Spatial Analysis on Histological Images Using Spark

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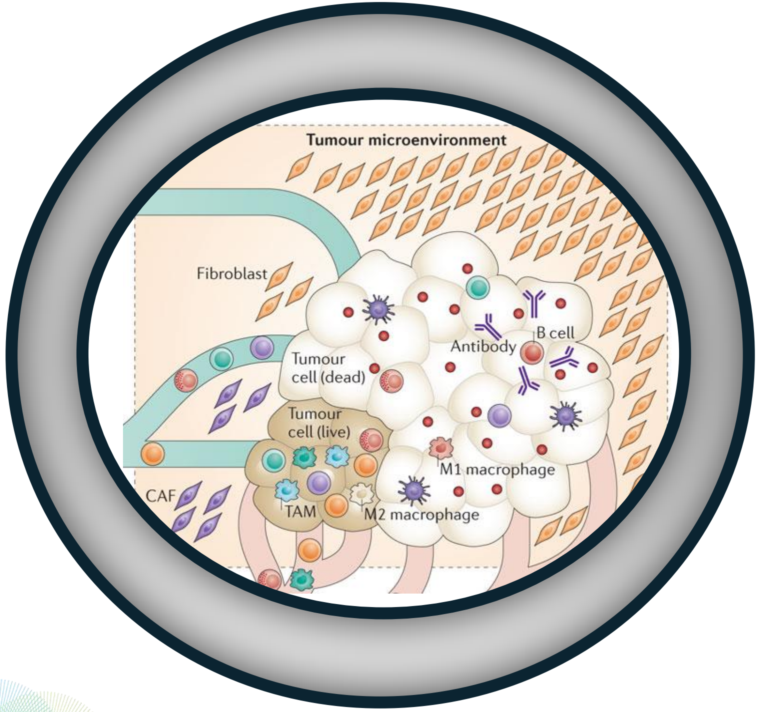
Disclaimer

- This presentation is …
  - – ❌ ***NOT*** about computer vision / image processing
  - – ❌ ***NOT*** about drug, biology, or biochemistry
  - – ❌ ***NOT*** about new algorithm or infrastructure

Disclaimer

- This presentation is …
  - ○ An application of Spark on spatial analysis on biomedical images
  - ○ A proof of concept of a small module in a complex pipeline
  - ○ A work in progress

Towards a systematic characterization of tumor context

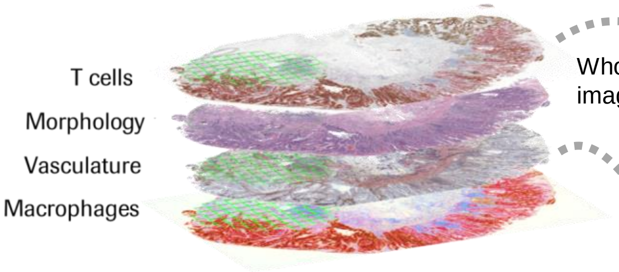


Challenges:

- Location and density of different immune cell populations are associated with patient prognosis and prediction outcome
- Huge variation in immune infiltrates across tumor entities and patients
- Inconsistent data in the literature

[Nat Rev Drug Discov.](#) 2015;14(9):603-22.

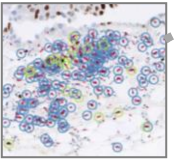
Roche pRED Tissue image analysis workflow



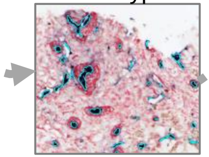
>10,000 slides per year
(~ 6 slides per block)

Whole slide image analysis

>100,000 objects per slide

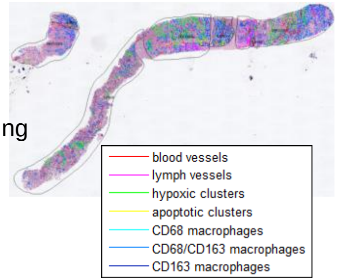


T cell location and subtype



Vessel location, class assignment and object features

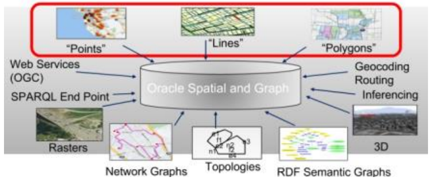
In silico multiplexing



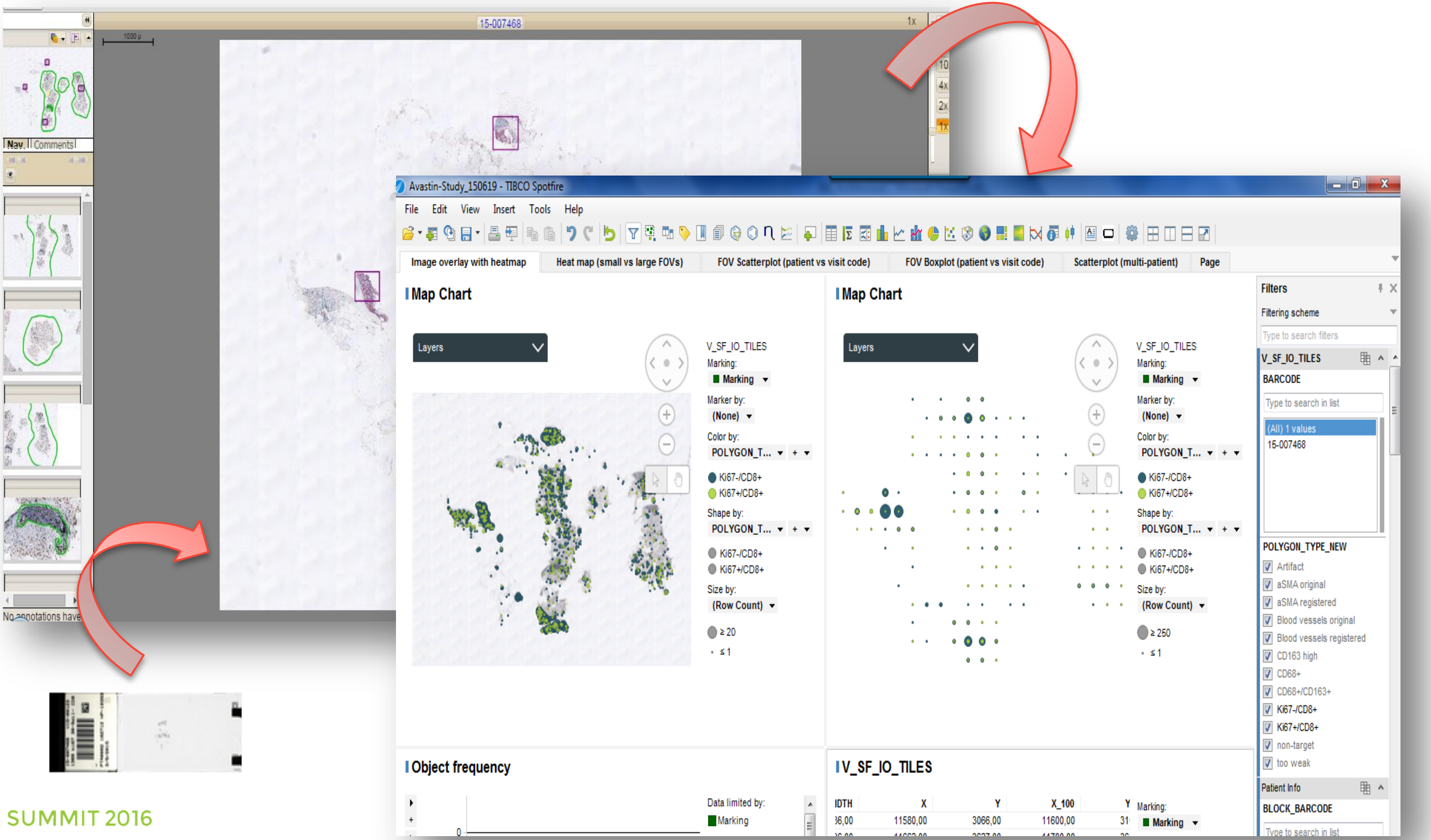
Objects in same reference coordinate system

Imaging results

Spatial profiling



Goal: actionable data



15-007468

Avastin-Study_150619 - TIBCO Spotfire

Map Chart

V_SF_IO_TILES
Marking: Marking
Marker by: (None)
Color by: POLYGON_T...
- ● Ki67-/CD8+
- ● Ki67+/CD8+

Shape by: POLYGON_T...
- ● Ki67-/CD8+
- ● Ki67+/CD8+

Size by: (Row Count)
- ≥ 20
- ≤ 1

Map Chart

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Shape by: POLYGON_T...
- ● Ki67-/CD8+
- ● Ki67+/CD8+

Size by: (Row Count)
- ≥ 250
- ≤ 1

Filters

Filtering scheme
Type to search filters

V_SF_IO_TILES
BARCODE
Type to search in list
(All) 1 values
15-007468

POLYGON_TYPE_NEW
- ☑ Artifact
- ☑ aSMA original
- ☑ aSMA registered
- ☑ Blood vessels original
- ☑ Blood vessels registered
- ☑ CD163 high
- ☑ CD68+
- ☑ CD68+/CD163+
- ☑ Ki67-/CD8+
- ☑ Ki67+/CD8+
- ☑ non-target
- ☑ too weak

Patient Info
BLOCK_BARCODE
Type to search in list

Object frequency

Data limited by: Marking

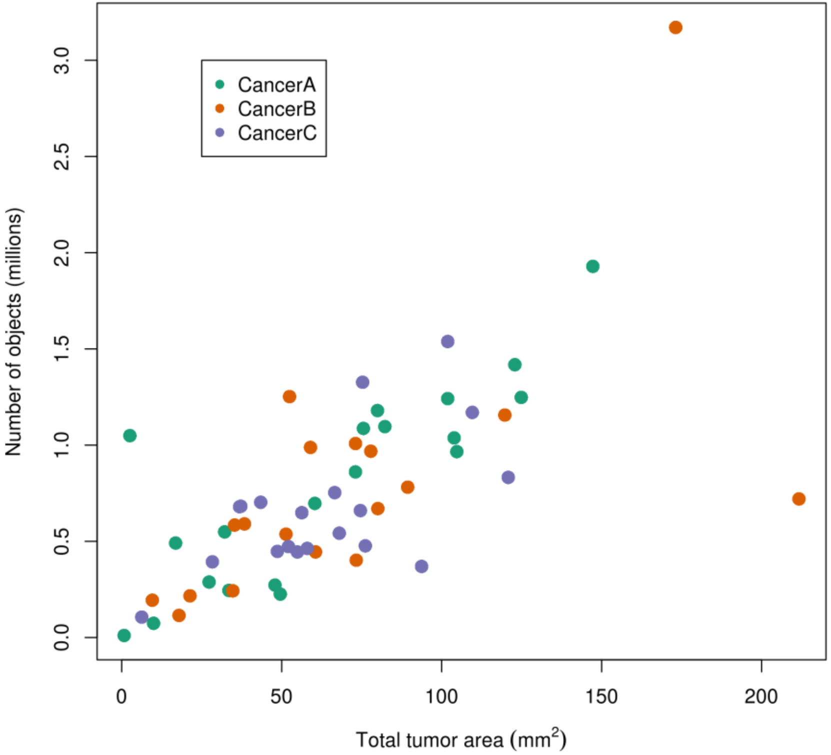
0

V_SF_IO_TILES

IDTH	X	Y	X_100	Y
36,00	11580,00	3066,00	11600,00	31

Marking: Marking

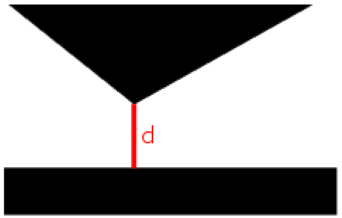
POC data set

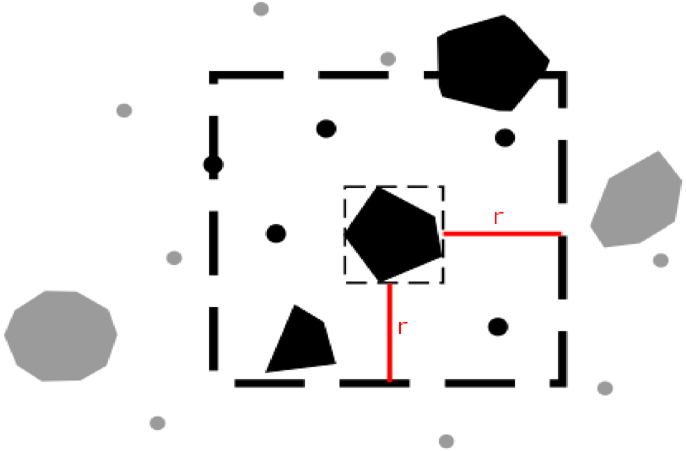


- 57 “blocks“ of 3 cancer types
- Each block contains 6 or 7 slides
  - histology stain
  - cancer biomarker
  - microenvironment biomarker
- Each object annotated with object type (T cell, lymph vessels, etc.), shape (point / polygon), and coordinate

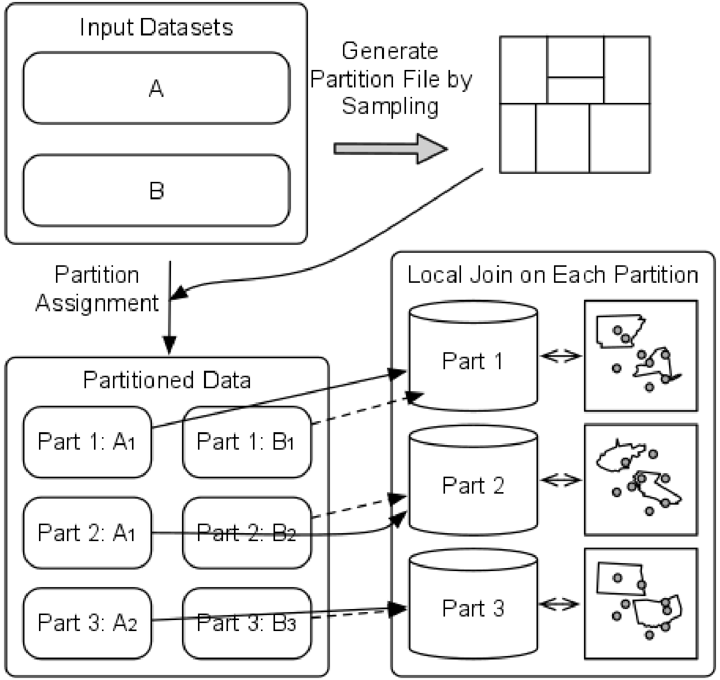
Distance calculation

- Basic statistic for distribution, co-localization, spatial clustering, etc.
- Distance: shortest distance between two contours
- Total number of pairwise distances: 5.3 trillion (10^{12}) pairs – prohibitive
- Workaround: only calculate the distance between each object and its "neighbors" within a window *r*.





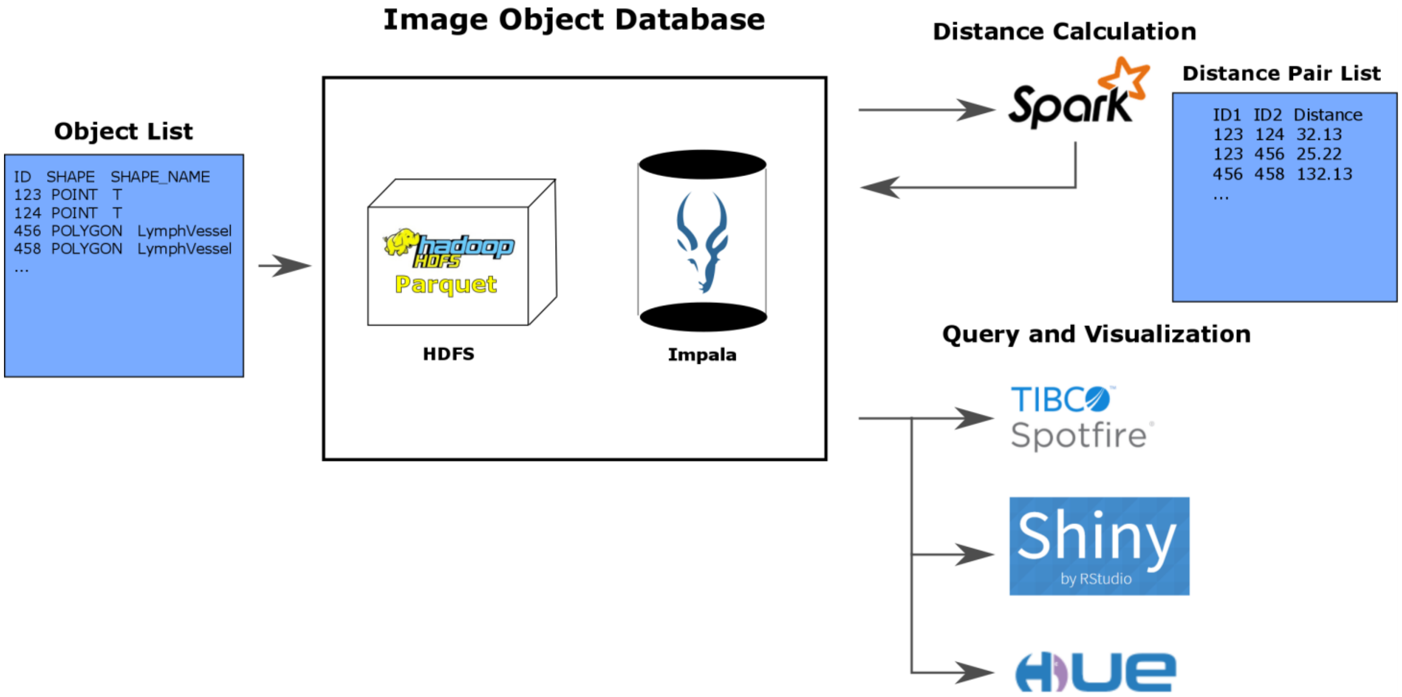
Spatial Spark



http://simin.me/projects/spatialspark/

- An open source library developed by Dr. Simin You and Prof. Jianting Zhang from CUNY.
- Divide-and-conquer, following similar designs of HadoopGIS.
- Support multiple spatial partitioning methods: sort-tile partition, binary-split partition, fixed-grid partition

Spatial profiling workflow



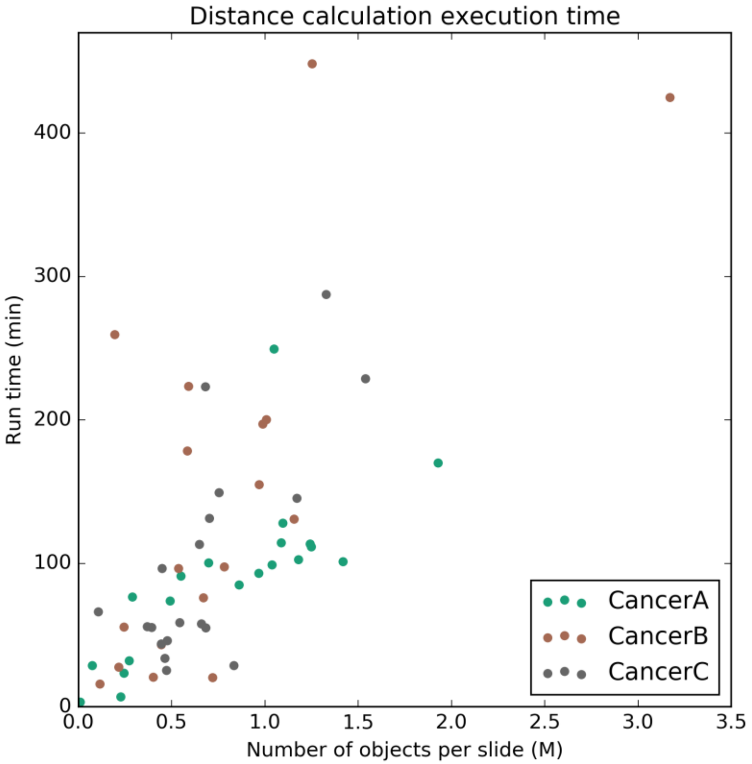
Object List

ID	SHAPE	SHAPE_NAME
123	POINT	T
124	POINT	T
456	POLYGON	LymphVessel
458	POLYGON	LymphVessel
…		

Distance Pair List

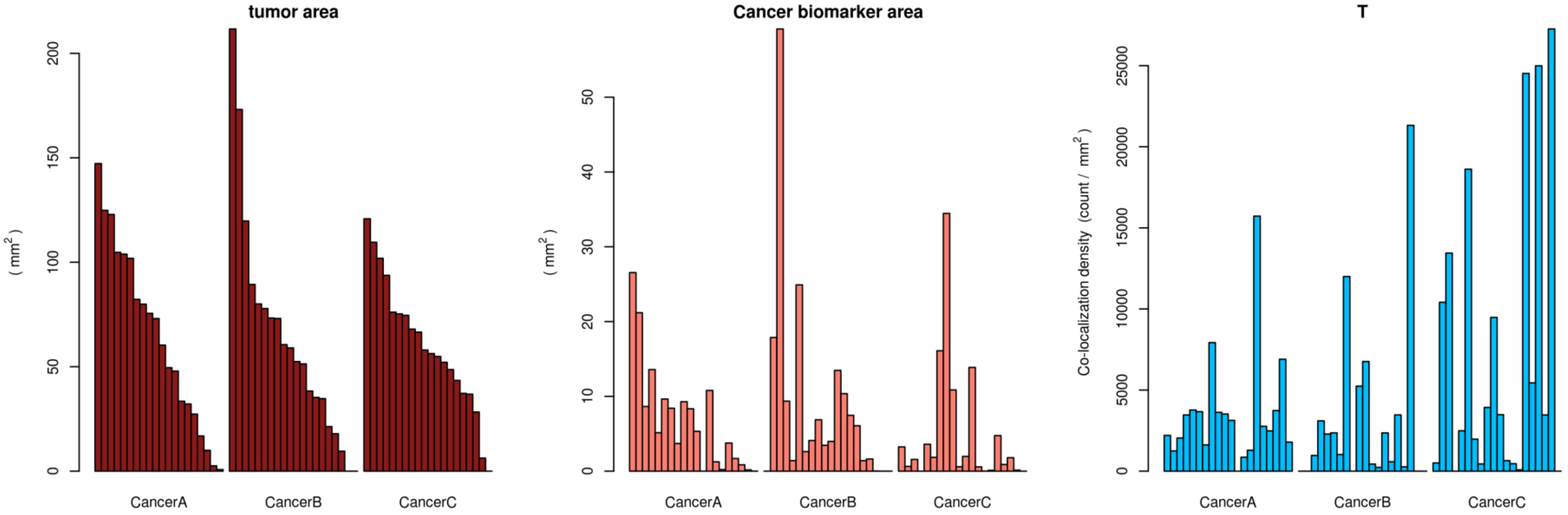
ID1	ID2	Distance
123	124	32.13
123	456	25.22
456	458	132.13
…		

Distance calculation: run time



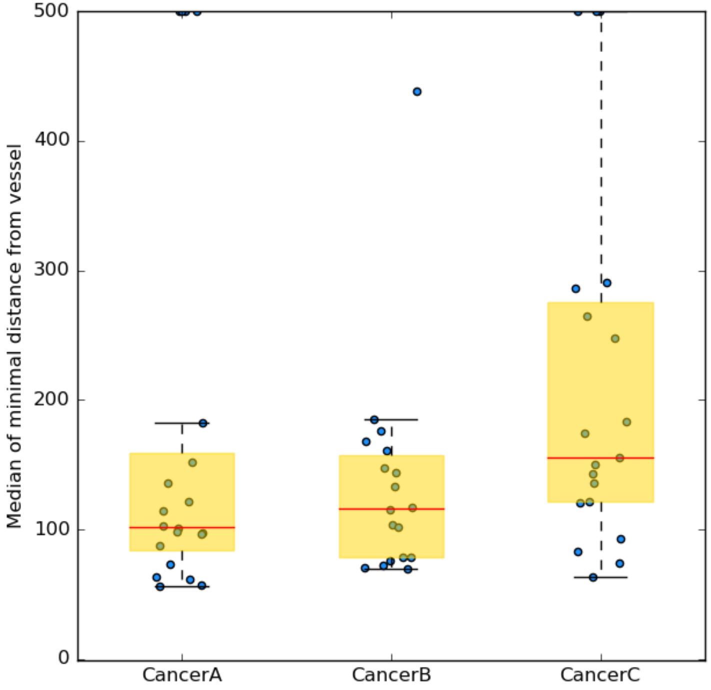
- Using 18 cores, 4 threads / core (72X parallelization).
- Radius = 232.5 µm
- Under shared test environment
- Execute time is roughly linear to number of object (theoretical time complexity).

Co-localization



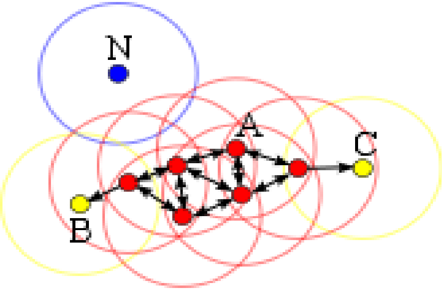
- Enables profiling of between-indication variation and between-tumor variation.

Distance distribution from immune cell to blood vessel



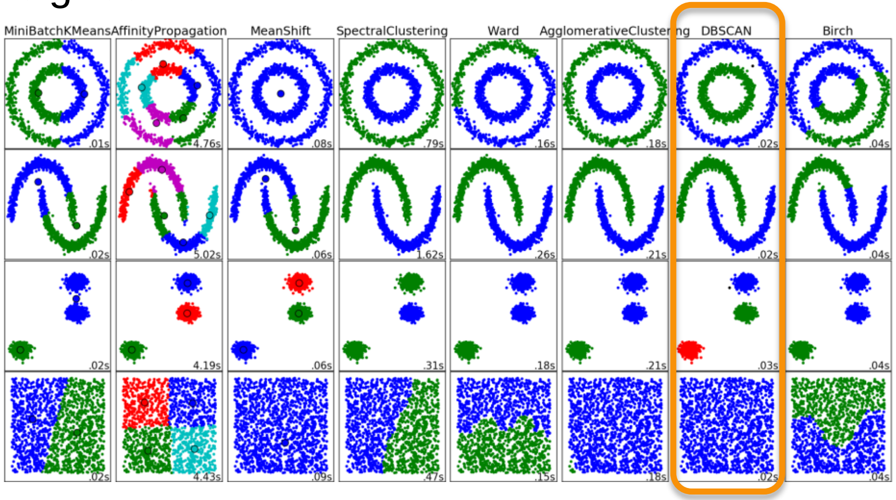
Spatial clustering of objects: DBSCAN

- **Density-based spatial clustering of applications with noise** (**DBSCAN**) clusters closely connected points into the same cluster, marking high-density regions.
- Parameters:
  - minPts: minimum number of neighbors
  - Eps: maximum distance to define a neighbor



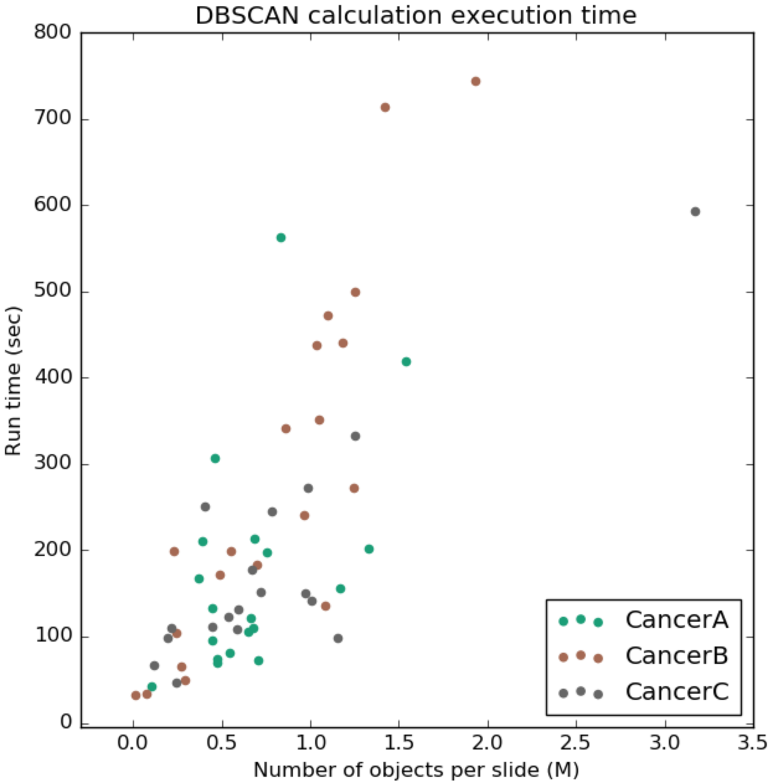
minPts = 3
A: core point
B, C: reachable
N: outlier

https://en.wikipedia.org/wiki/DBSCAN



http://scikit-learn.org/stable/modules/clustering.html

DBSCAN: run time



- Directly load distance from parquet.
- Run time is linear to the number of objects (given already calculated distances).

Future works

- Clinical information
- Genomic data
- Scale up and upstream integration
- UI integration

Acknowledgement

- Spark exploratory / support
  - Sittichoke Saisanit *(Roche pREDi)*
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  - Gerlind Herberich *(Roche pREDi)*
  - Jurriaan Brouwer *(Roche pREDi)*
- Spatial Spark
  - Jianting Zhang *(CUNY)*
  - Simin You *(CUNY)*

Doing now what patients need next

THANK YOU.

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