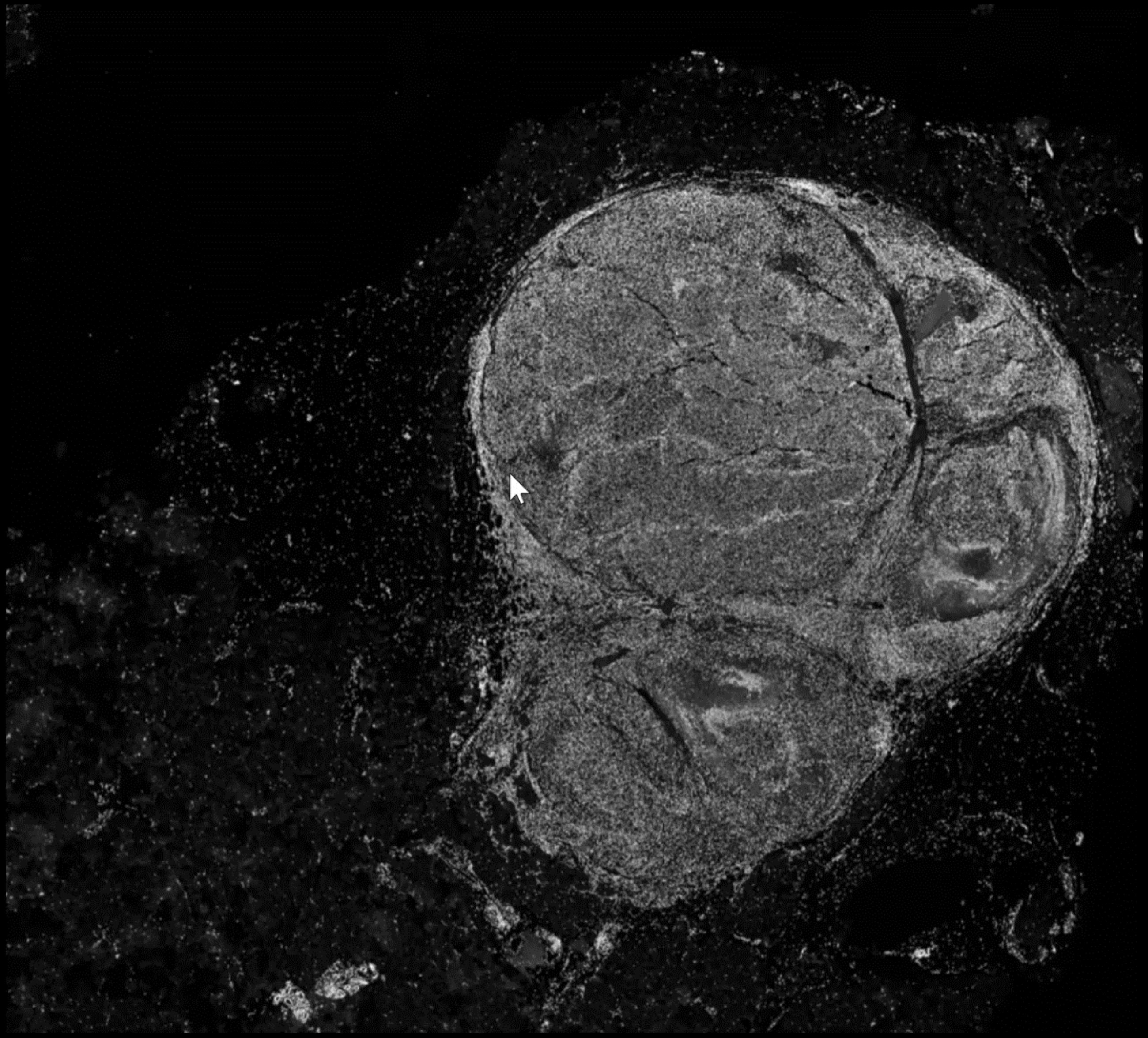


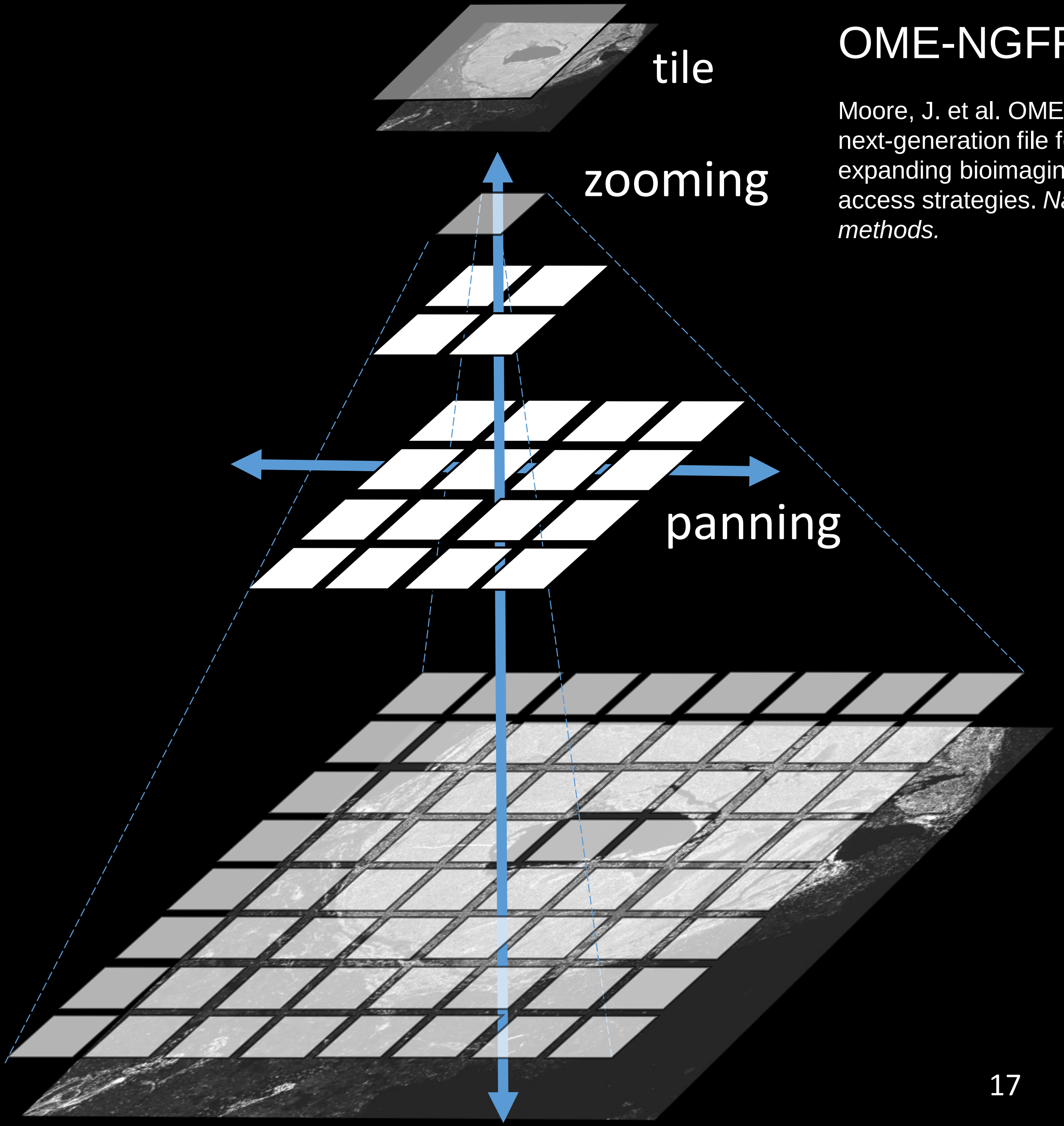


How to achieve flexible and scalable image rendering in the web?

Scalable Multiplex Image Rendering for the Web

- Big data: up to 1TB image



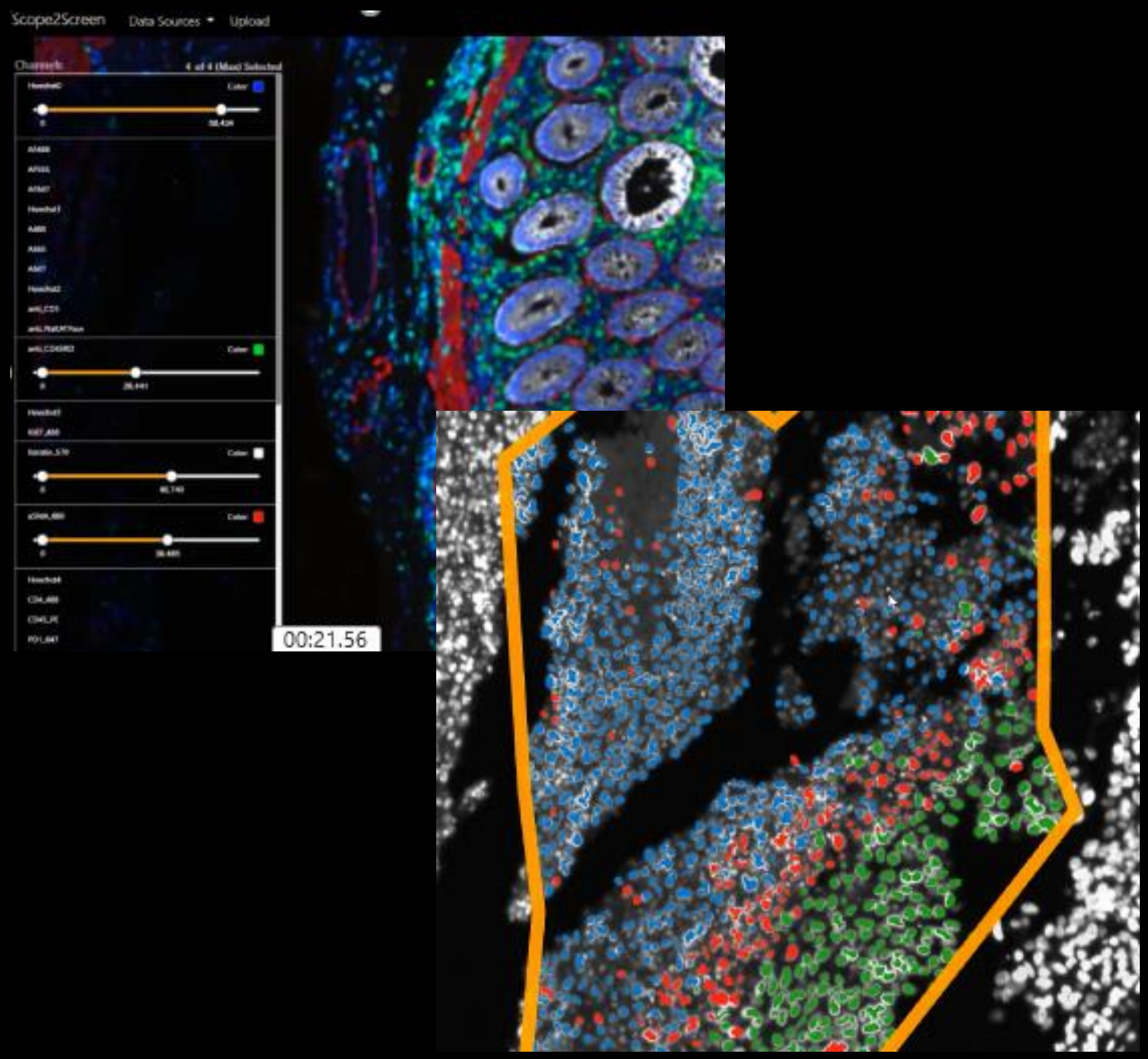


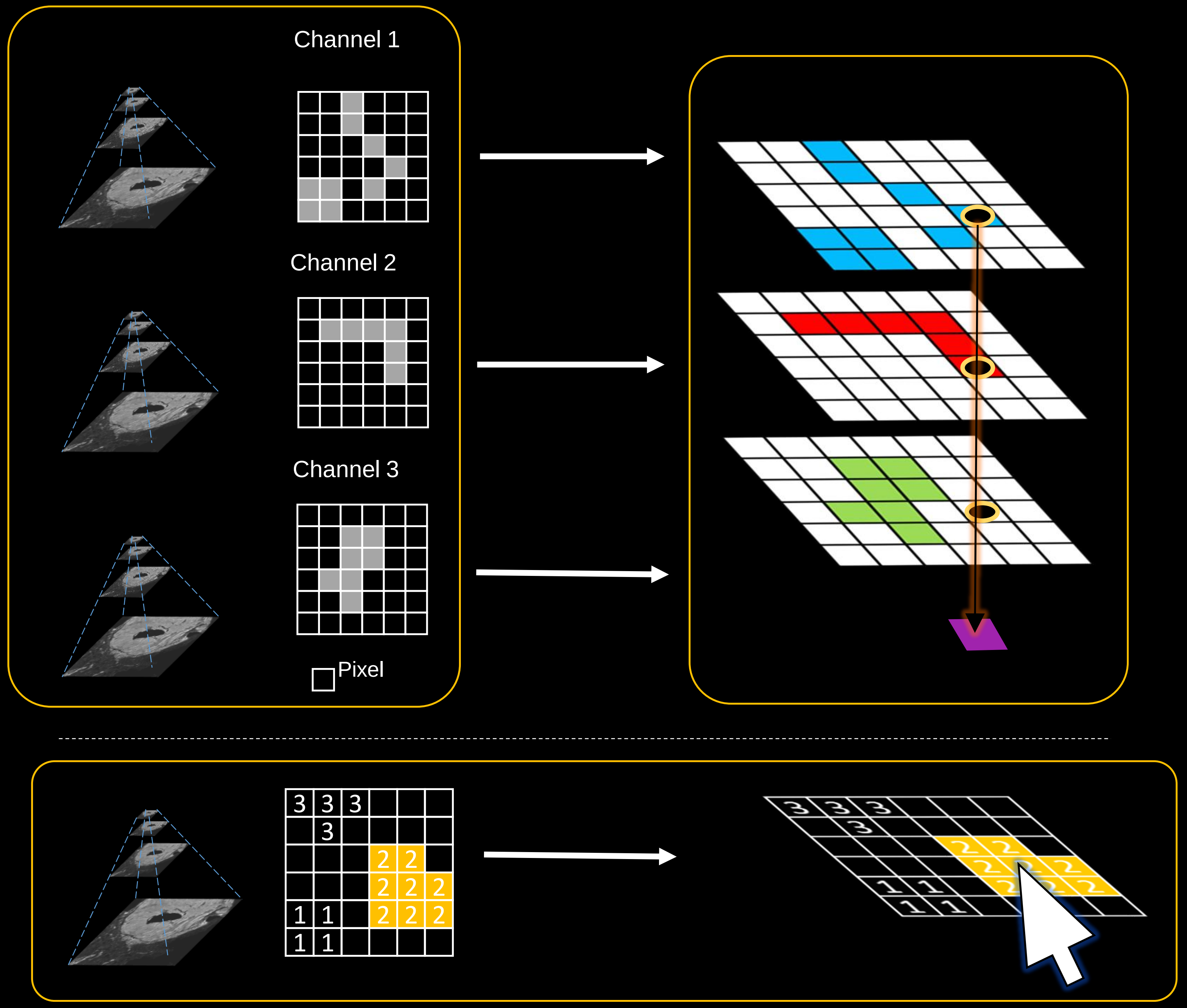
OME-TIFF

OME-NGFF

Moore, J. et al. OME-NGFF: a next-generation file format for expanding bioimaging data-access strategies. *Nature methods.*

Scalable Multiplex Image Rendering for the Web





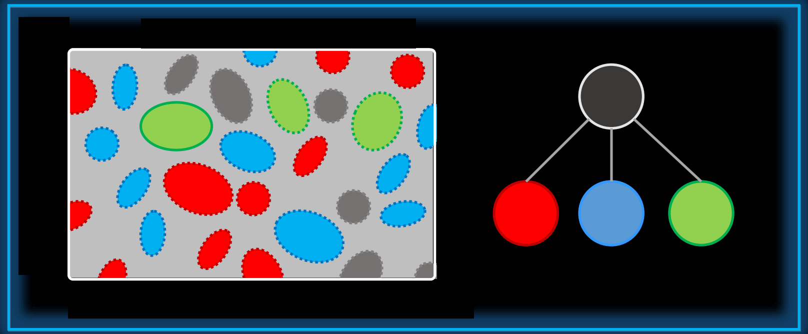
Visual Analytics Tasks

Visual Analysis of Multiplexed Immunofluorescence Data

Annotation
Focus+Context Pathology Assessment

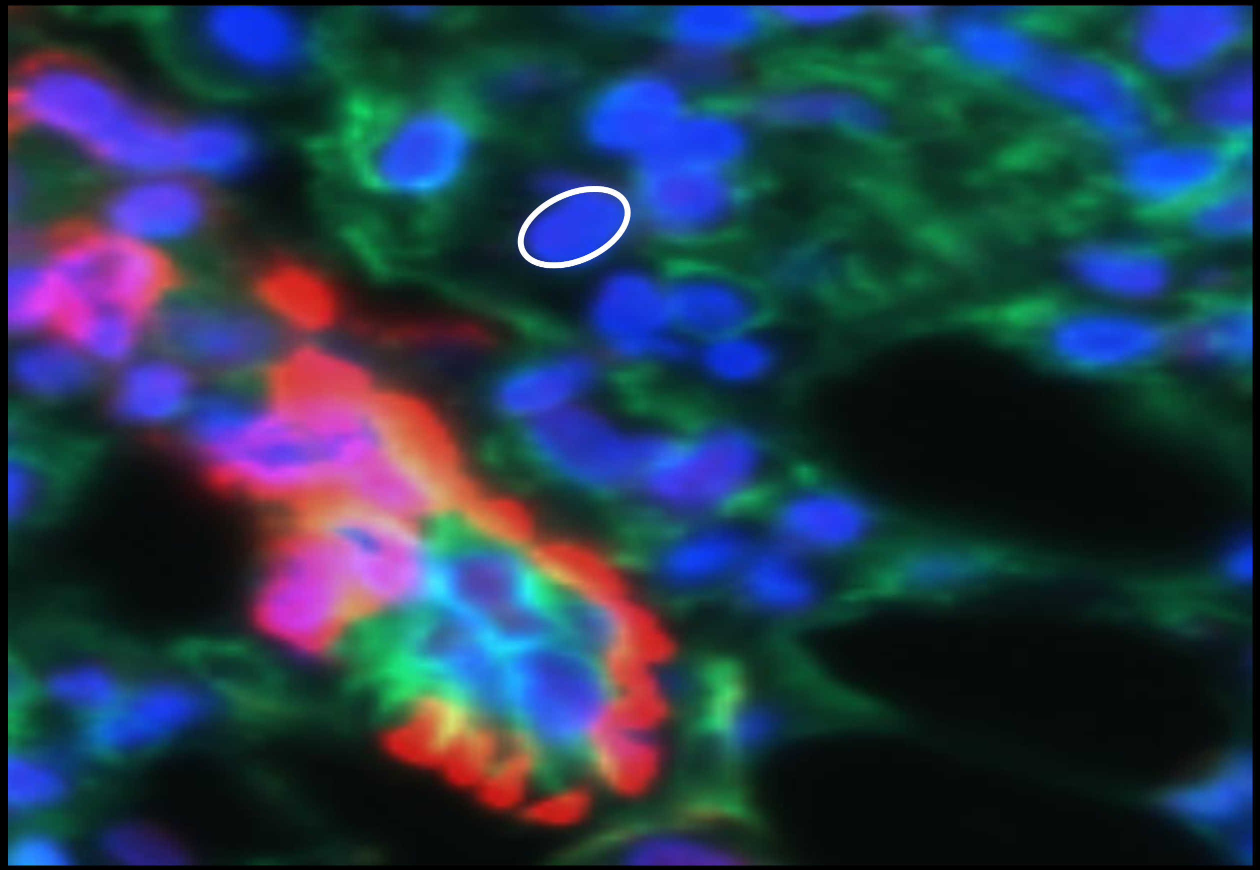
Interaction Analysis
Cellular Neighborhoods

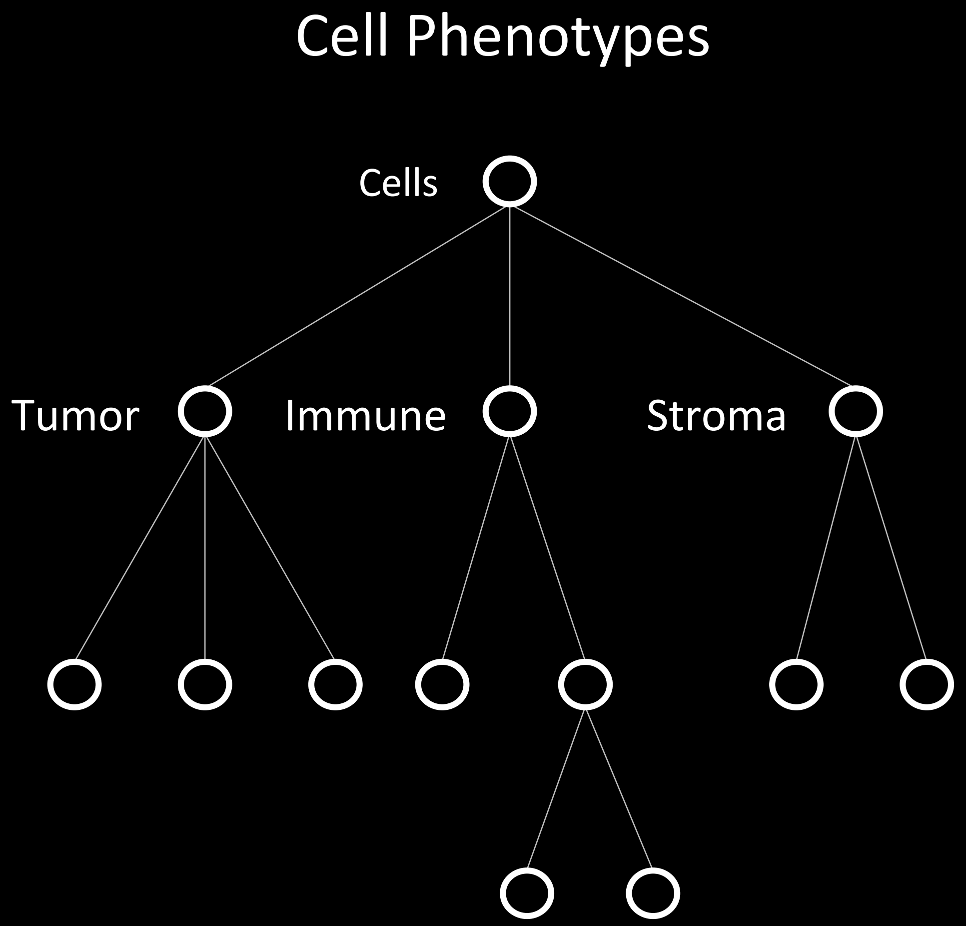
Cell Classification
Data Facetting with Machine Learning



Facet Data into Cell Types

- Identify cell types based on protein expressions in image channels



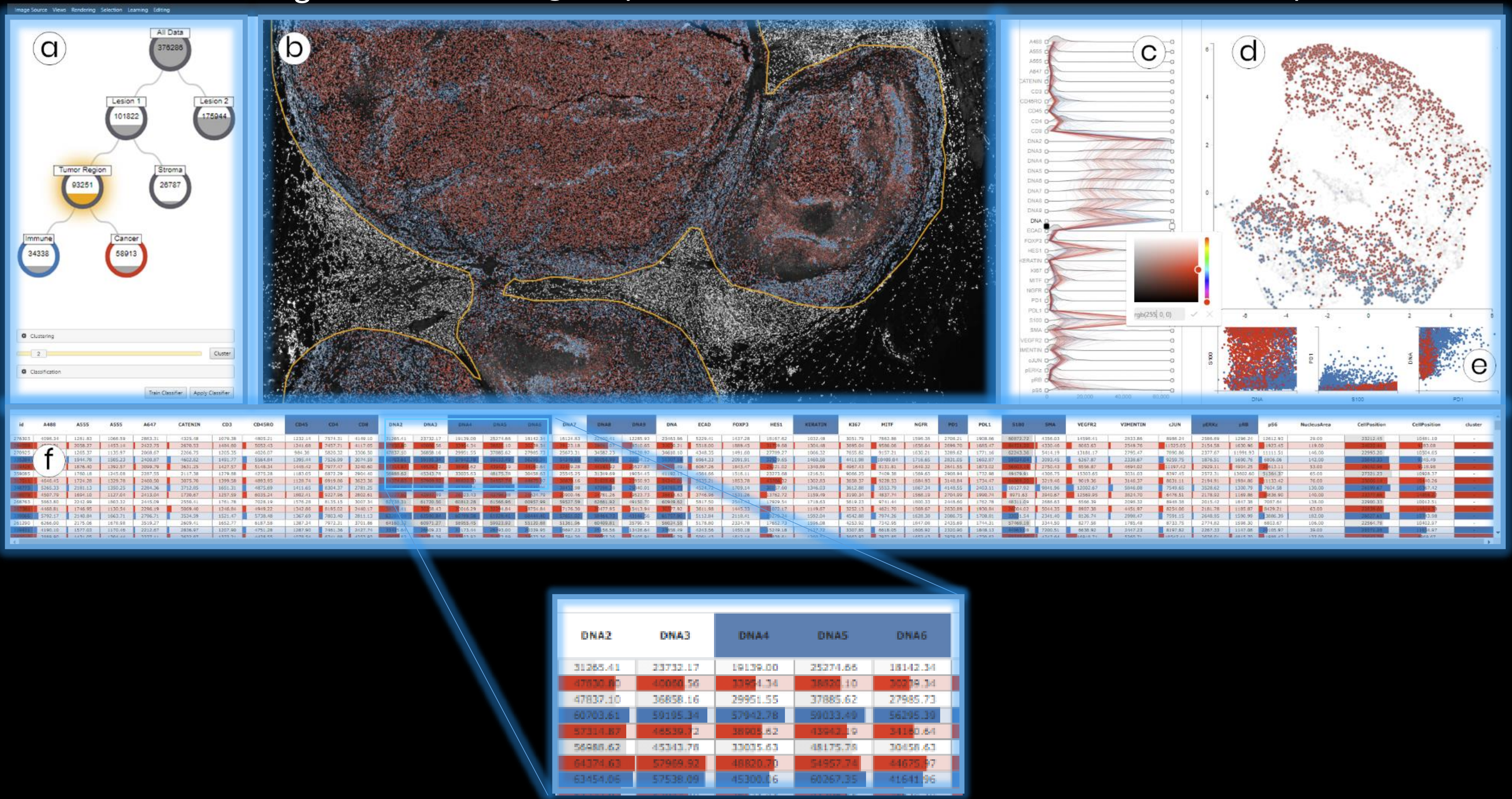


Facetto

Hierarchical Faceting

Image Exploration

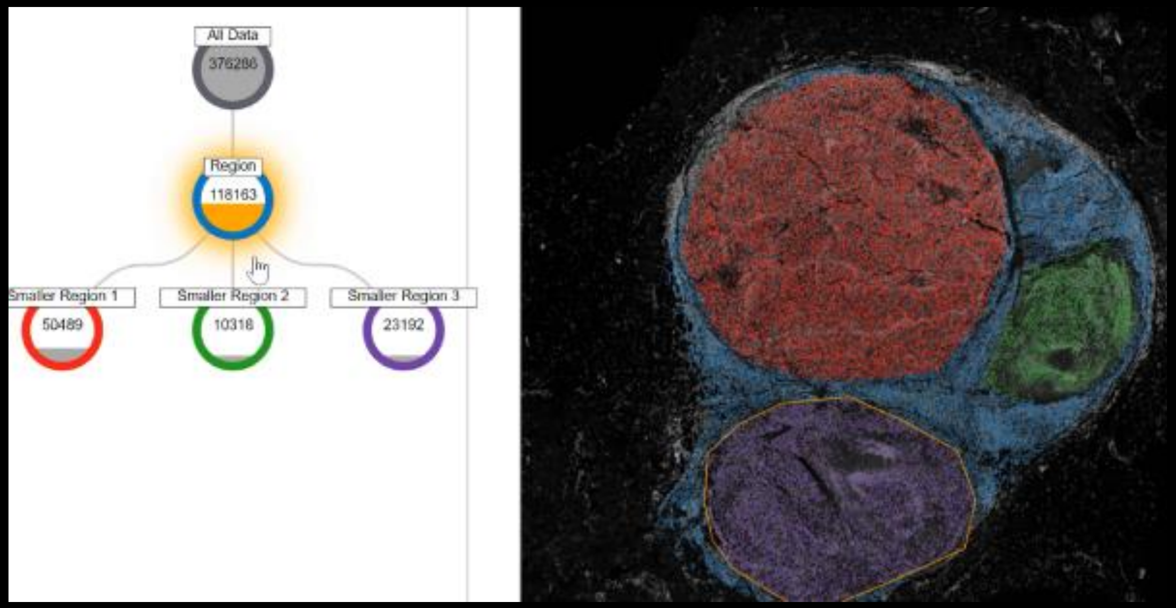
Feature Exploration

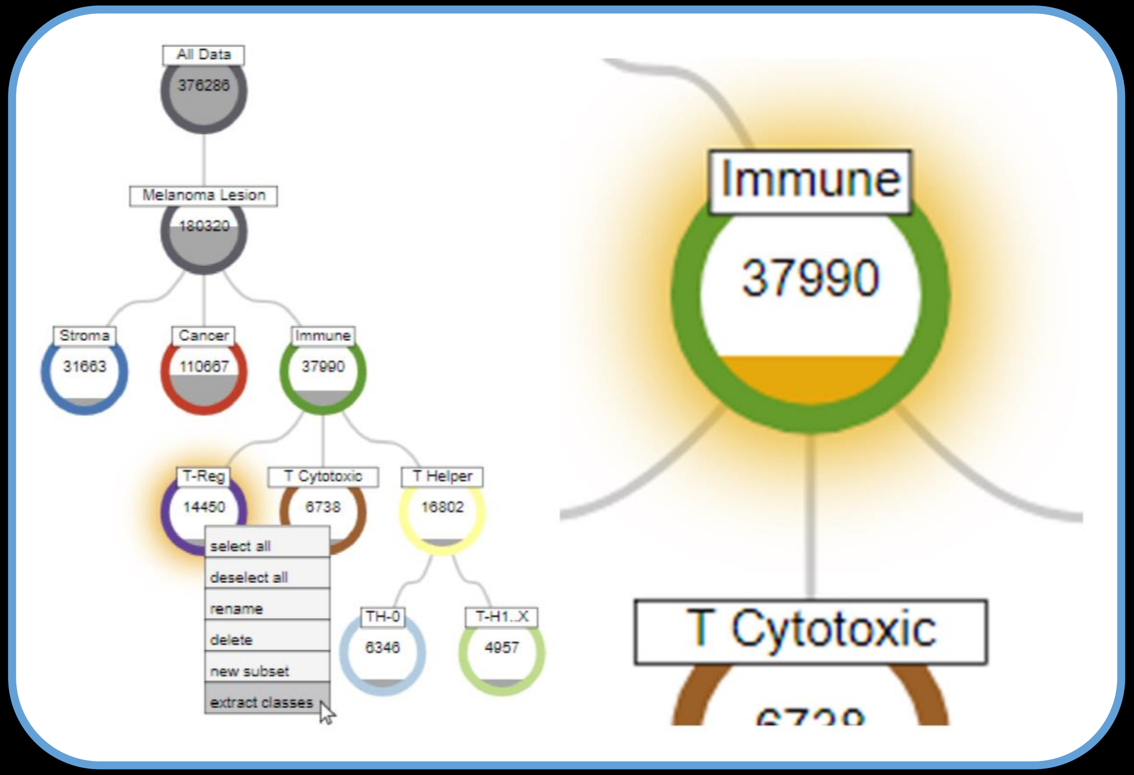


Krueger, R., et al., 2019. Facetto: Combining unsupervised and supervised learning for hierarchical phenotype analysis in multi-channel image data. *IEEE TVCG*

Manual Faceting

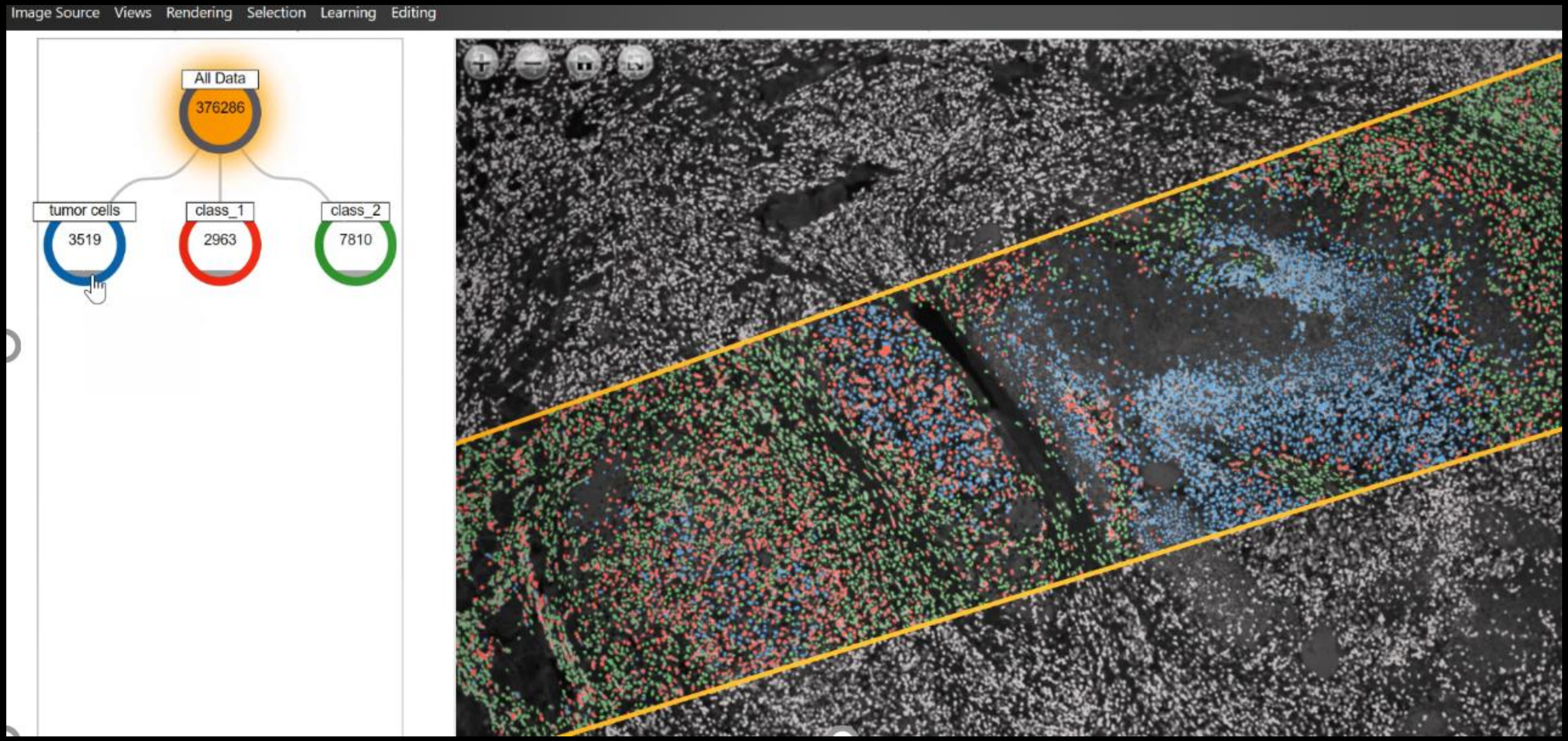
- Facet data into meaningful subsets (cell types, regions)
- Keep track of consecutive filtering actions





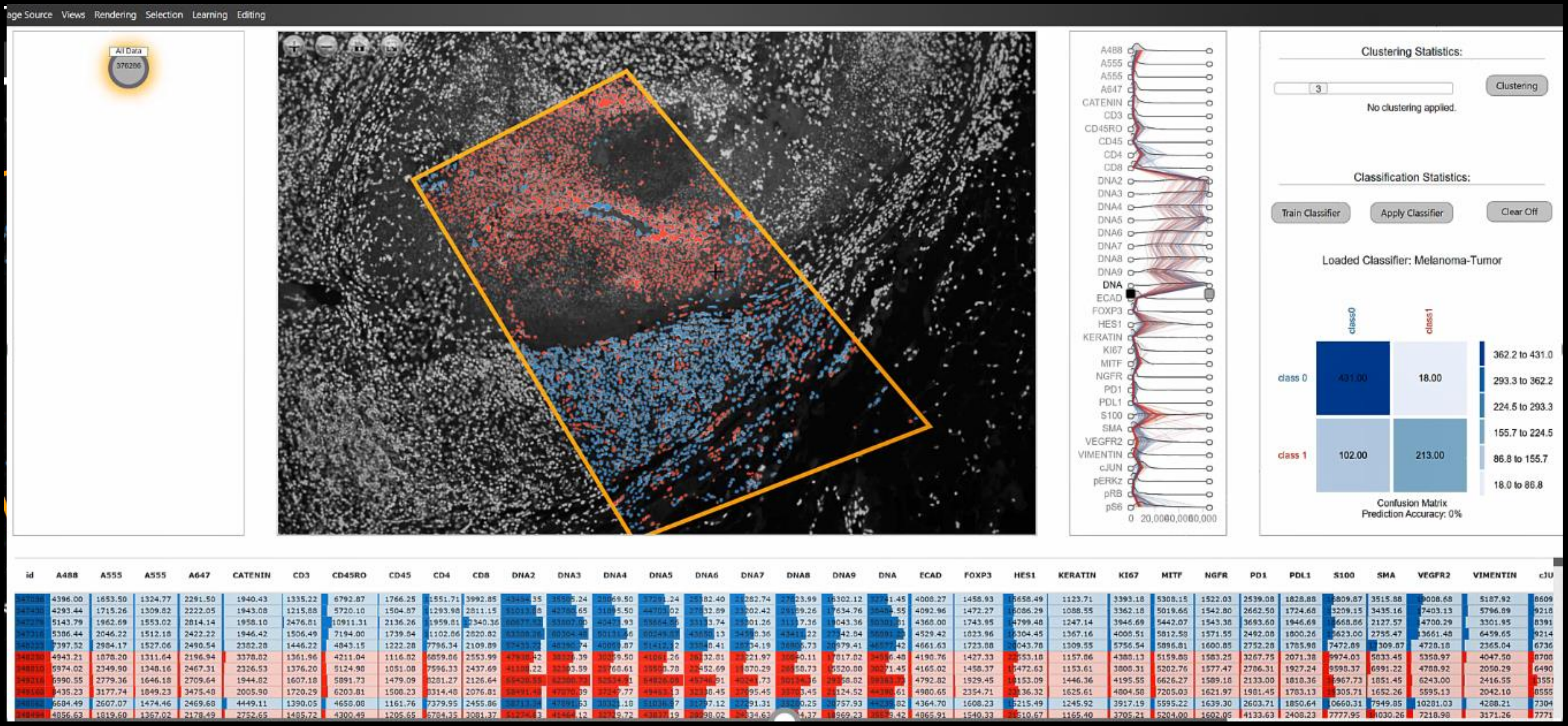
How can ML Support Analysis & Faceting?

- Bottom-Up Analysis
  - Unsupervised learning supports exploration and faceting
  - EM-Clustering
    is fast, detects clusters of different size, density, shape



How can ML Support Analysis & Faceting?

- Top-Down Analysis
  - Supervised learning applies gained knowledge to new data
  - Train classifier on manually refined clustering results
  - CNN Classification uses image tiles as input to classify cell phenotypes



Visual Analysis of Multiplexed Immunofluorescence Data

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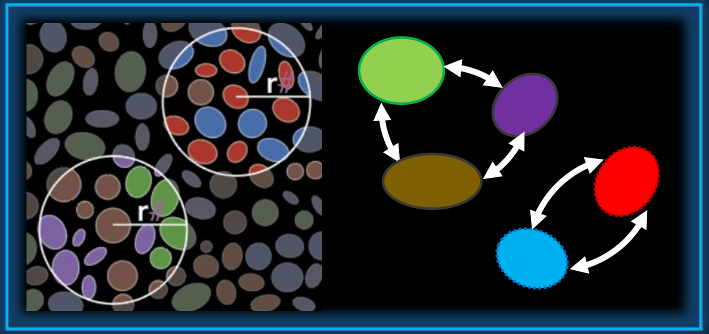
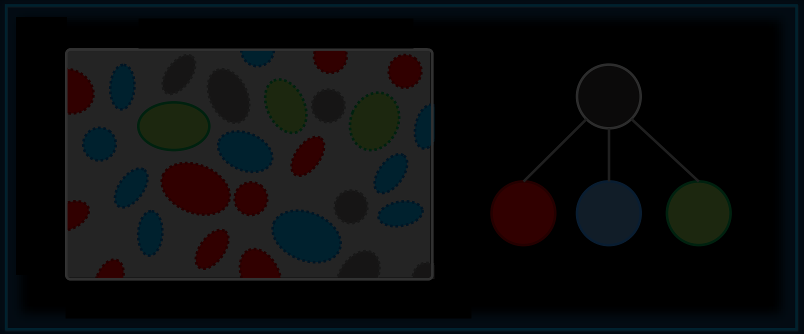
Focus+Context Pathology Assessment

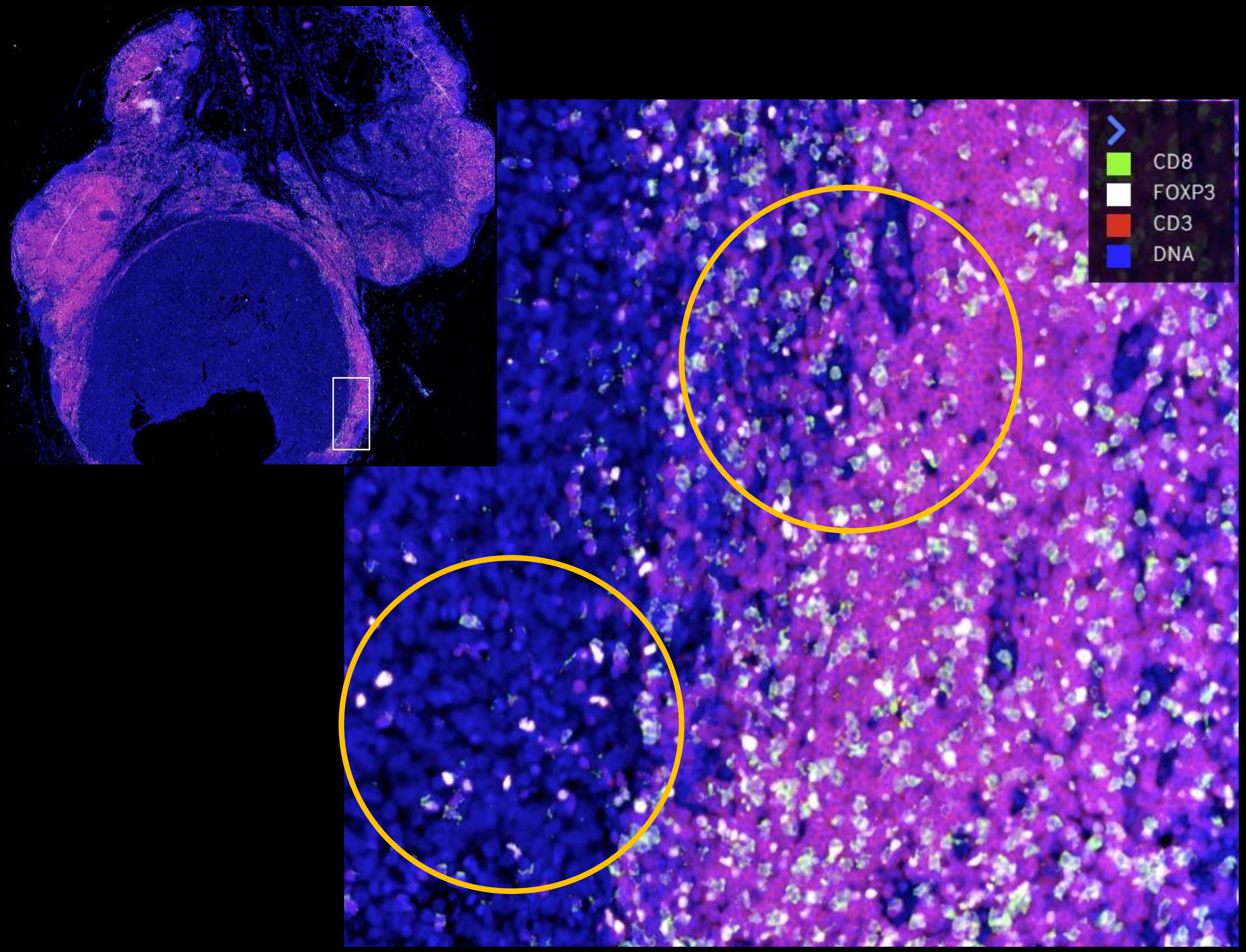
Interaction Analysis
Cellular Neighborhoods

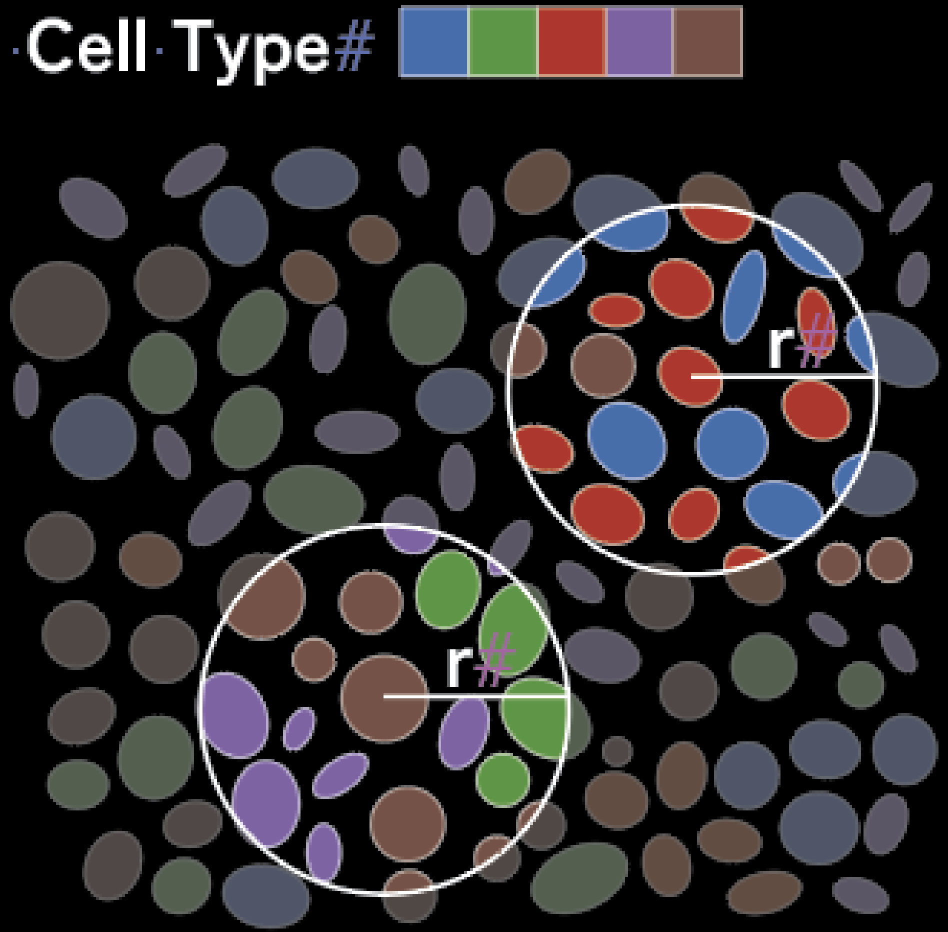


Cell Classification
Data Facetting with Machine Learning

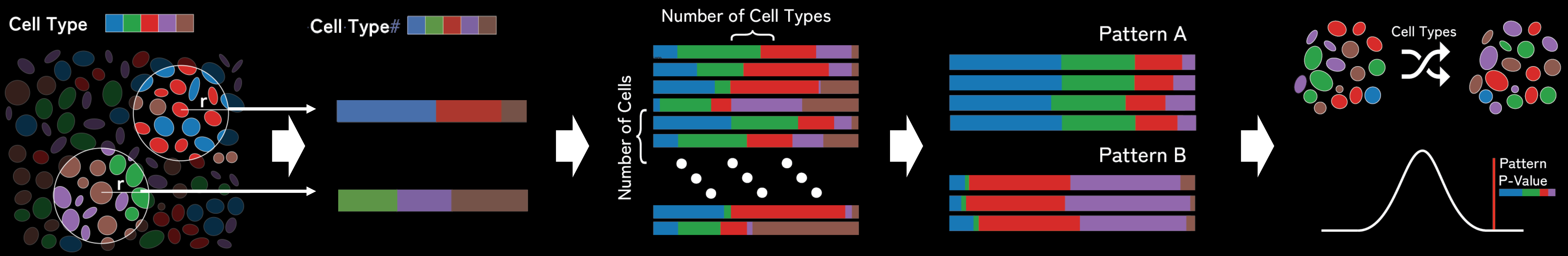


From Single-Cell Analysis to Cellular Neighborhoods

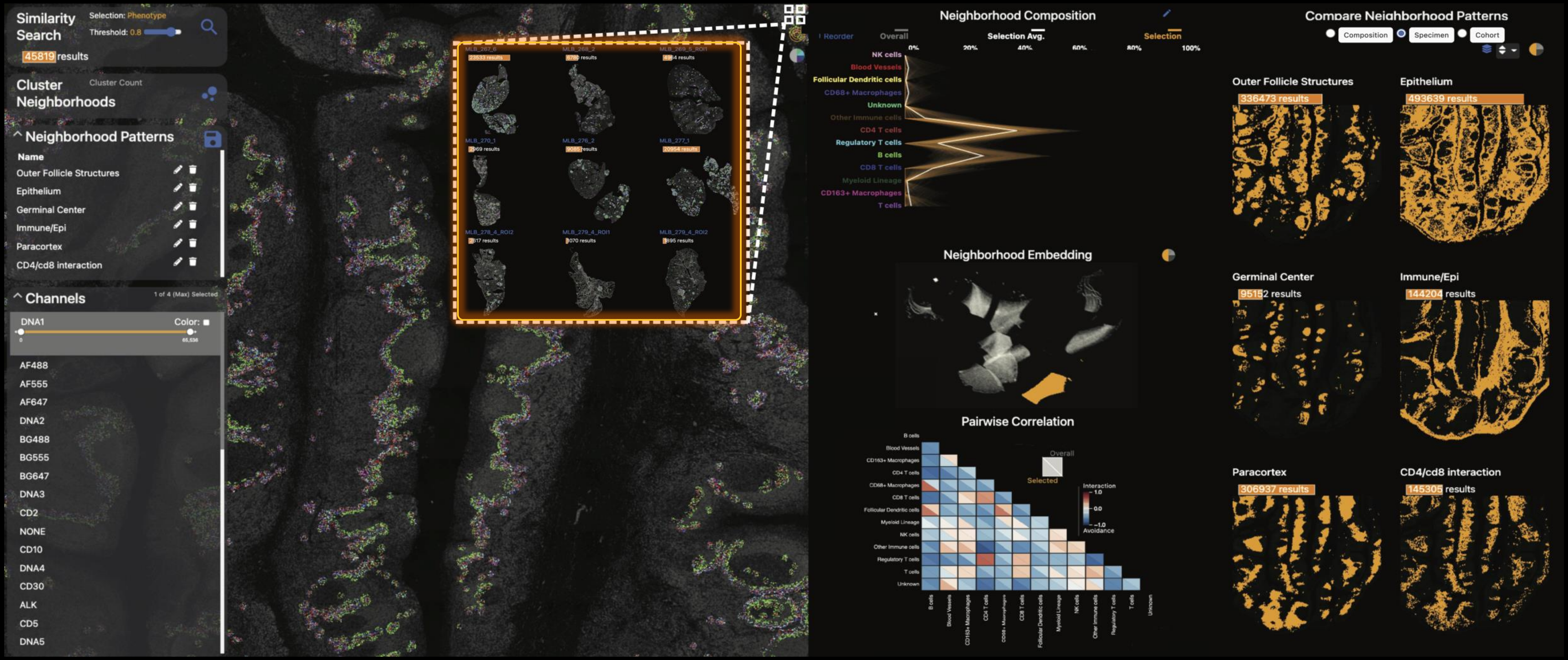




Neighborhood Quantification

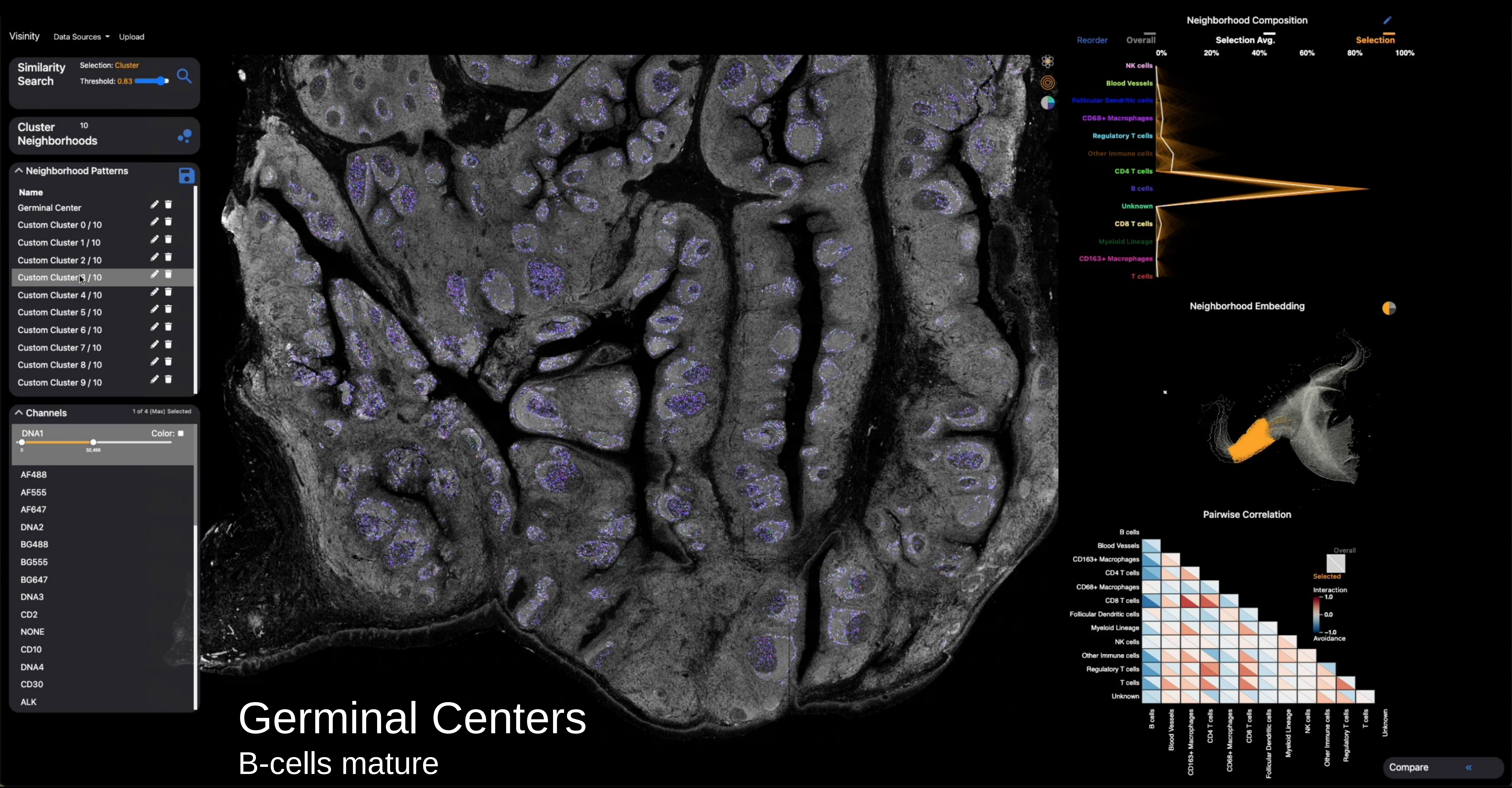


Visinity: Visual Spatial Neighborhood Analysis



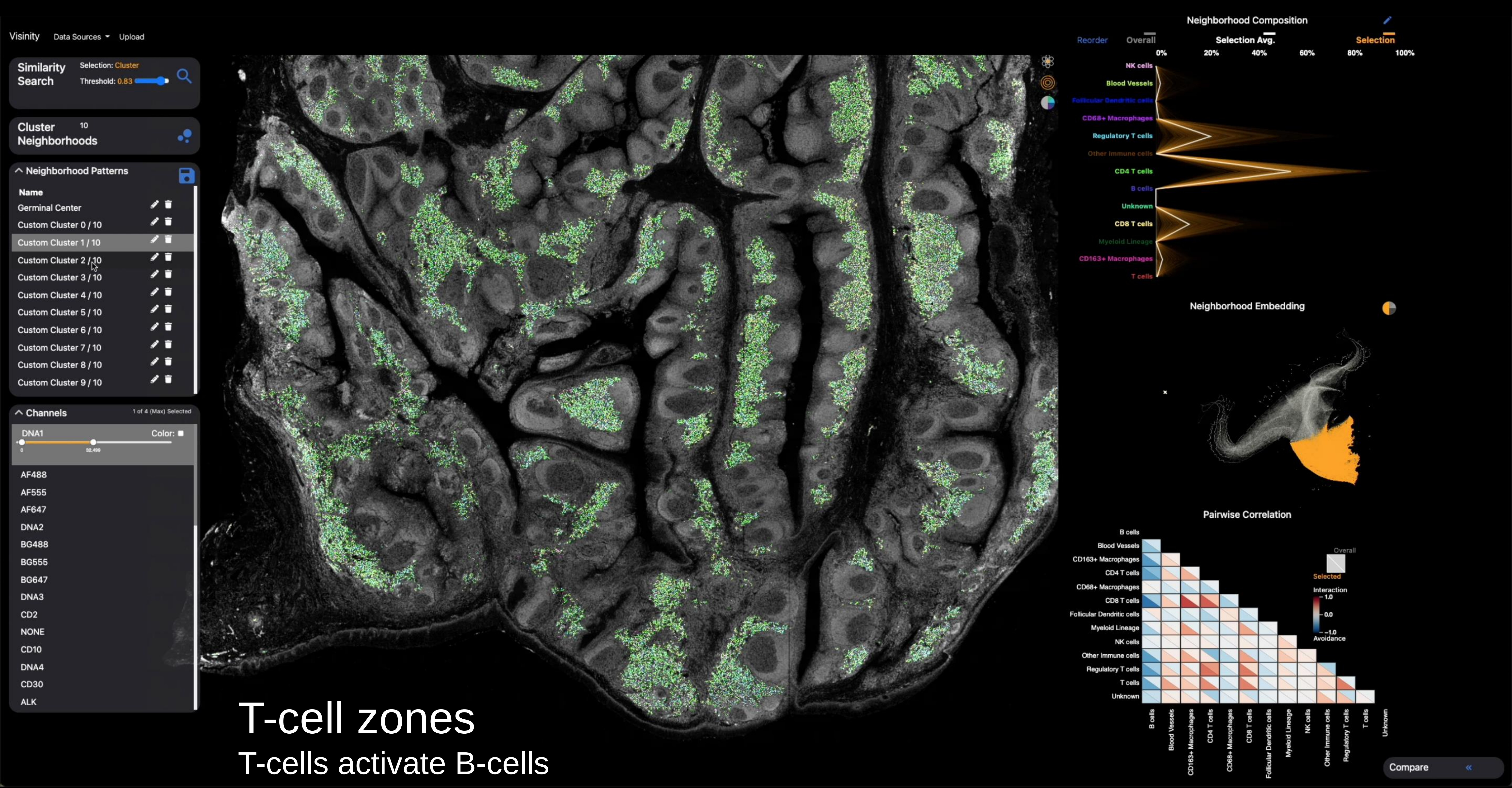
Warchol, S., Krueger, R. et al., *2022.* **Visinity: Visual Spatial Neighborhood Analysis for Multiplexed Tissue Imaging Data**. *IEEE TVCG.*

Gaglia, Giorgio, et al., 2023. **Lymphocyte networks are dynamic cellular communities in the immunoregulatory landscape of lung adenocarcinoma**. Cancer Cell.



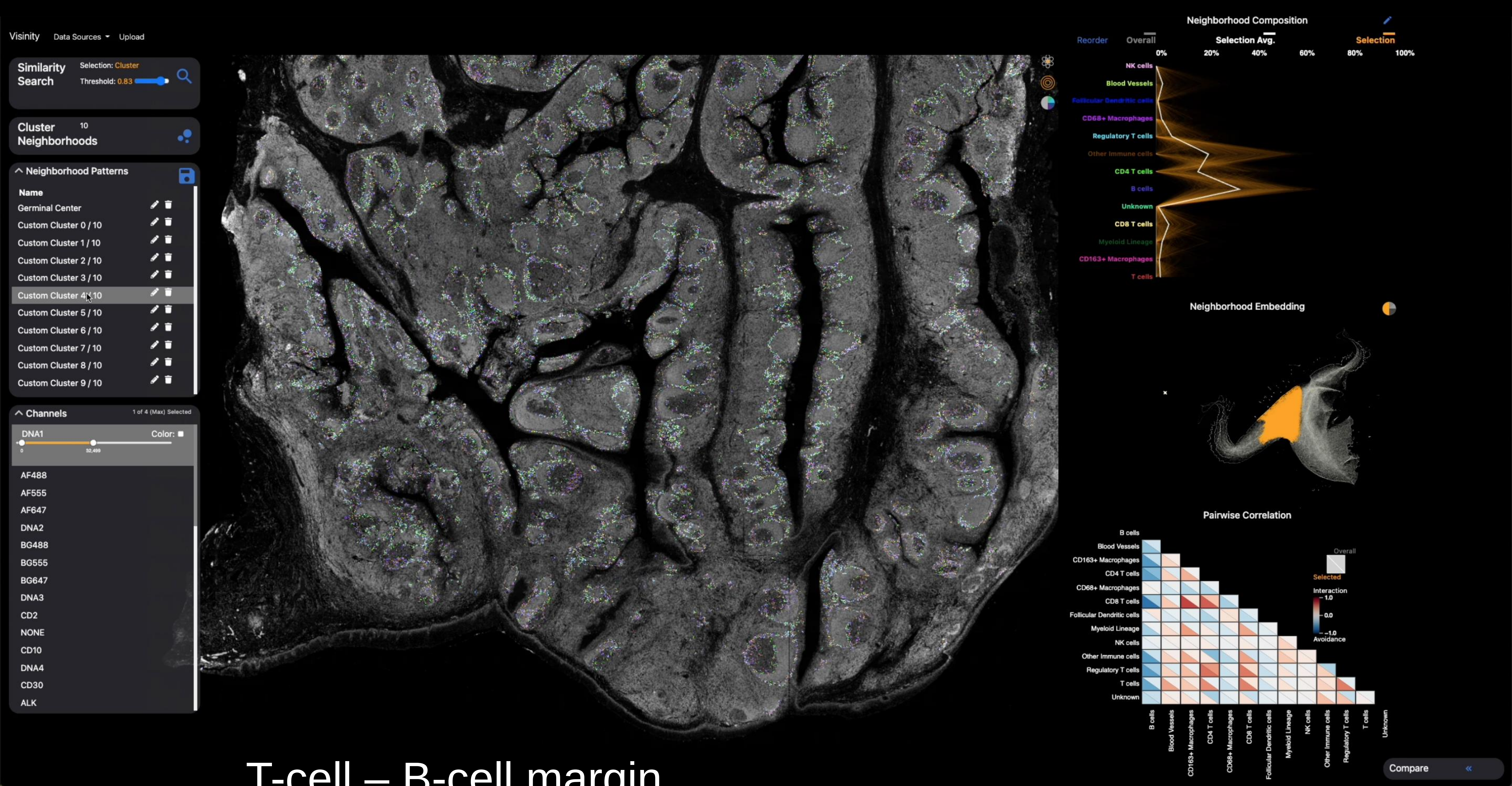
Germinal Centers

B-cells mature

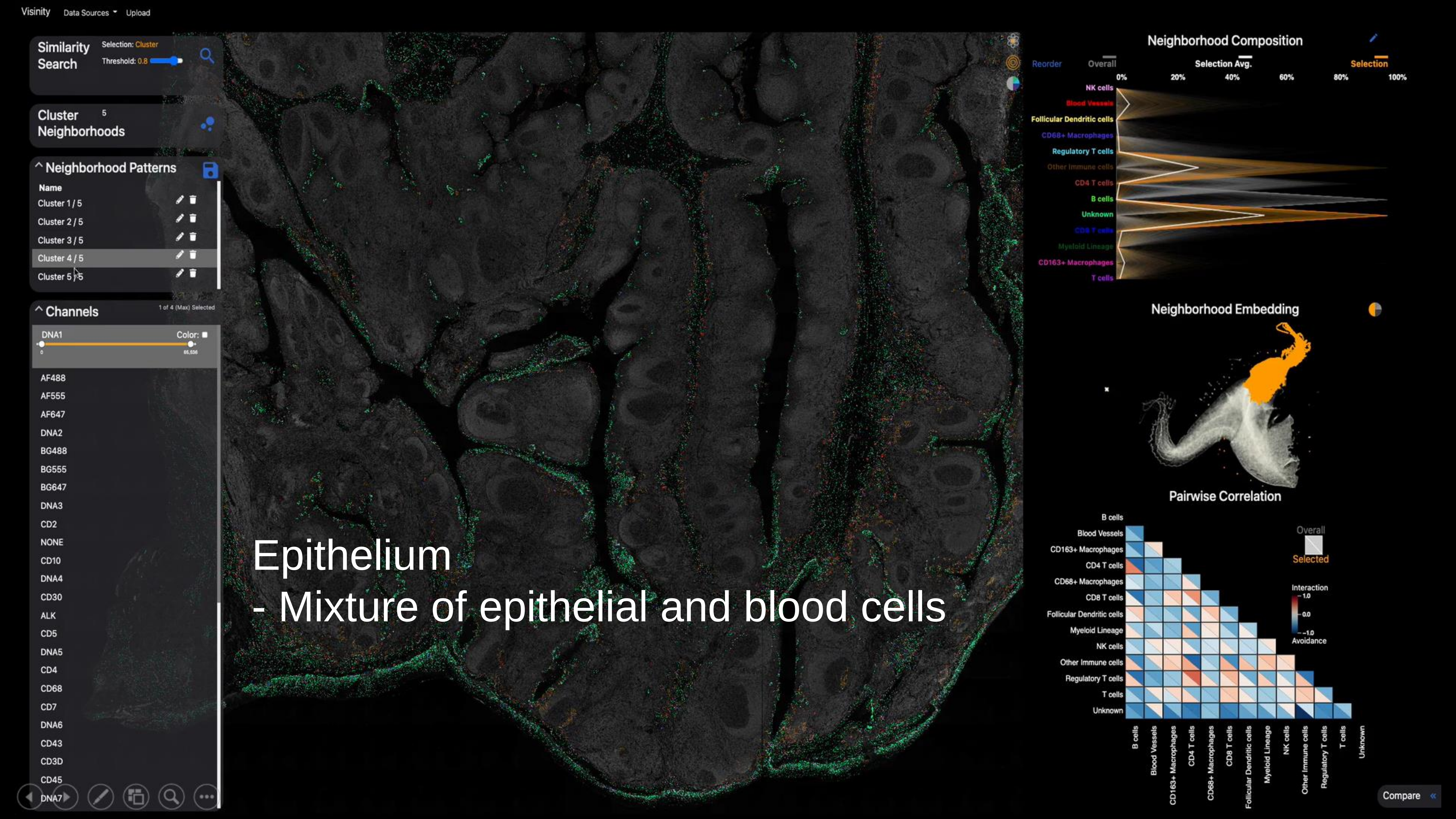


T-cell zones

T-cells activate B-cells



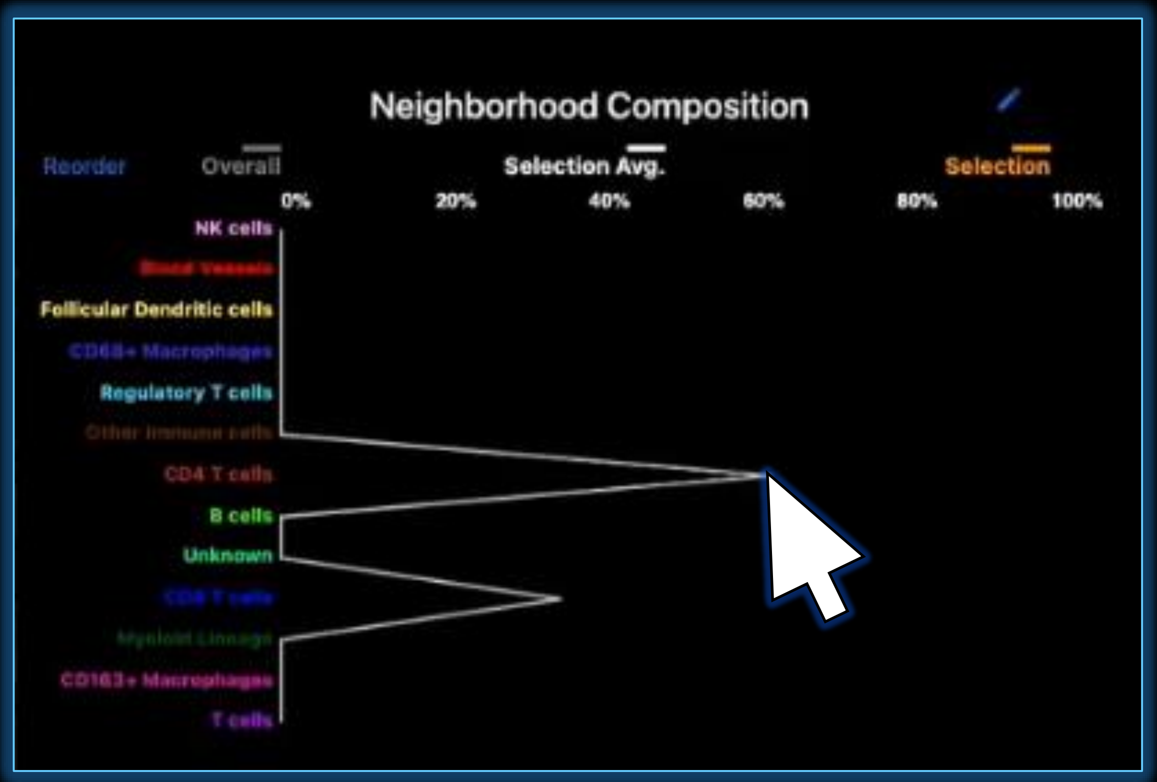
T-cell – B-cell margin

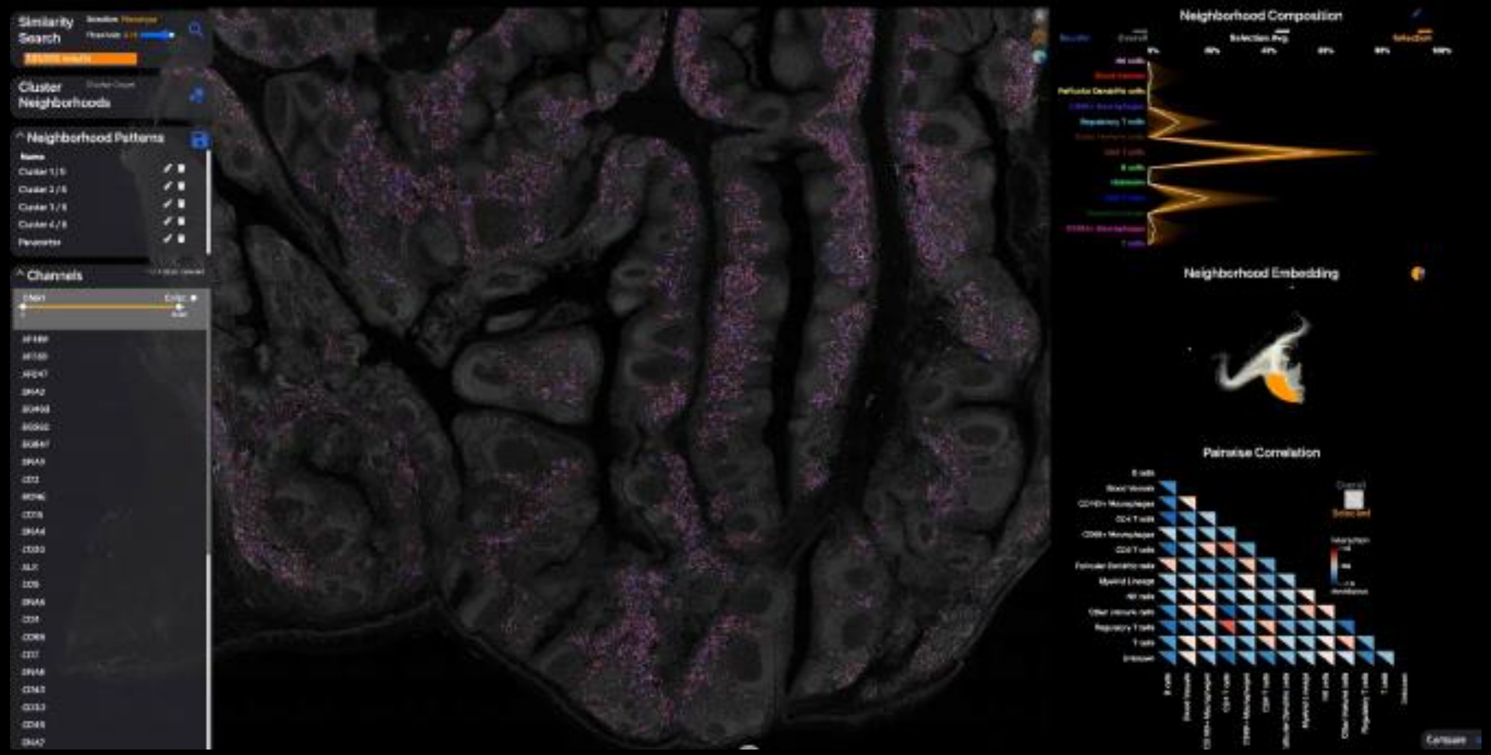


Epithelium

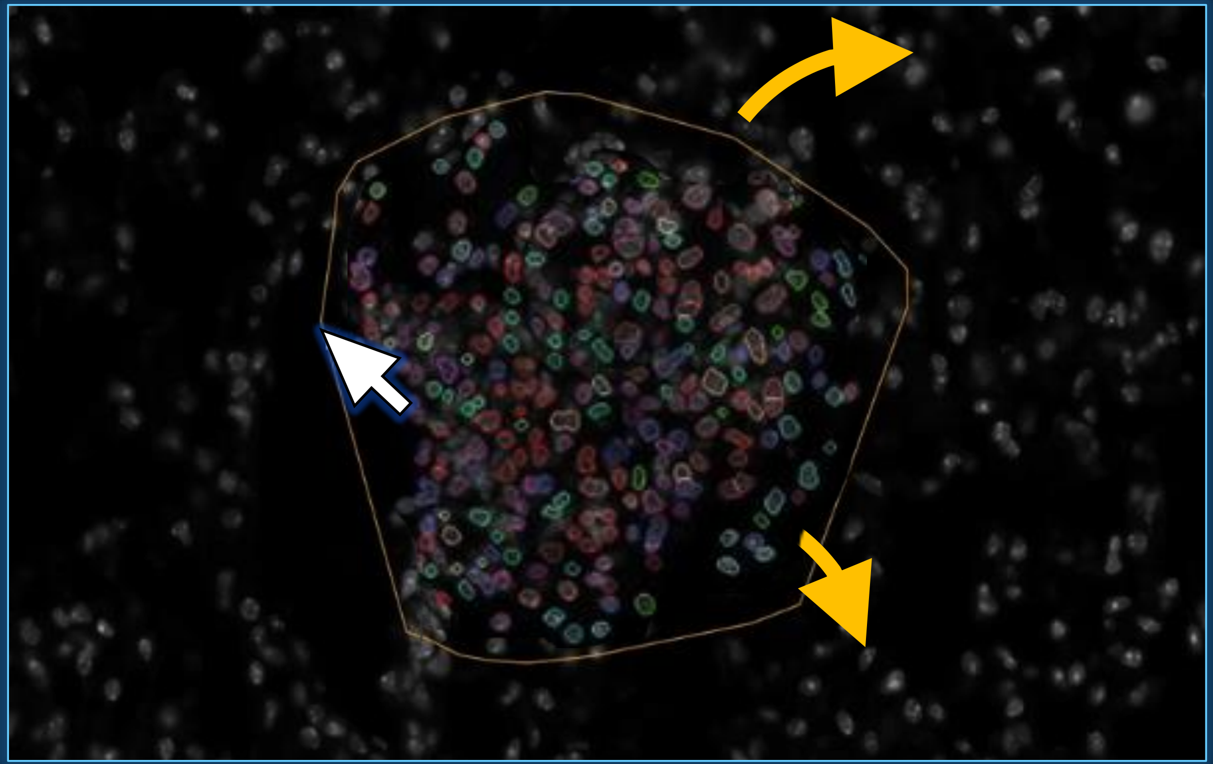
- Mixture of epithelial and blood cells

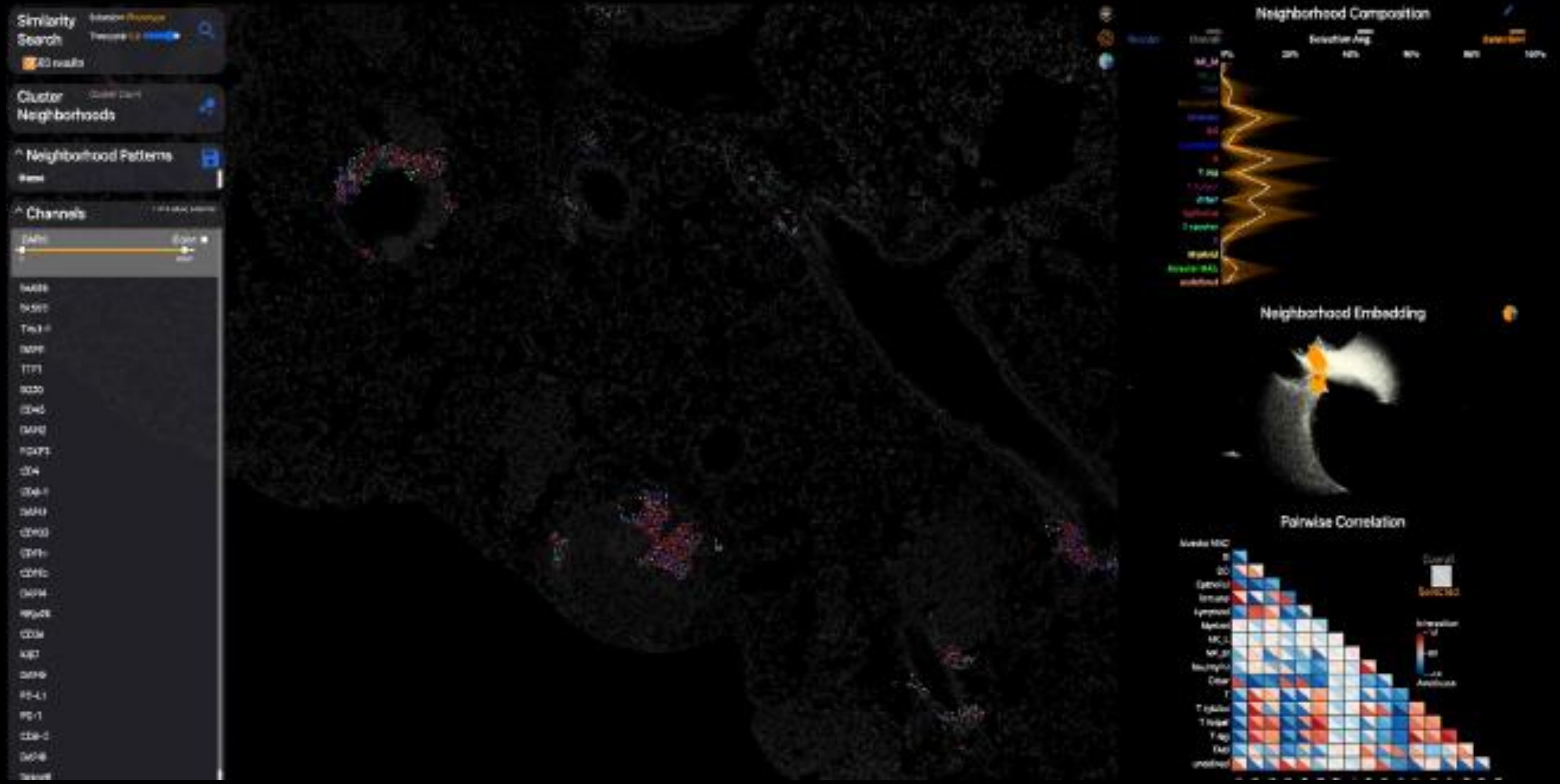
Top-Down: Hypothesis Formulation & Query





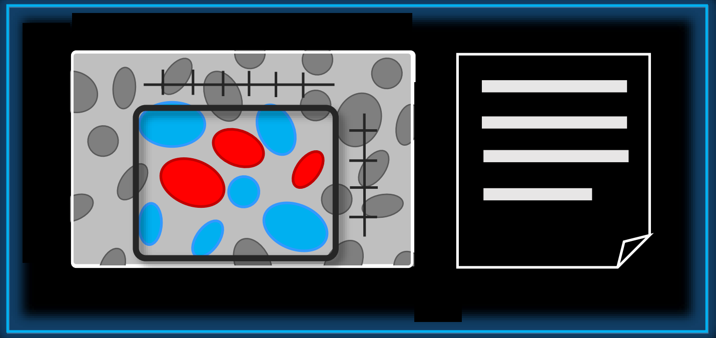
Top-Down: Search/Find by Example





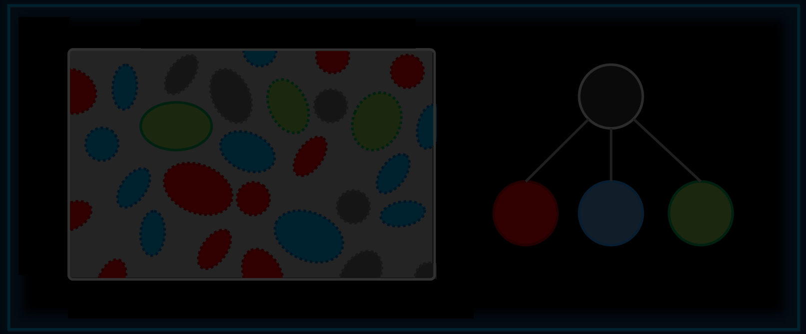
Visual Analysis of Multiplexed Immunofluorescence Data

Annotation
Focus+Context Pathology Assessment

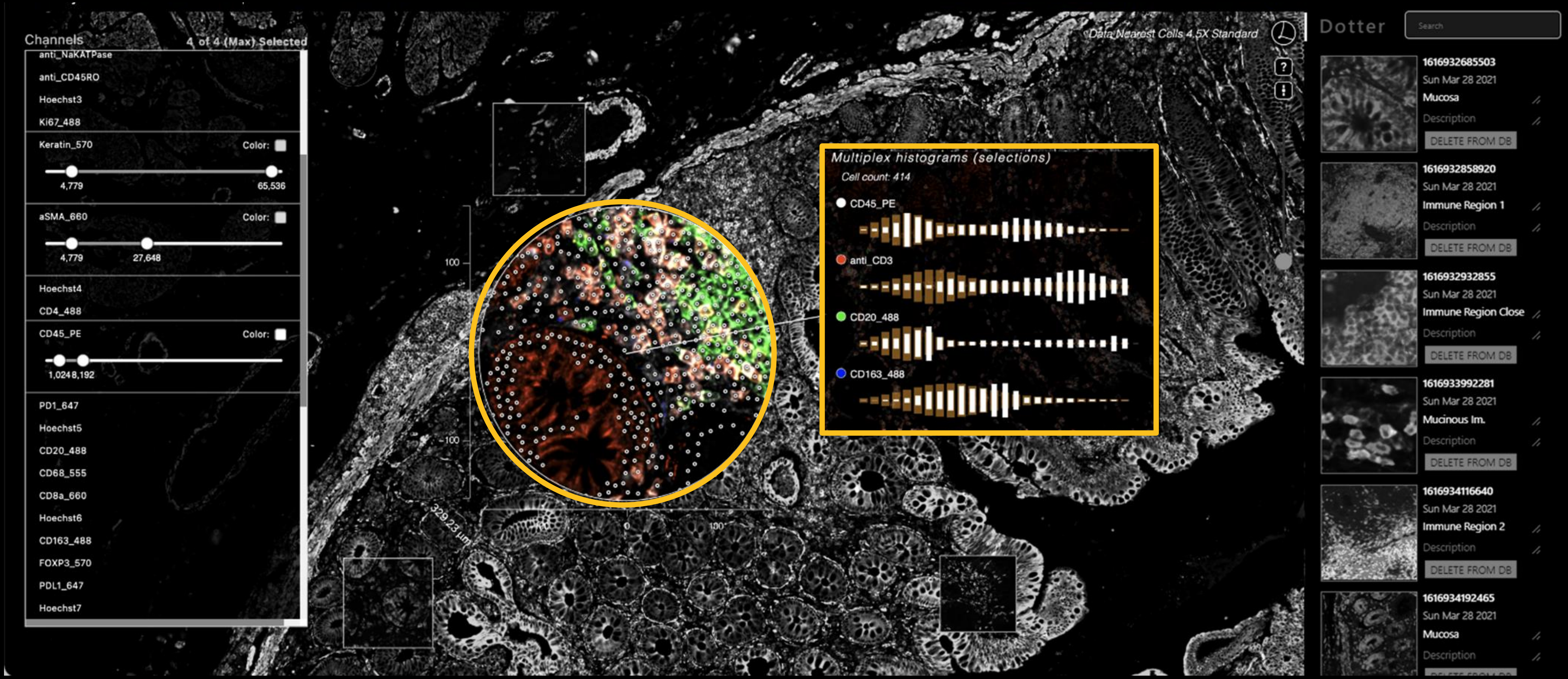


Interaction Analysis
Cellular Neighborhoods

Cell Classification
Data Facetting with Machine Learning

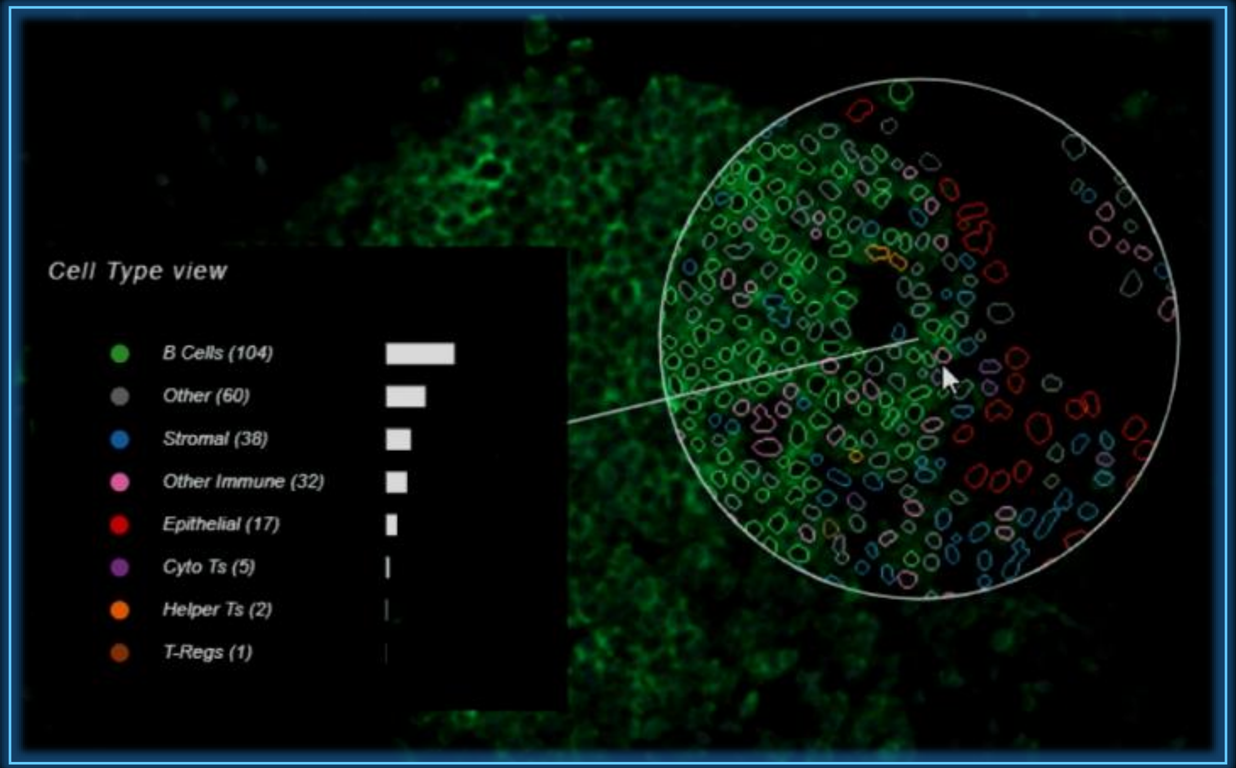


From Scope 2 Screen



Jessup, J.& Krueger, R., et al., 2021. Scope2Screen: Focus+Context Techniques for Pathology Tumor Assessment in Multivariate Image Data. *IEEE TVCG.*

Filters



Feature-based

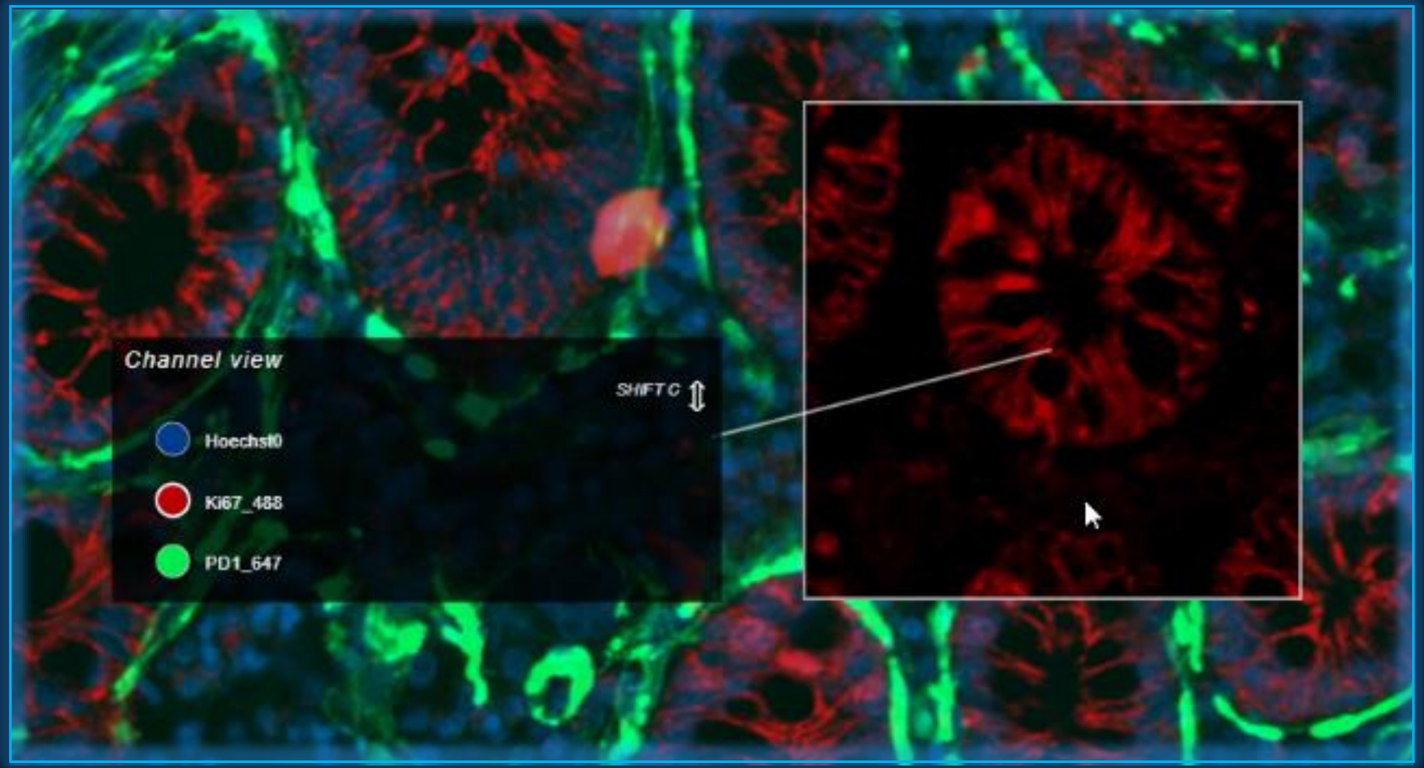
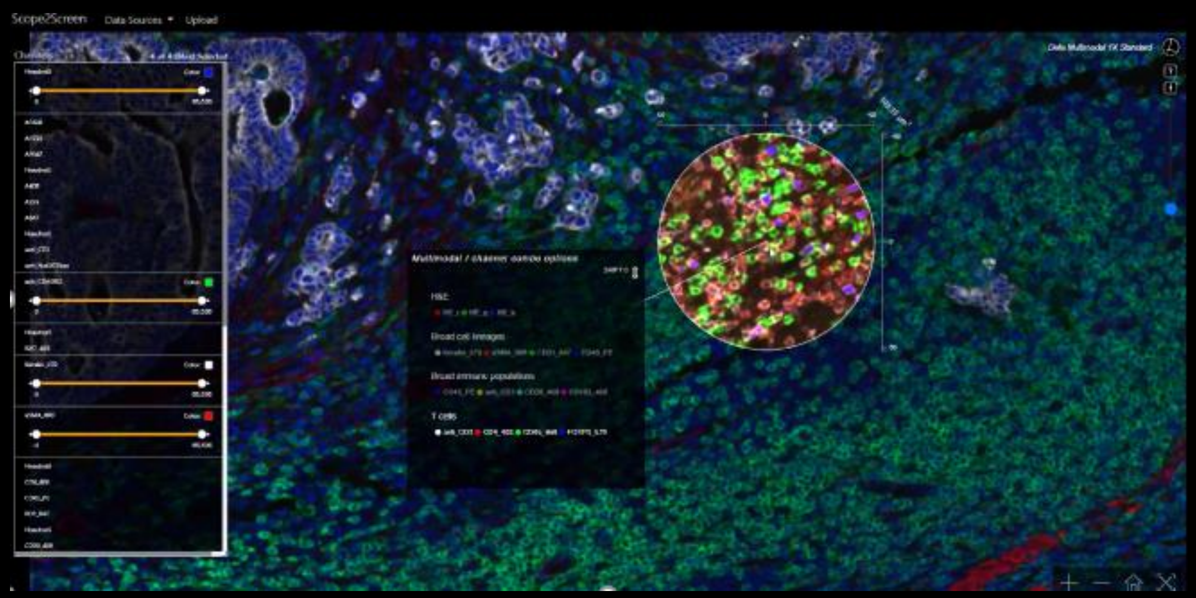
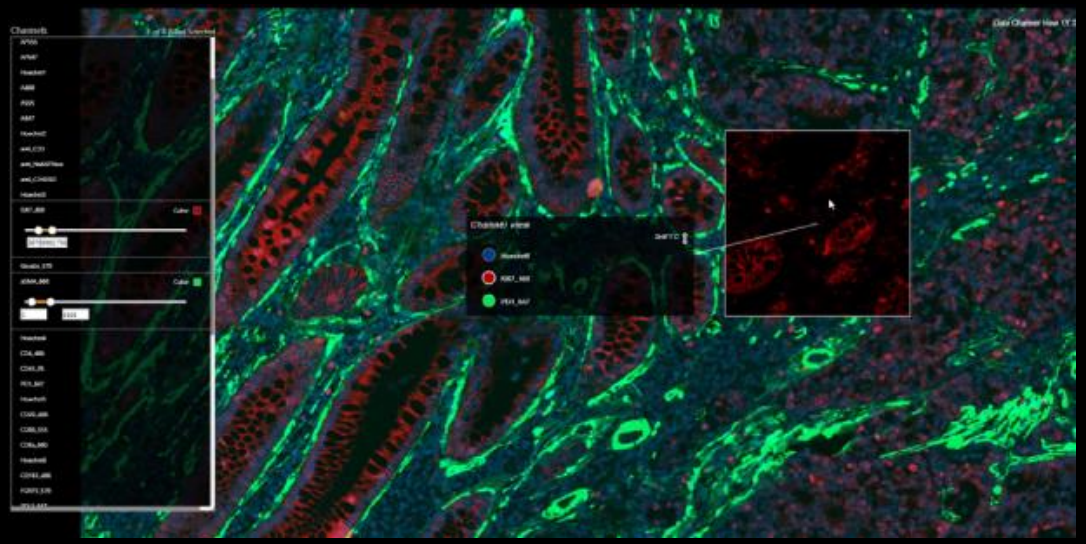
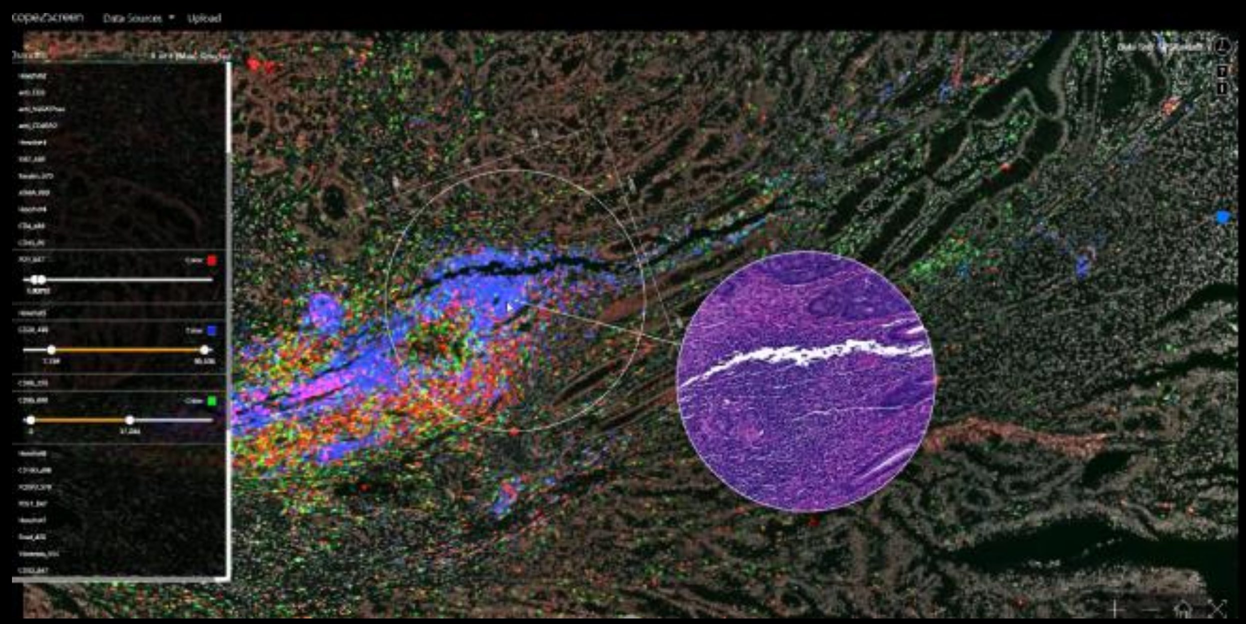


Image-based

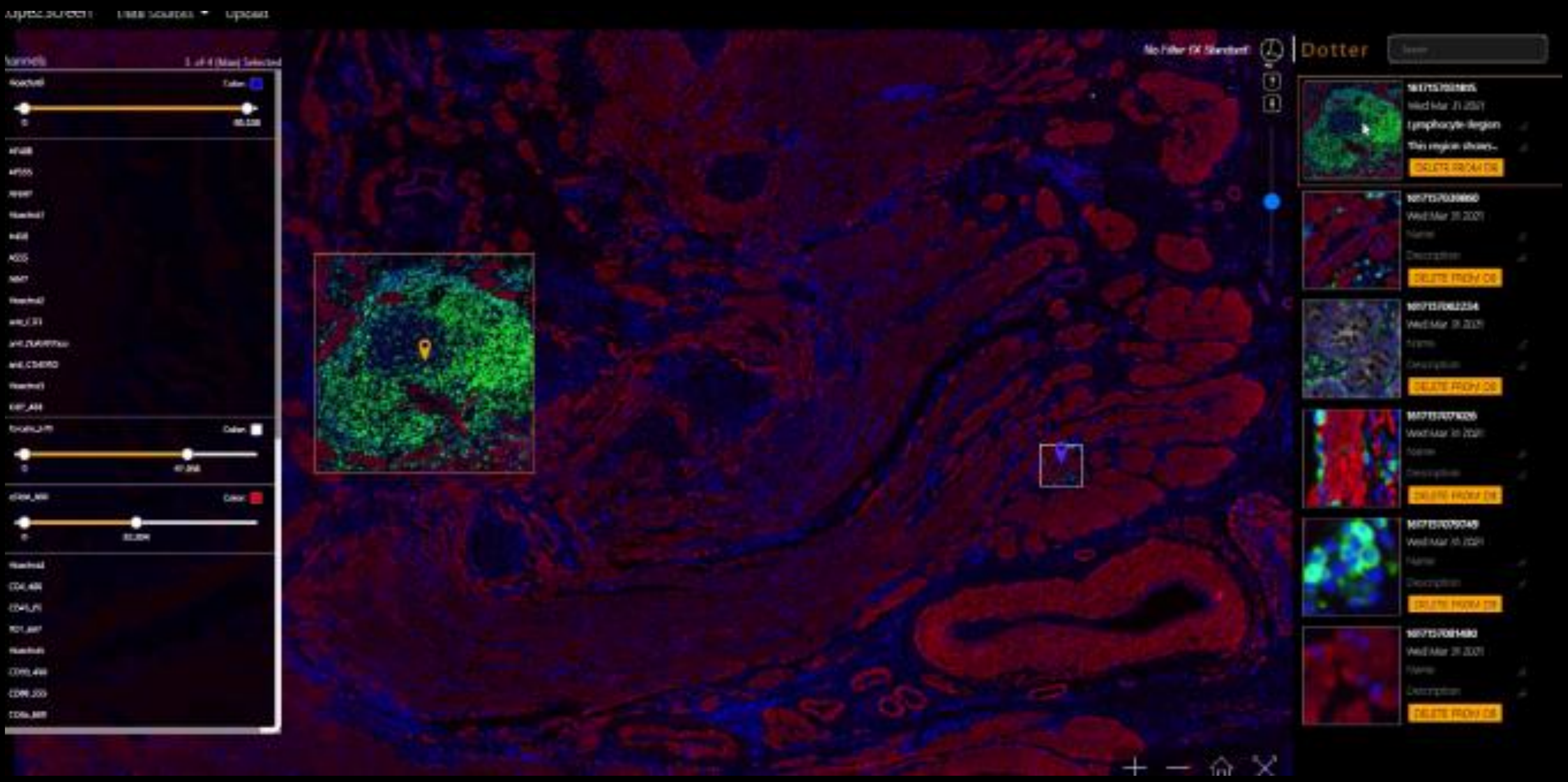
Image-Based Filters

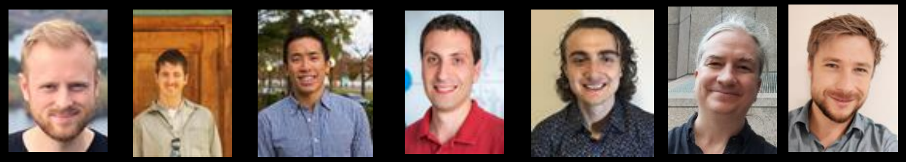




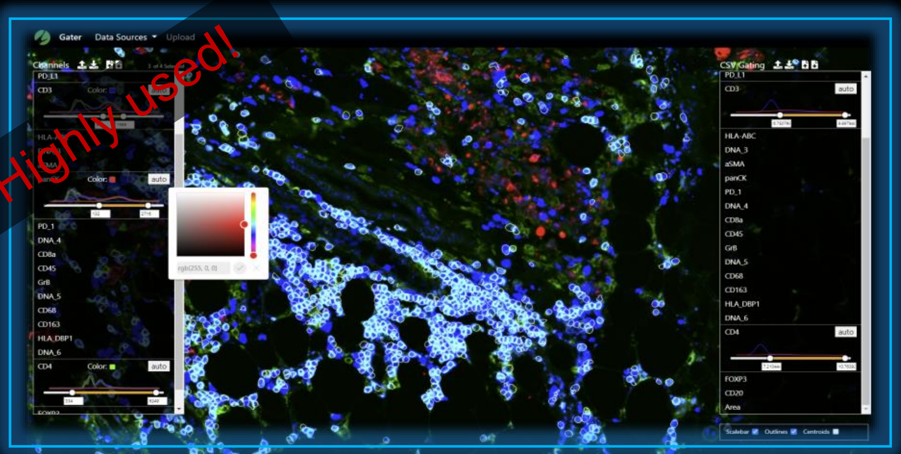


Annotation



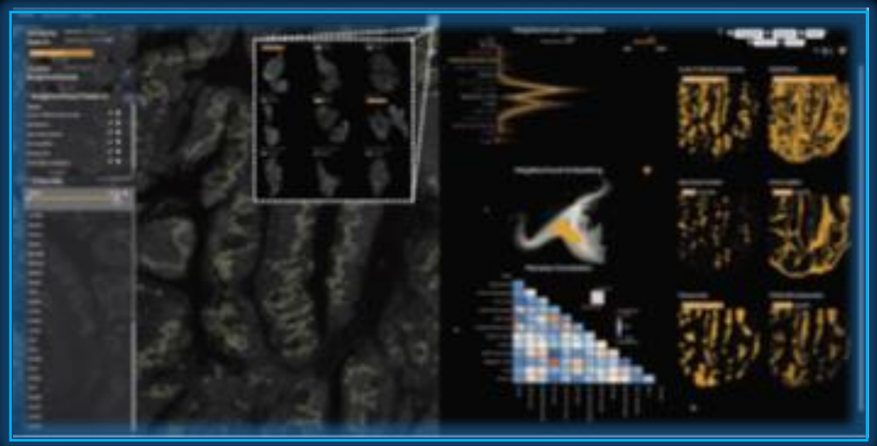


Analysis Suite: 3 Tools



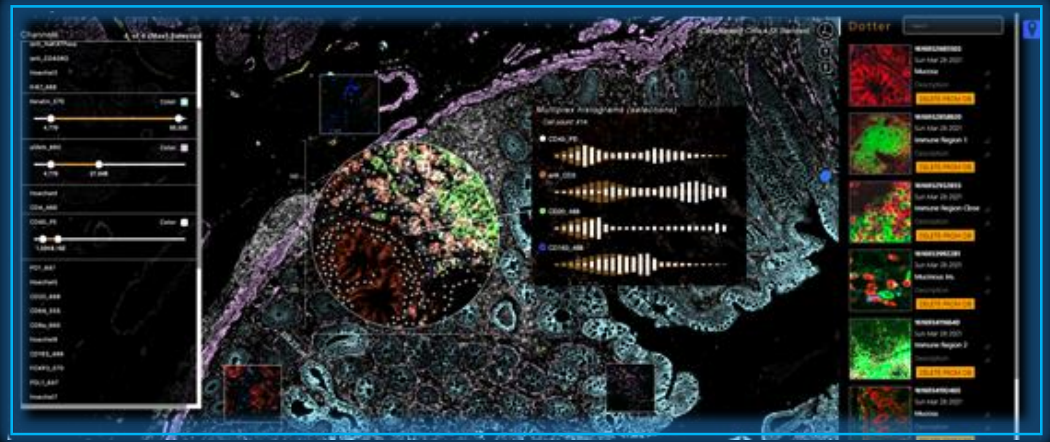
Gater: Tabular Data Cleaning with Visual Feedback

https://github.com/labsyspharm/gater



Visinity (Facetto): Cell Typing and Neighborhood Analysis

https://github.com/labsyspharm/visinity



Scope2Screen: Focus+Context ROI Exploration and Annotation

https://github.com/labsyspharm/scope2screen

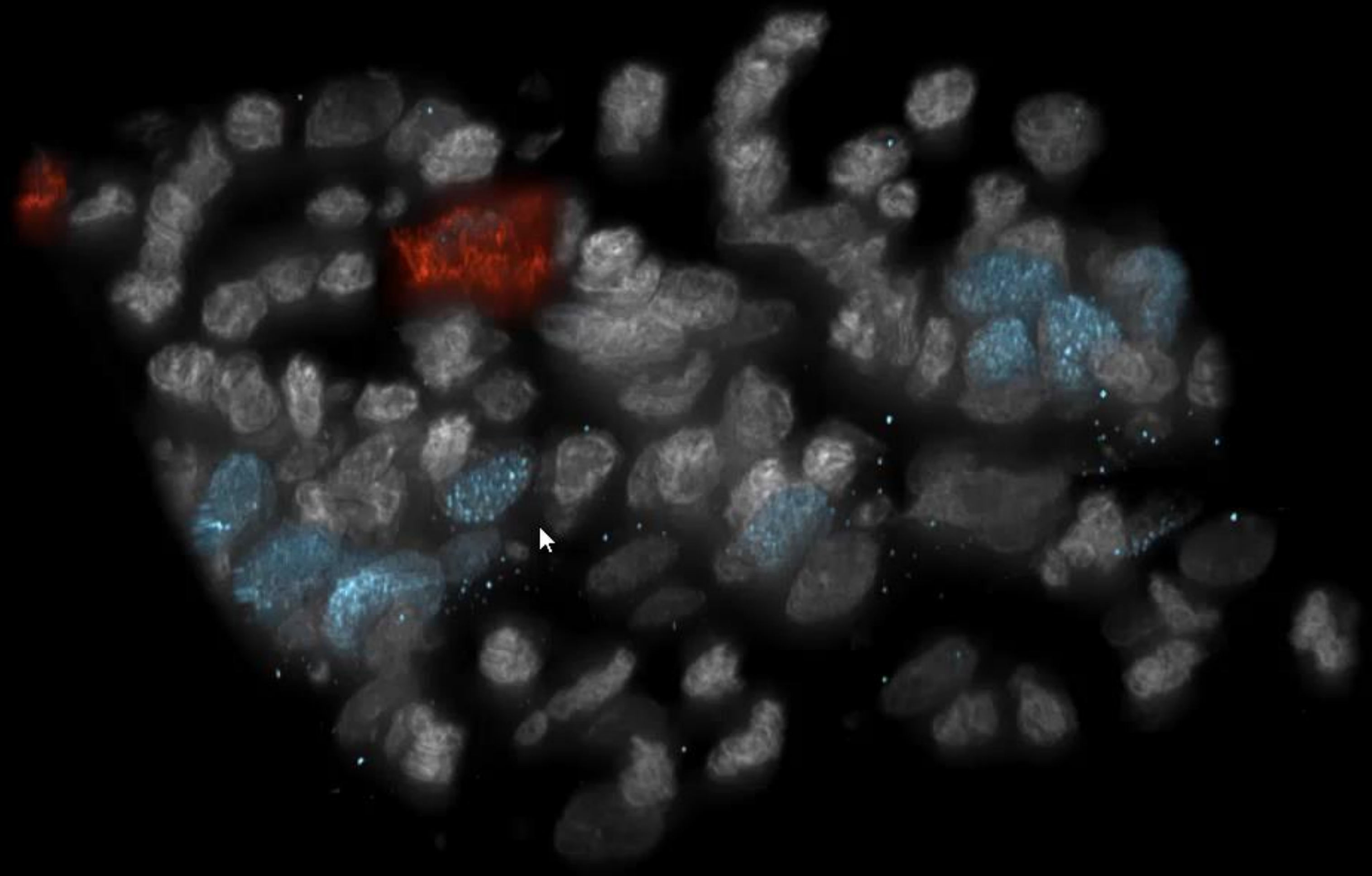
Visual Computing Group @ Harvard School of Engineering and Applied Sciences

Laboratory of Systems Pharmacology @Harvard Medical School

Future Research Areas

2D to 3D

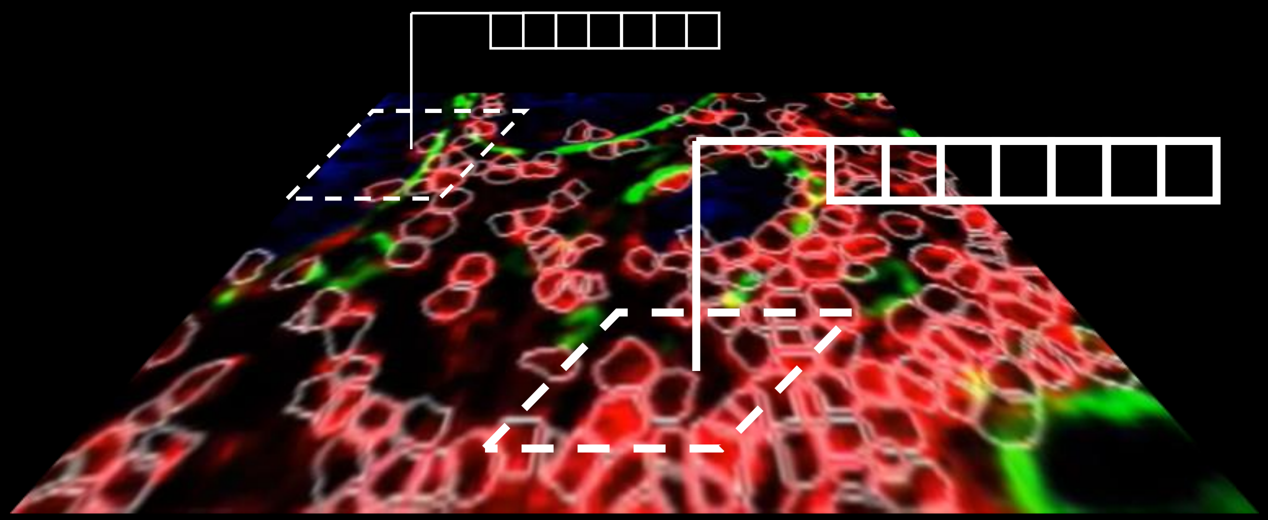
- TB-sized multi-volumetric data
- Scalable multi-resolution rendering
- Image-based cell and interaction analysis



Herzberger, Lukas et al. 2023. Residency Octree: A Hybrid Approach for Scalable Web-Based Multi-Volume Rendering. IEEE TVCG.

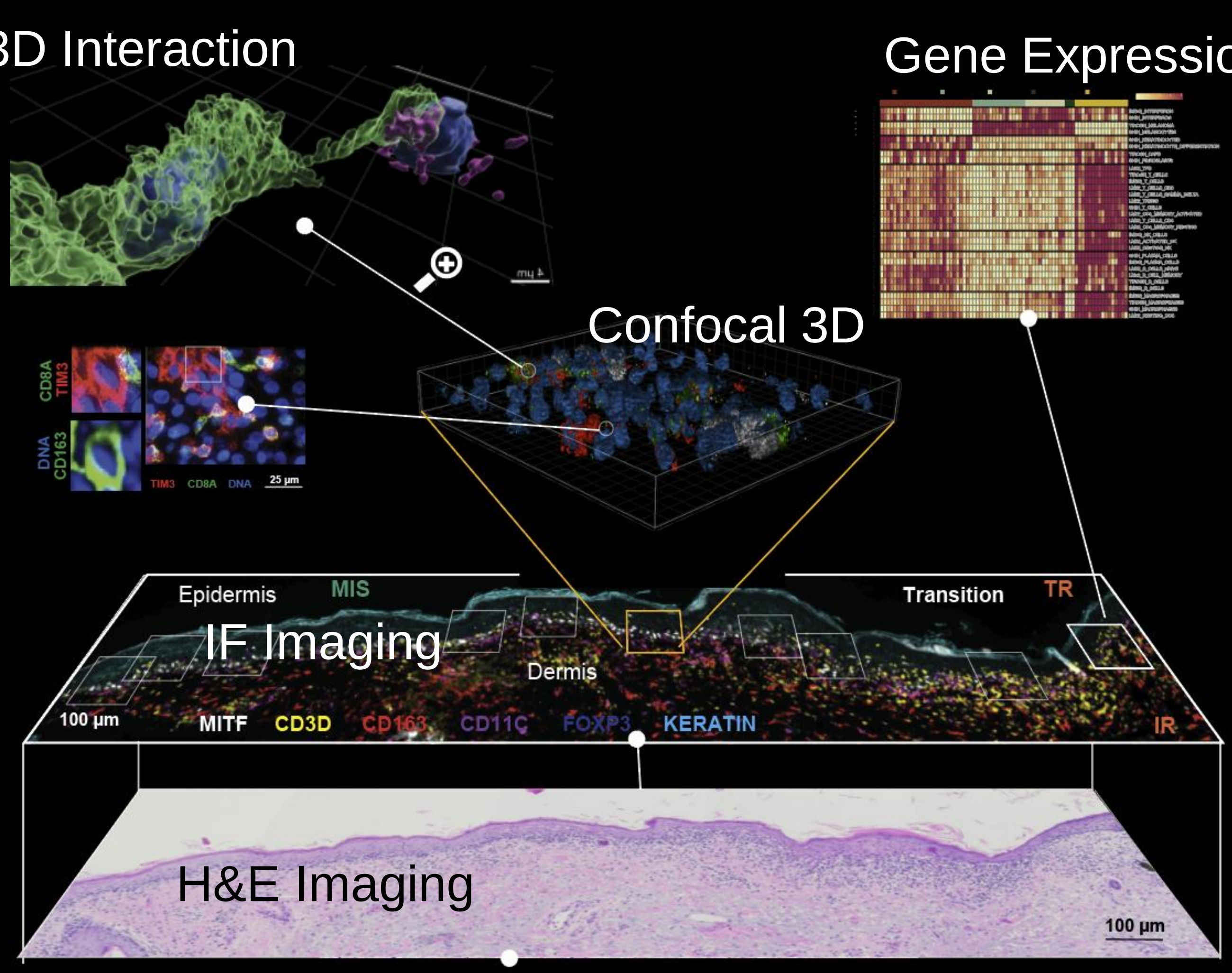
Future Research Areas

- 2D to 3D
  - TB-sized multi-volumetric data
  - Scalable multi-resolution rendering
  - Image-based cell and interaction analysis
- Holistic Orchestration and Analysis
  - Multiple modalities
  - Spatially referenced gene expressions
  - Textual data (annotations, meta data)

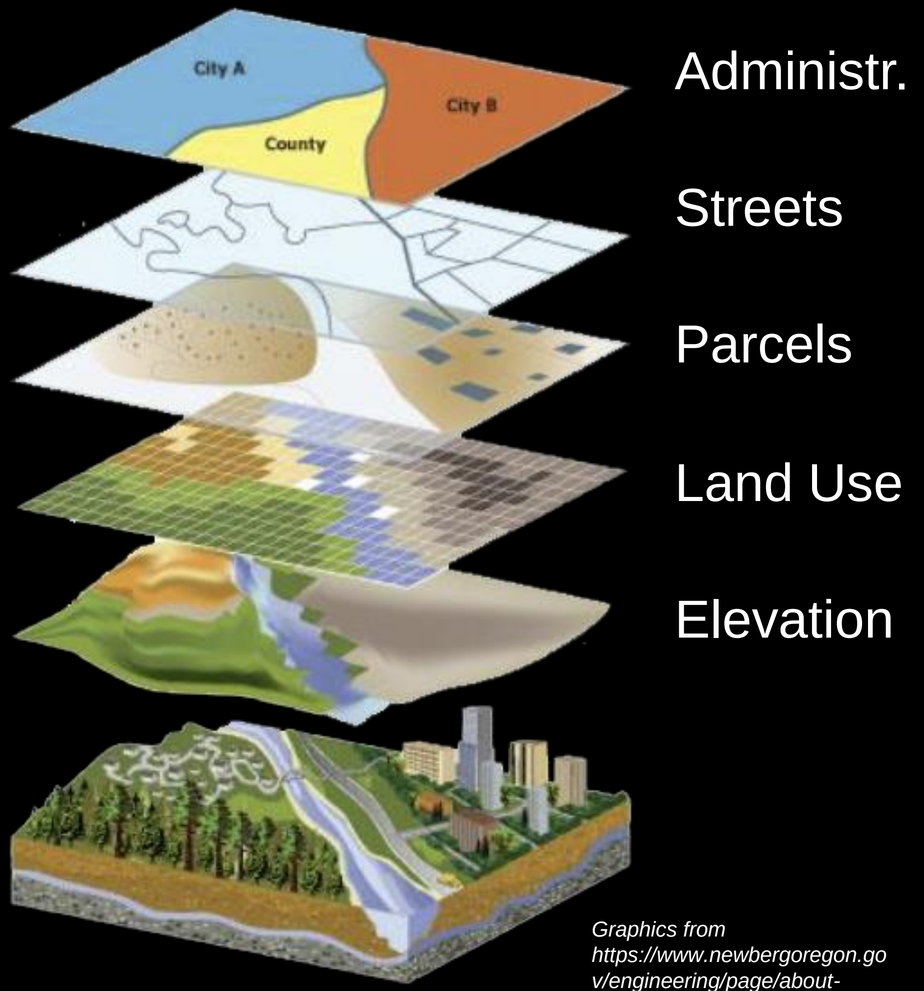


Spatial Analysis in Other Domains

Nirmal et al. The Spatial Landscape of Progression and Immunoediting in Primary Melanoma at Single-Cell Resolution, Cancer Discovery, 2022.



Biomedical Spatial Information Systems



Graphics from https://www.newbergoregon.gov/engineering/page/about-newberg-gis

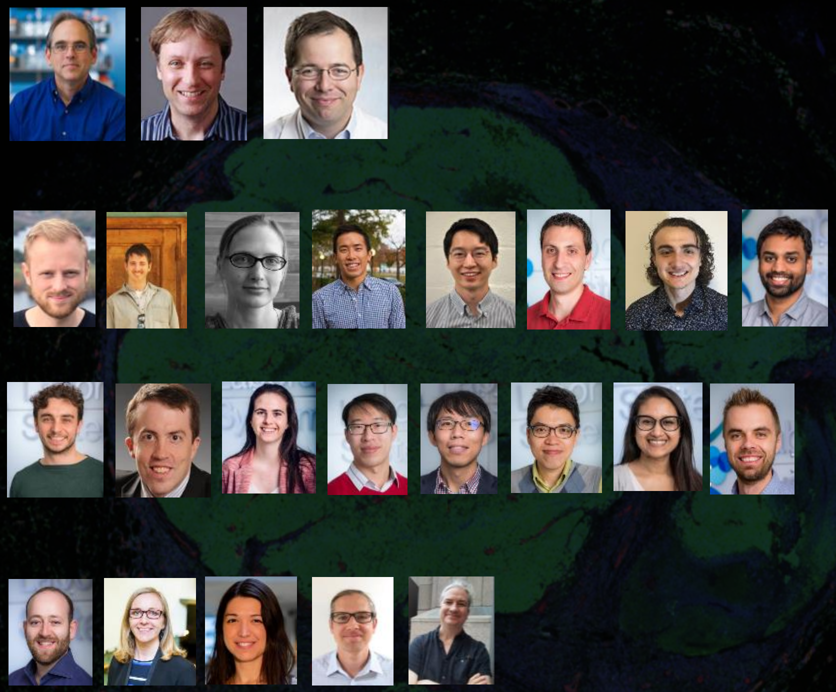
Geographical Information Systems

Thank You!

Questions?

rk4815@nyu.edu

Acknowledgments:



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Visual Computing Group
@School of Engineering and Applied Sciences

HiTS

Laboratory of Systems Pharmacology,
@Harvard Medical School