Introduction to Spatial Transcriptomics (STx)

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- History of STx
- Current STx technologies
  - 10X Genomics Visium
  - NanoString GeoMx

RNA SEQUENCING IN SITU

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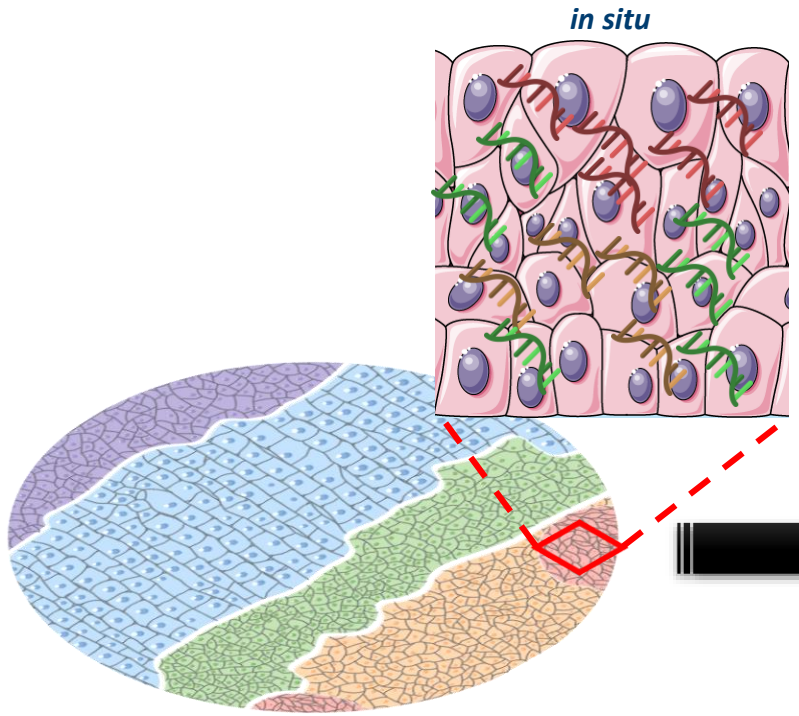

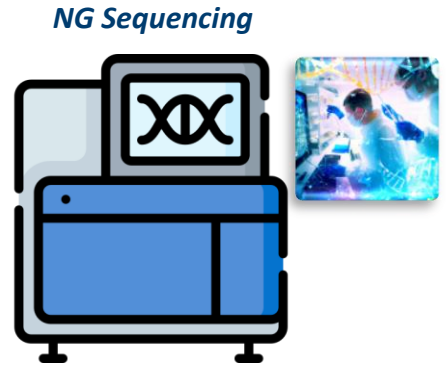

nanoString (GeoMx)

BGI (Stereo-Seq)

10X GENOMICS (Visium)

curio BIOSCIENCE (Slide-Seq)

- ✓Whole transcriptome characterisation
- ✓Almost single-cell resolution
- ✓Spatial information is retained

ANALYTICAL CHALLENGES OF SPATIALLY-RESOLVED 'OMICS DATA

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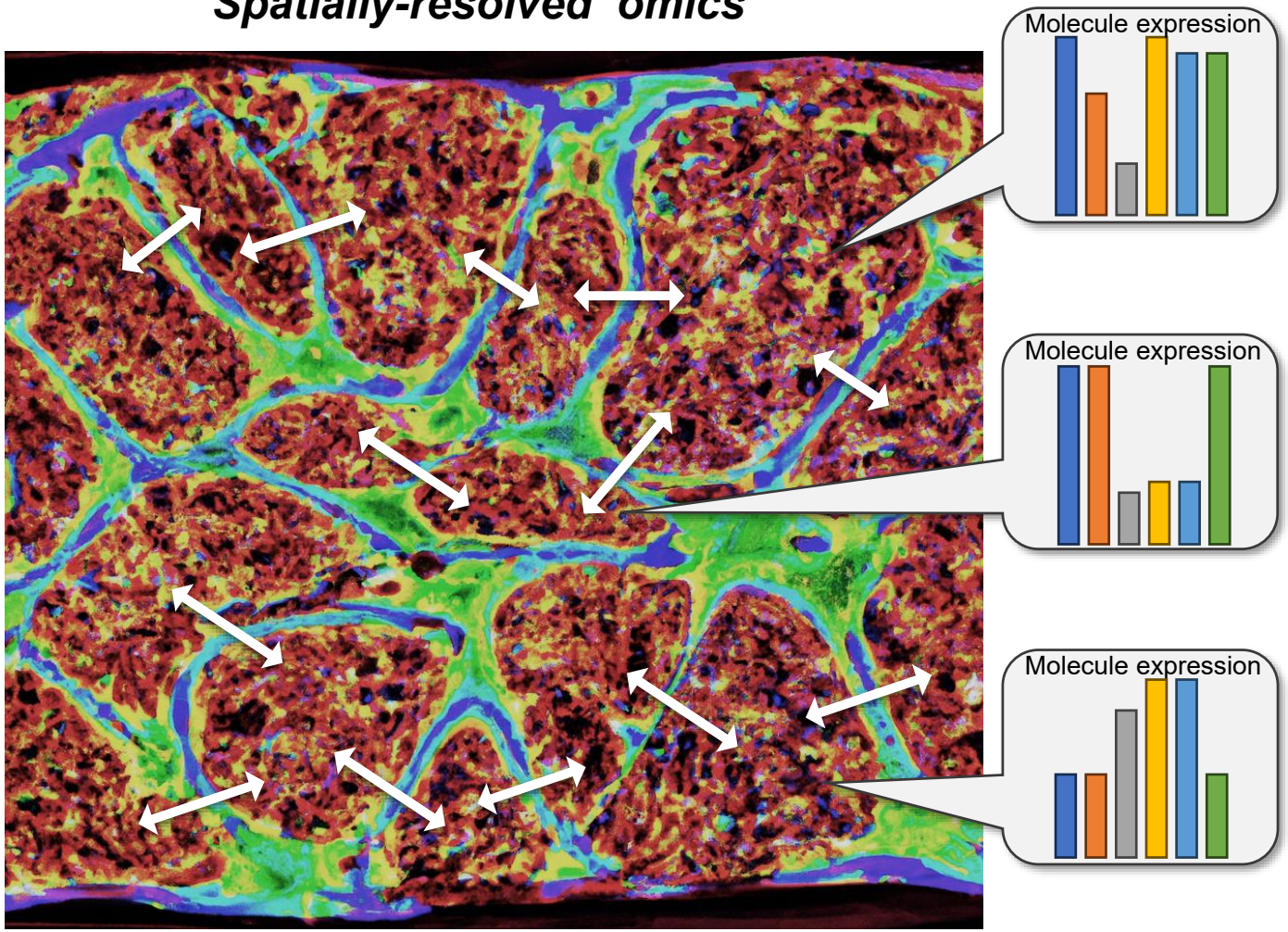
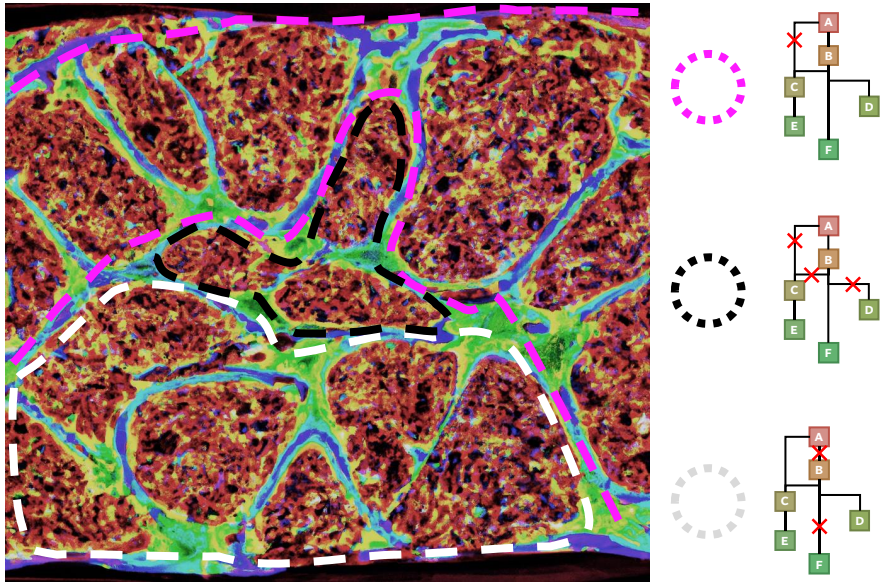
Spatially-resolved 'omics



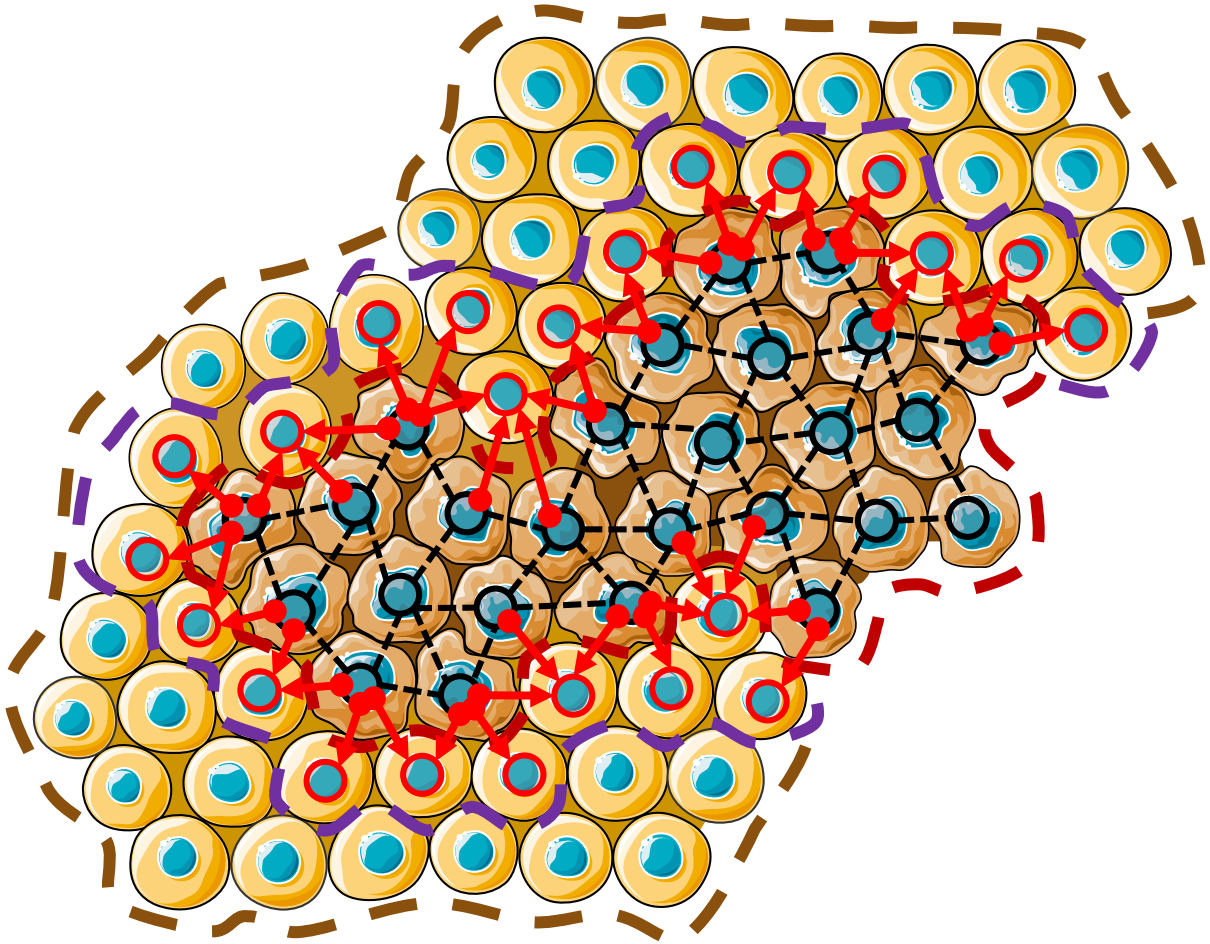
How to leverage the spatial aspect of the data effectively?

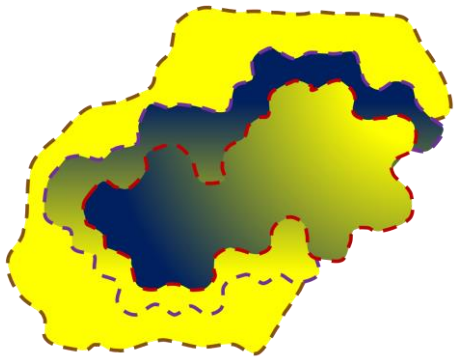


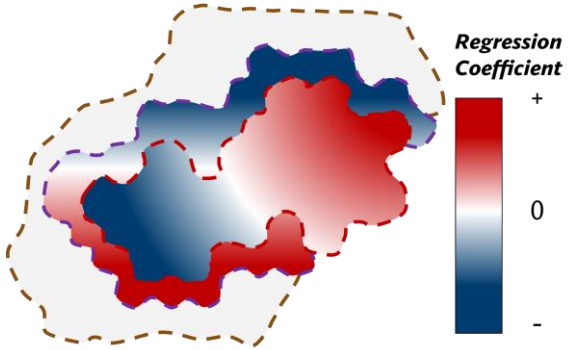
SPATIAL DATA ANALYSIS IN MOLECULAR BIOLOGY

Data with a spatial dimension have distinct properties

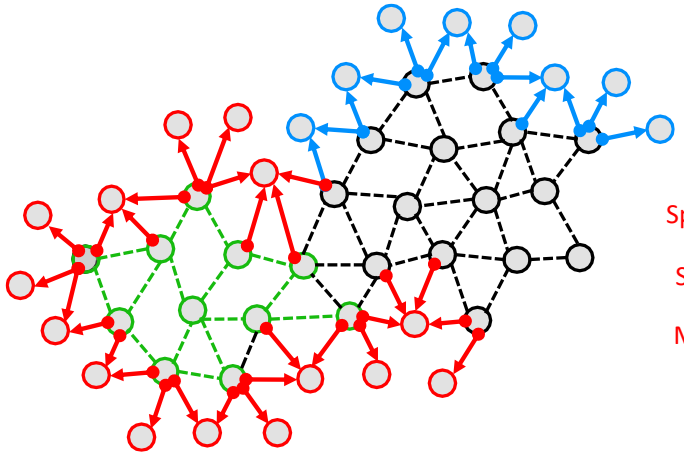
A different set of statistical and inferential considerations.







Complex spatial associations



Spatial Autocorrelation

Spatial Heterogeneity

Modifiable Aerial Unit Problem

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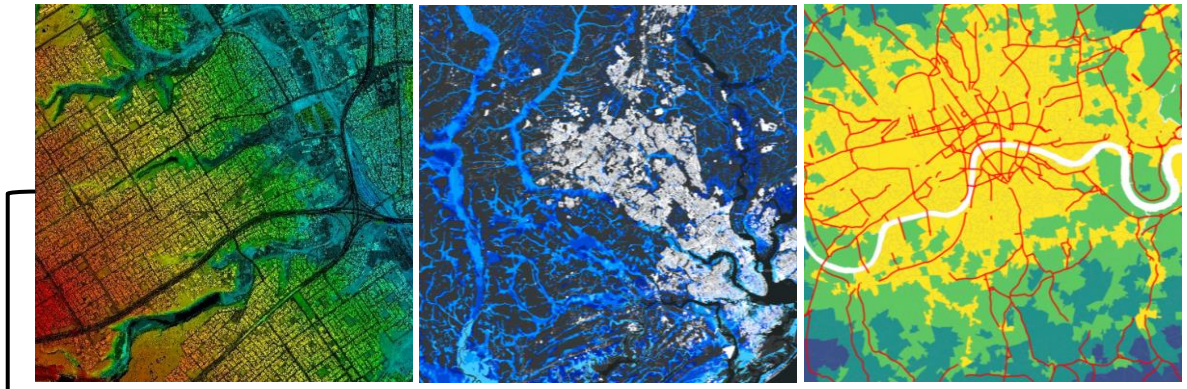
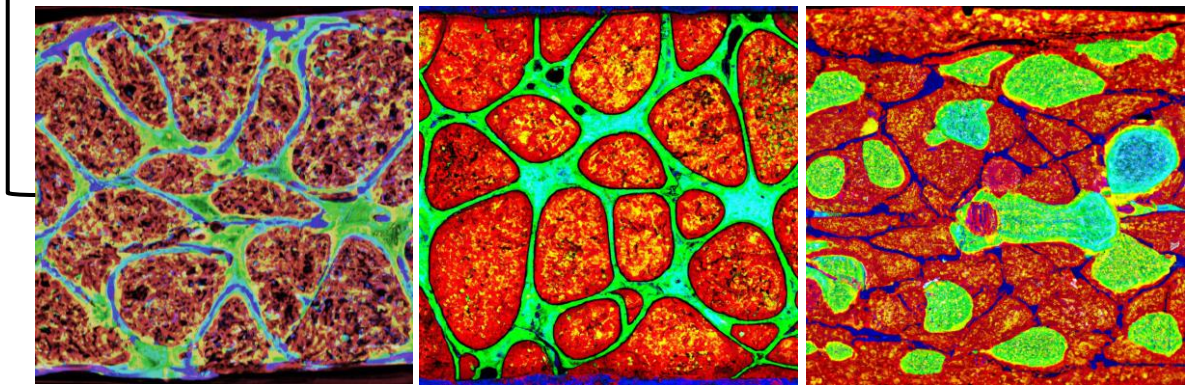
APPLICATION OF GEOSPATIAL METHODS IN BIOLOGY

Space has the **same features** in all disciplines

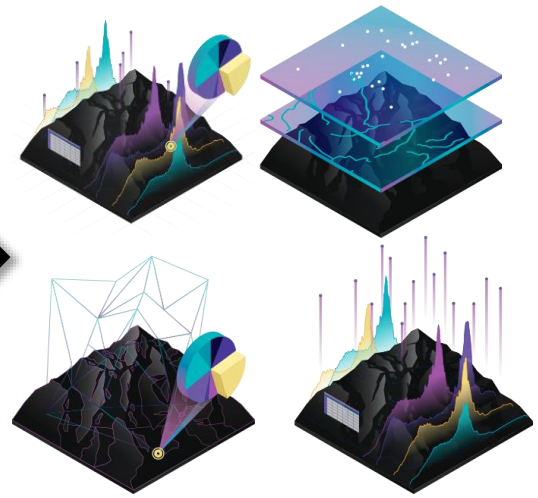
Geographical maps



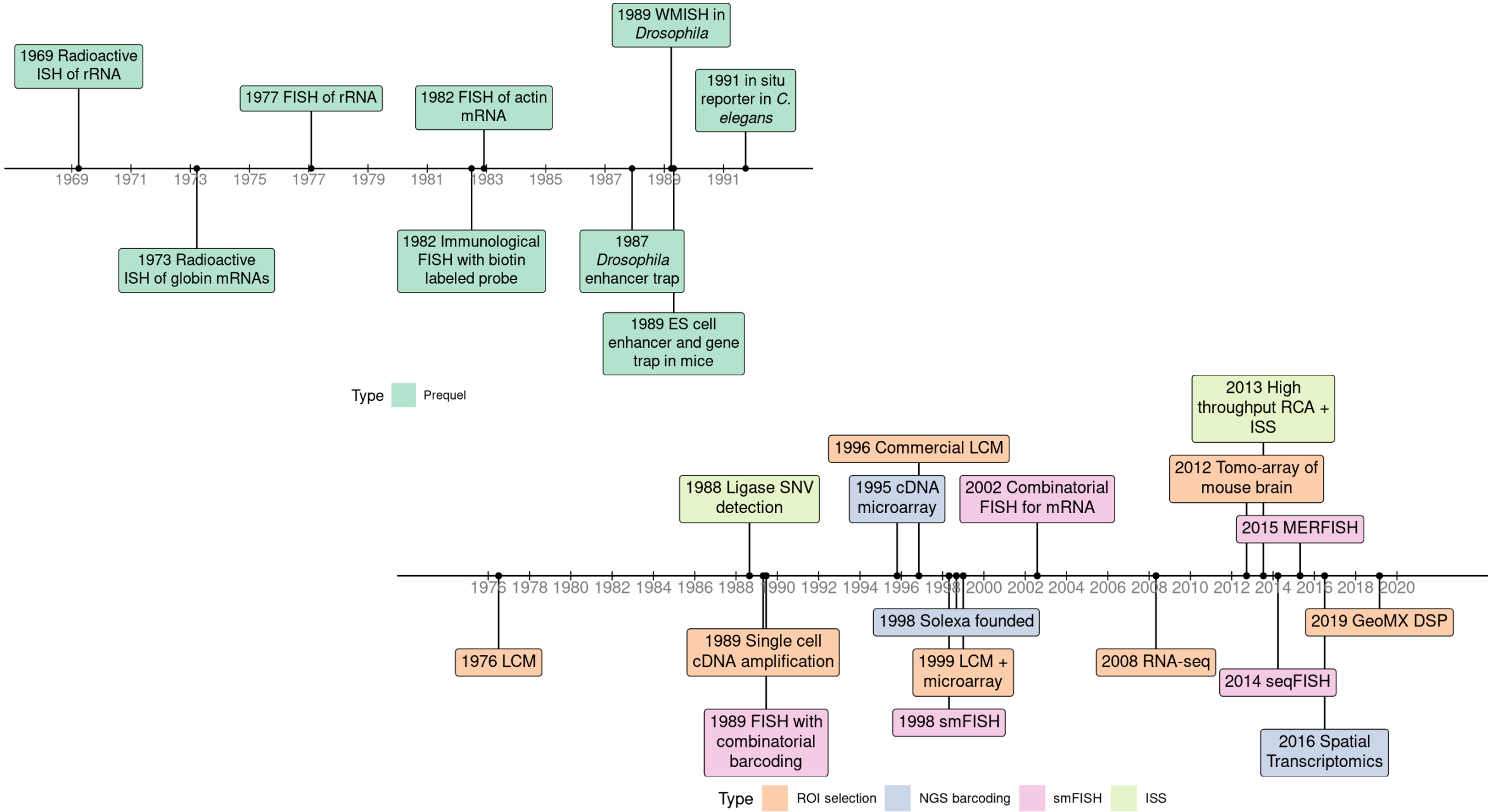
Biological maps



Geospatial analyses



SPATIAL TRANSCRIPTOMICS IS NOT NEW…



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Source: Museum of spatial transcriptomics (https://doi.org/10.1038/s41592-022-01409-2)

CURRENT METHODS OF SPATIAL TRANSCRIPTOMICS

Technology	Highest Resolution	Max Number of Targets	Number of unique spatial barcodes
smFISH	single cell	10	N/a (probe-based)
seqFISH	single cell	10421	N/a (probe-based)
seqFISH+	single cell	10000	N/a (probe-based)
MERFISH	single cell	4209	N/a (probe-based)
STARmap	single cell	1020	N/a (probe-based)
MOSAICA	single cell	10	N/a (probe-based)
original ST	100µm	transcriptome	1007
10X Visium	55µm	transcriptome	~5000
HDST	2µm	transcriptome	~1.54 million
Slide-seq	10µm	transcriptome	10000
Slide-seqV2	10µm	transcriptome	10000
DBiT-seq	10µm	transcriptome	2500
PIXEL-seq	1.22µm	transcriptome	N/a (Illumina flow-like)
space-TREX	55µm	transcriptome	~5000
sci-Space	73.2µm	transcriptome	7506
GeoMx DSP	5µm	20175	N/a (probe-based)
Stereo-seq	500nm	transcriptome	Approx. 800m

Current spatial transcriptomics technologies and their main specifications.

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ARRAY AND PROBE EXAMPLES

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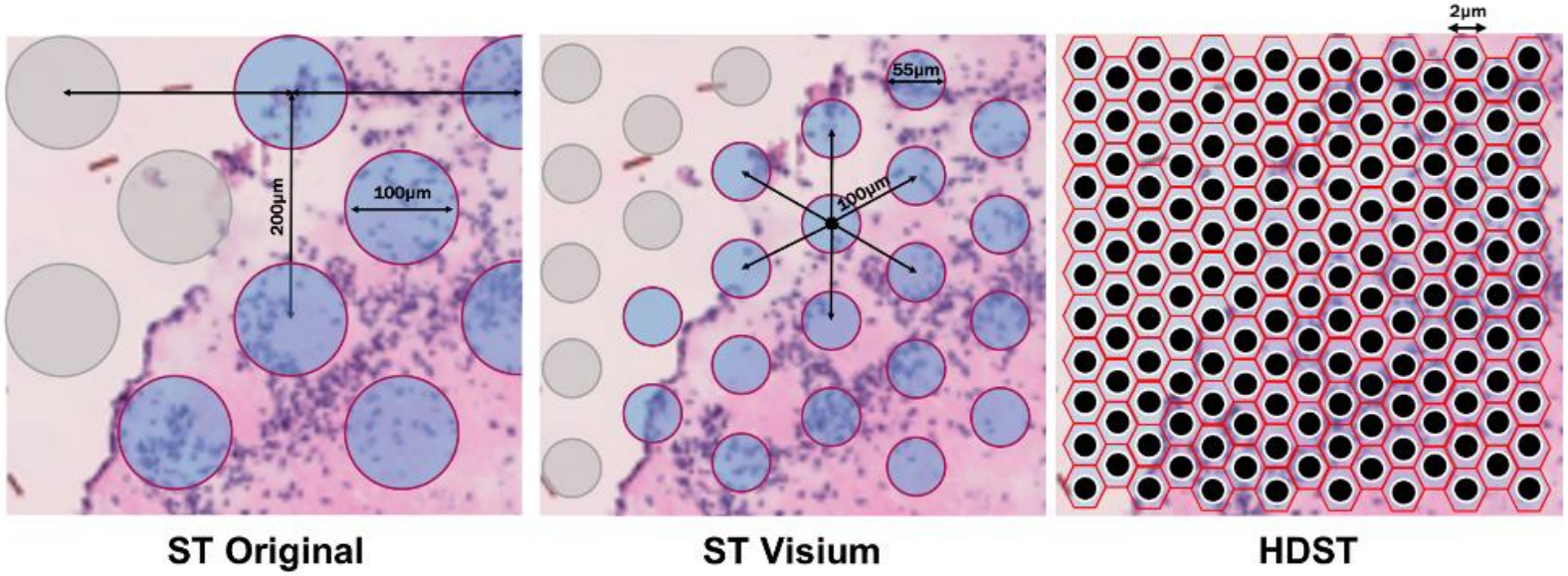
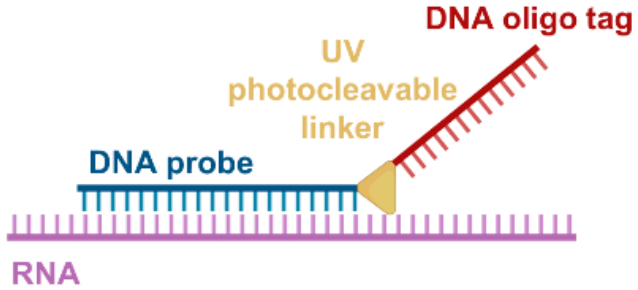


Array examples

10X Visium



GeoMx

Probe examples

THE 10X GENOMICS – VISIUM PLATFORM

Visium Slide

Sample Prep & Staining

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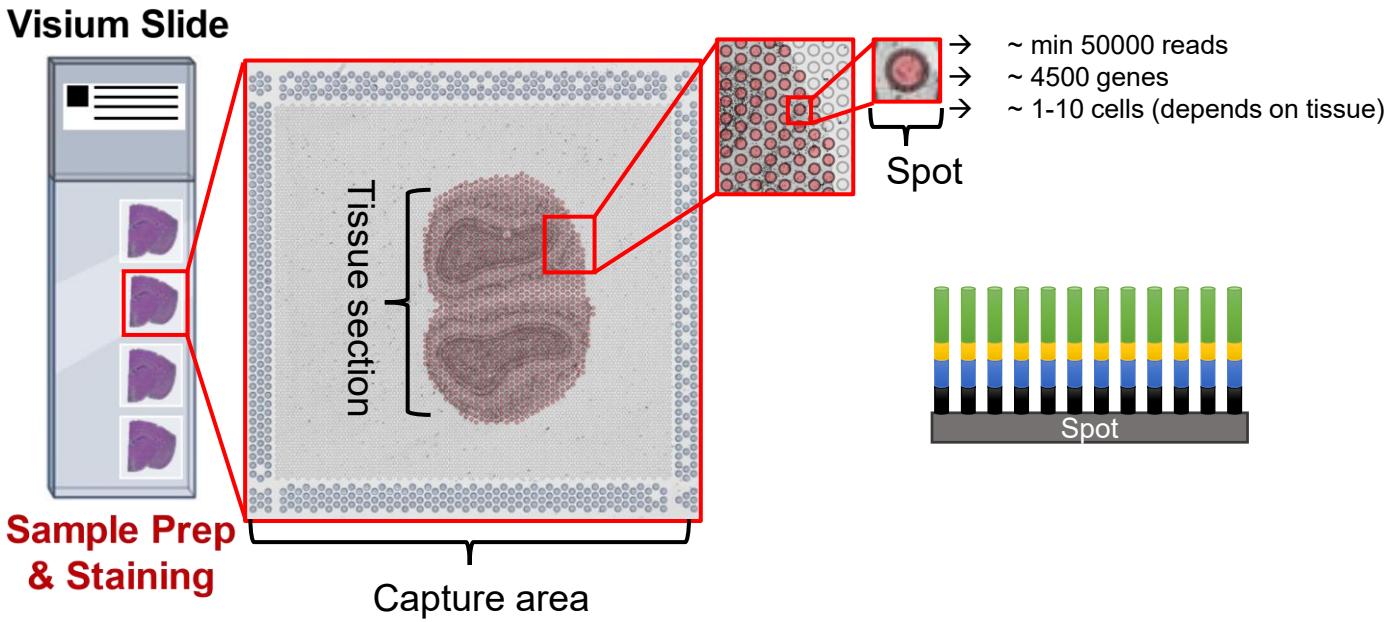
THE 10X GENOMICS – VISIUM PLATFORM



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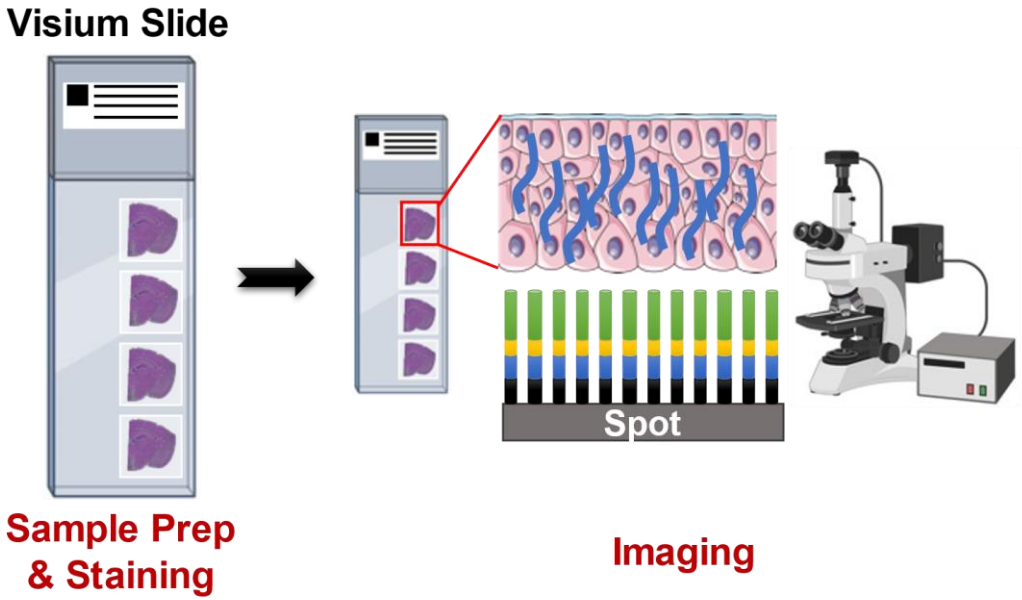
THE 10X GENOMICS – VISIUM PLATFORM



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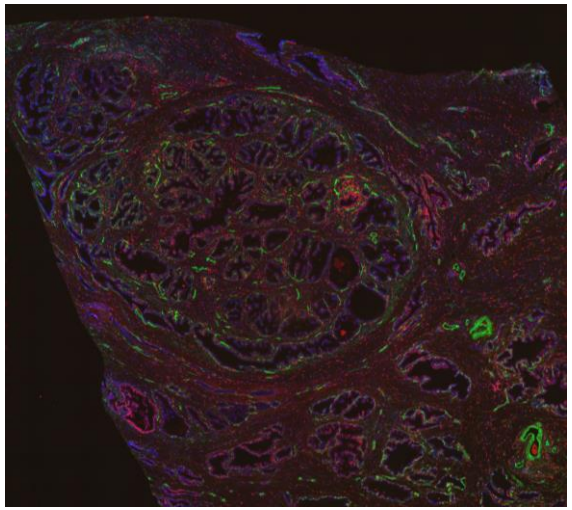
Fluorescent

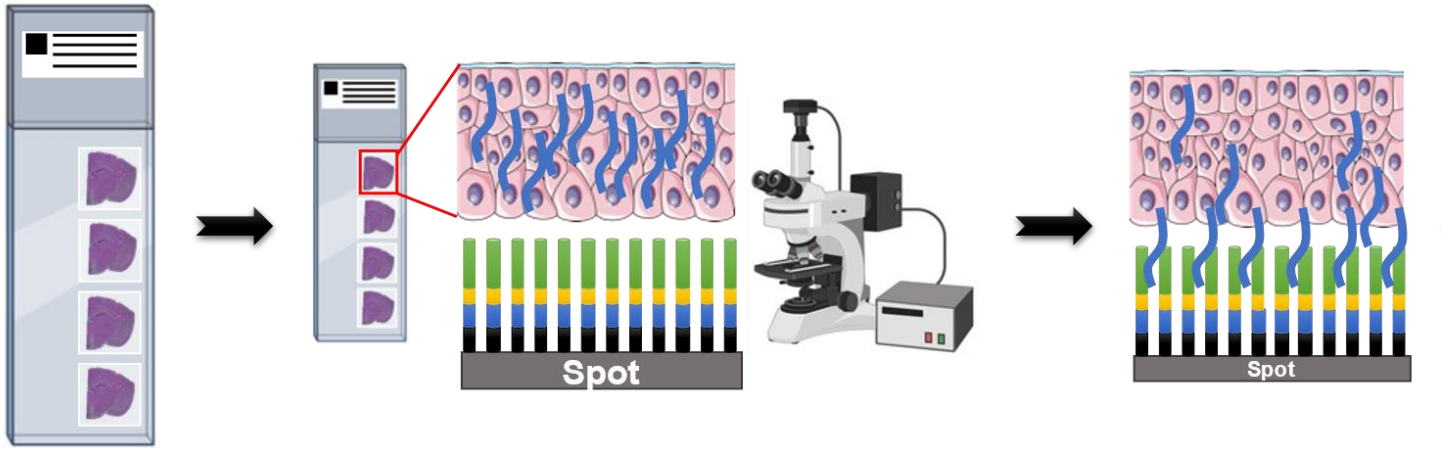


H&E

H&E: Haematoxylin & Eosin staining

THE 10X GENOMICS – VISIUM PLATFORM

Visium Slide



Sample Prep & Staining

Imaging

Permeabilisation & RNA Diffusion

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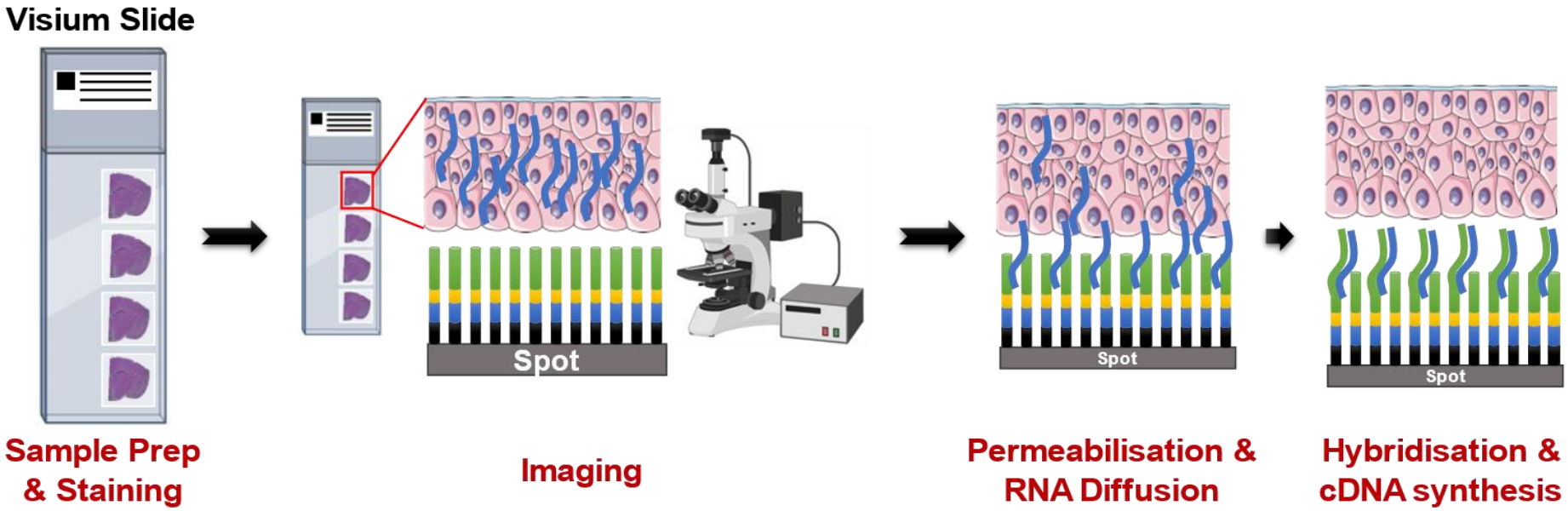
THE 10X GENOMICS – VISIUM PLATFORM



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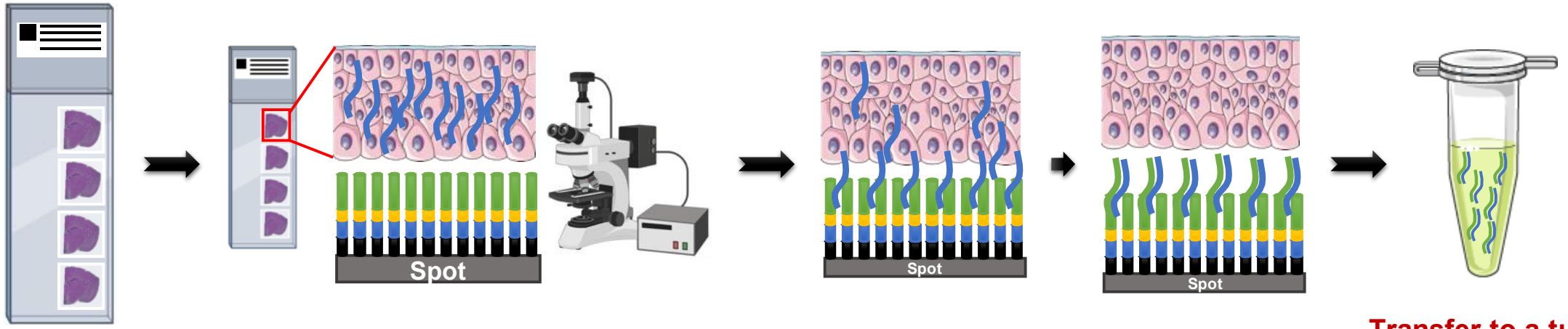
THE 10X GENOMICS – VISIUM PLATFORM

Visium Slide



Sample Prep & Staining

Imaging

Permeabilisation & RNA Diffusion

Hybridisation & cDNA synthesis

Transfer to a tube and prepare NGS library

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THE NANOSTRING - GEOMX PLATFORM

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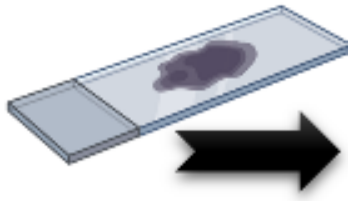

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Tissue on slide

THE NANOSTRING - GEOMX PLATFORM

10X

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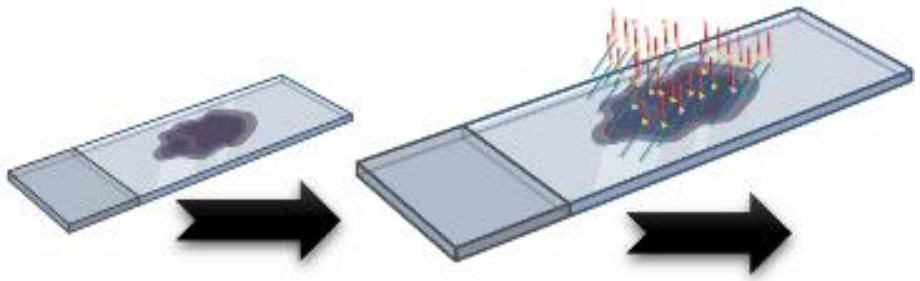
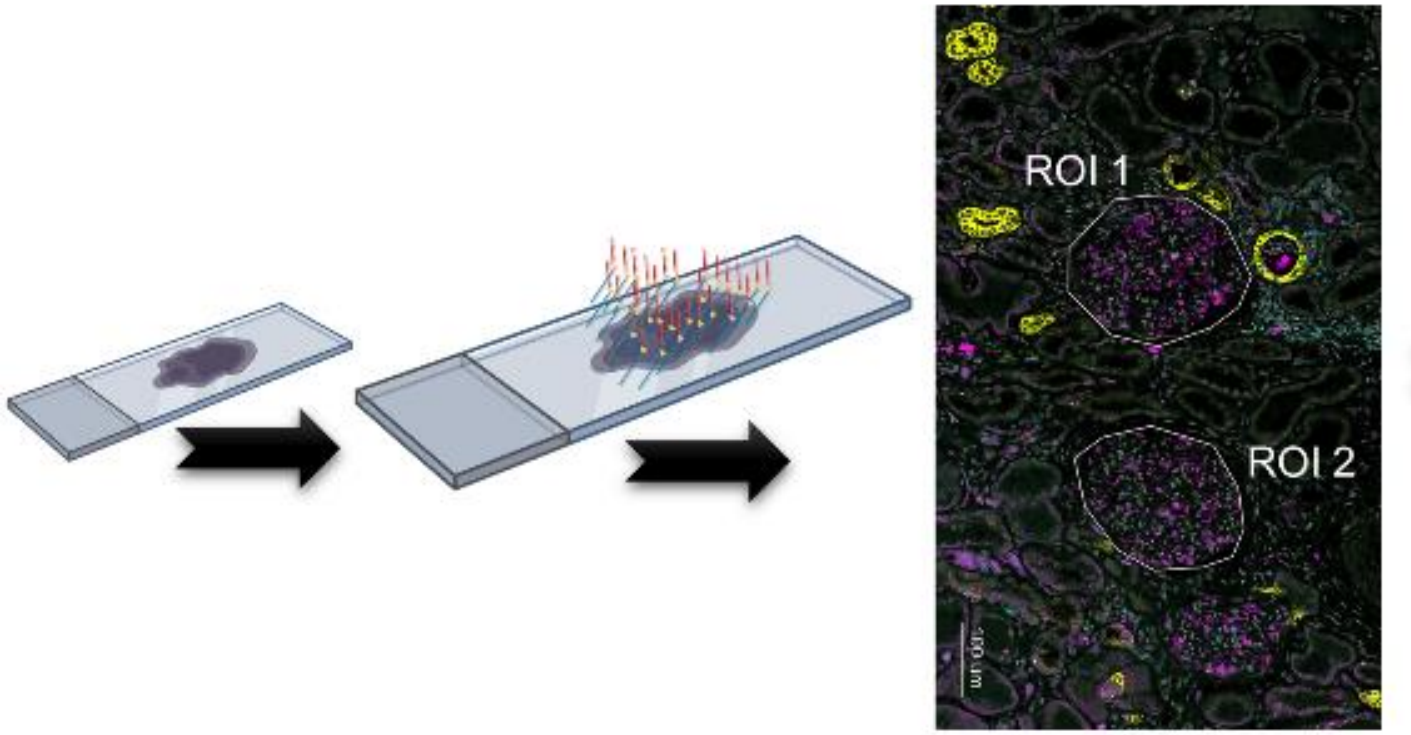


Tissue on slide Probes incubation

THE NANOSTRING - GEOMX PLATFORM

10X

GMX



Tissue on slide Probes incubation Imaging and ROI selection

THE NANOSTRING - GEOMX PLATFORM

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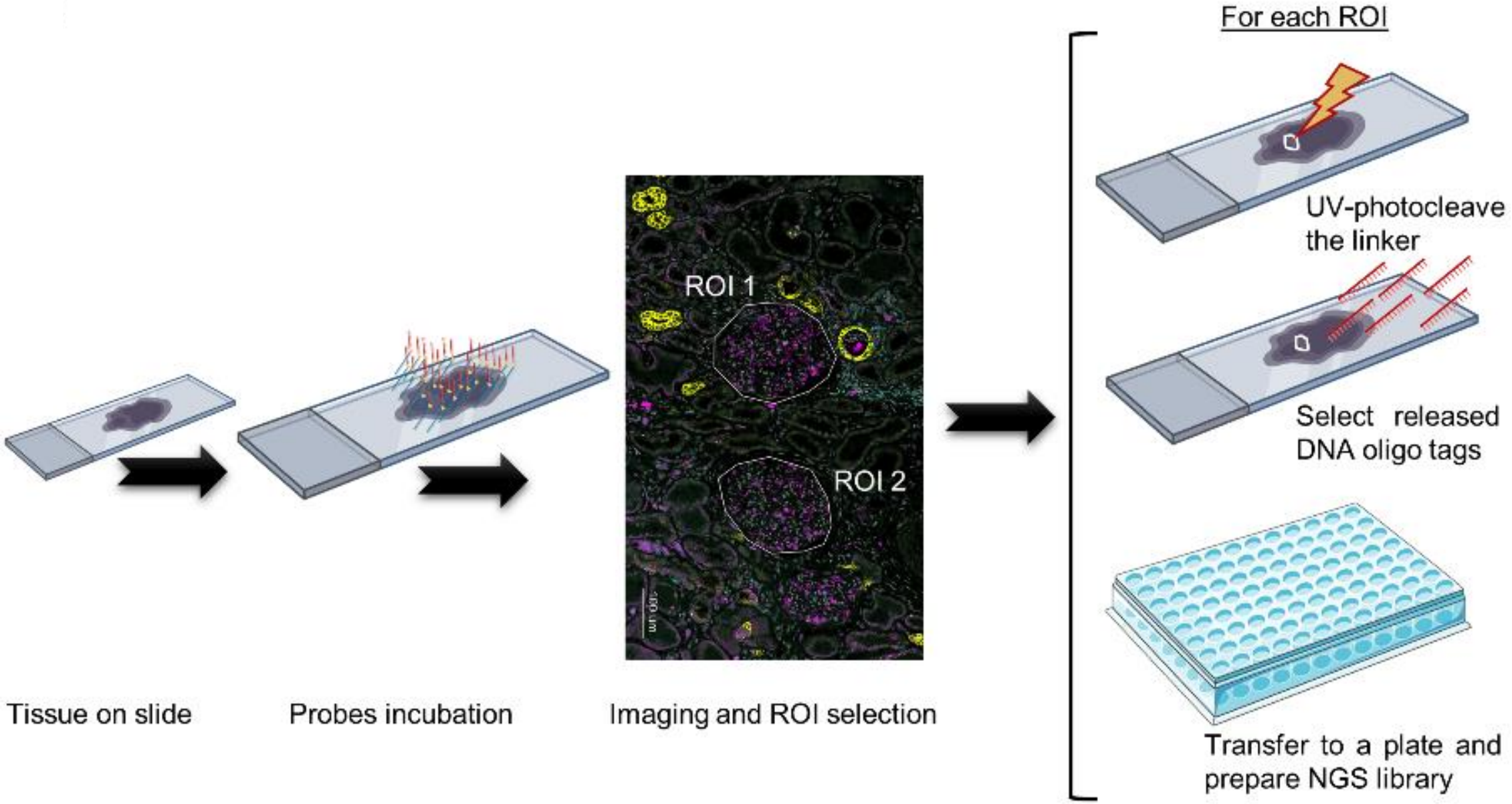

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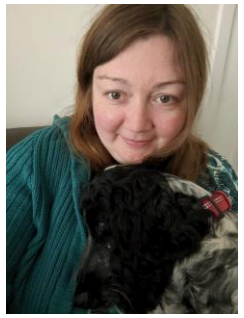

Newcastle University

Prof. Alex Comber

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