TOPOLOGICAL FEATURES IN CANCER GENE EXPRESSION DATA

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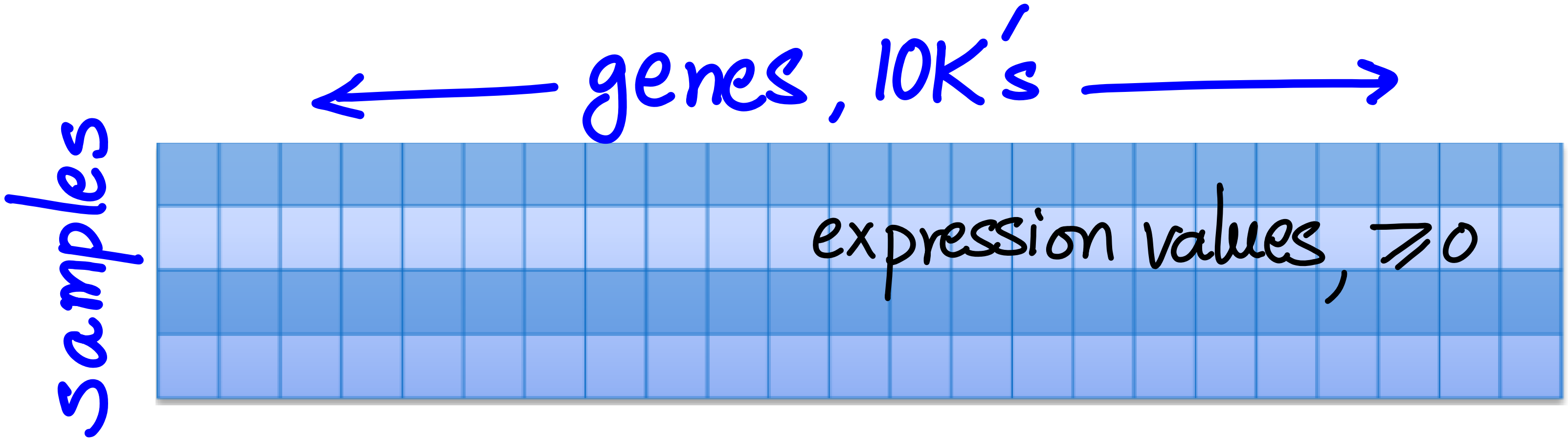
Bala Krishnamoorthy
Washington State University

PSB, 2015;   arXiv: 1410.3198

CANCER GENE EXPR. DATA



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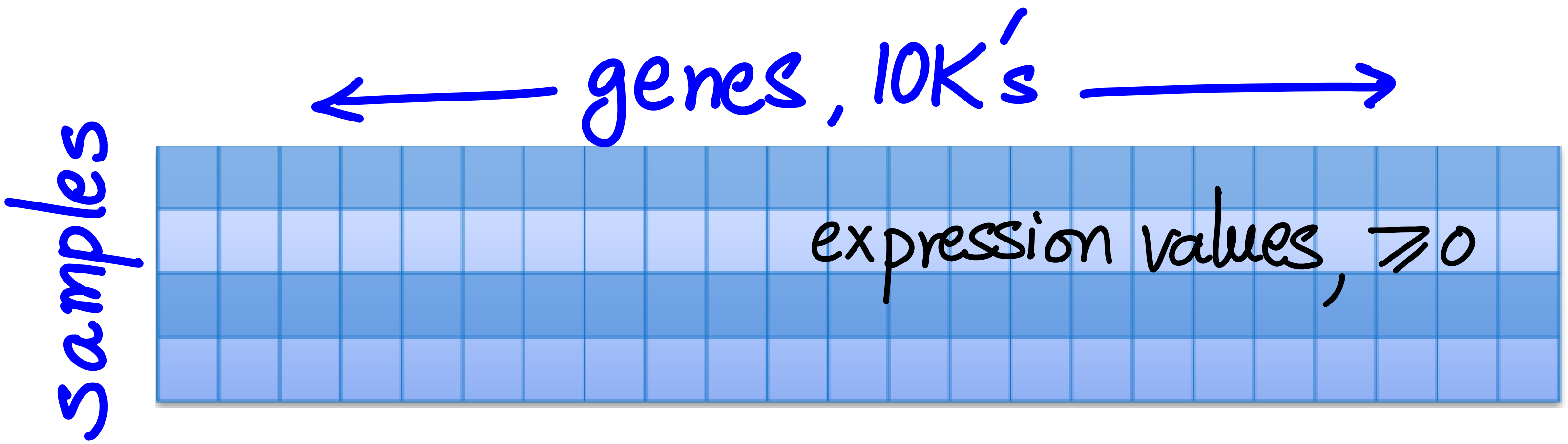

- ~50,000 genes
- 10s to a few 100 samples

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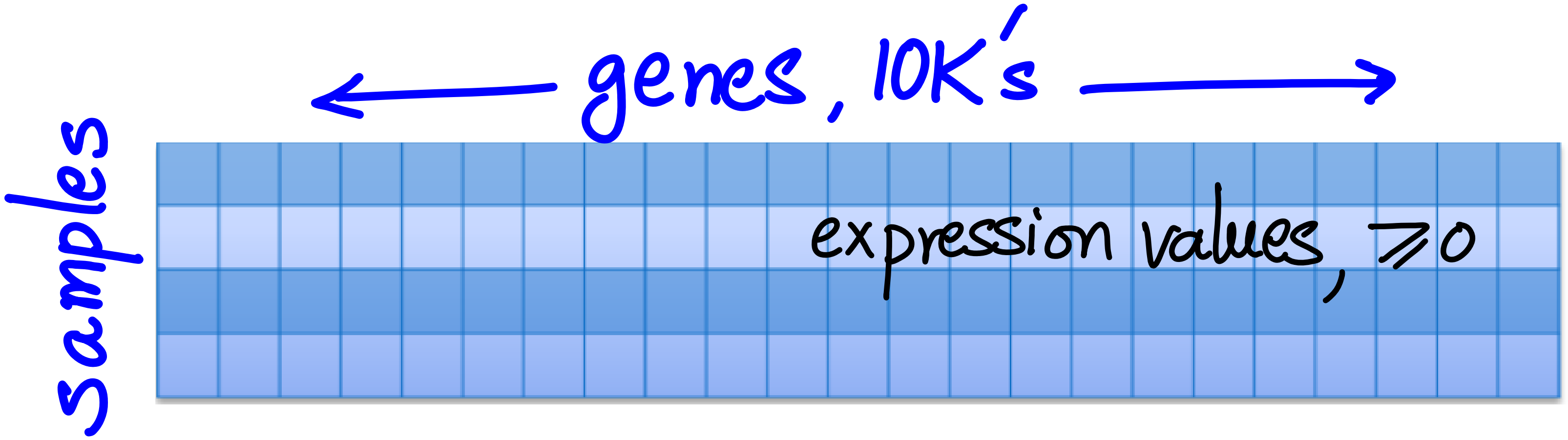

- ~50,000 genes
- 10s to a few 100 samples
- select a few "biologically relevant" genes ?

THE CHALLENGE

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- concentration of measure in high dim. (Beyer et.al, 1999)
  - clustering, PCA, ... might not work
- "higher order" method ?

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- genes in samples space

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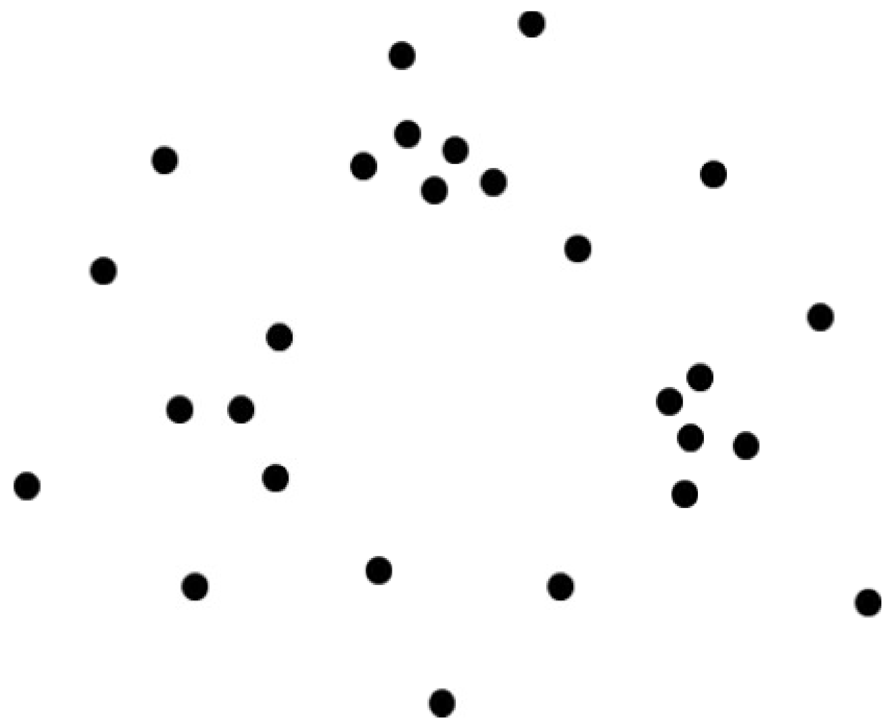
✱ a method for data exploration...

Higher-Order Structures

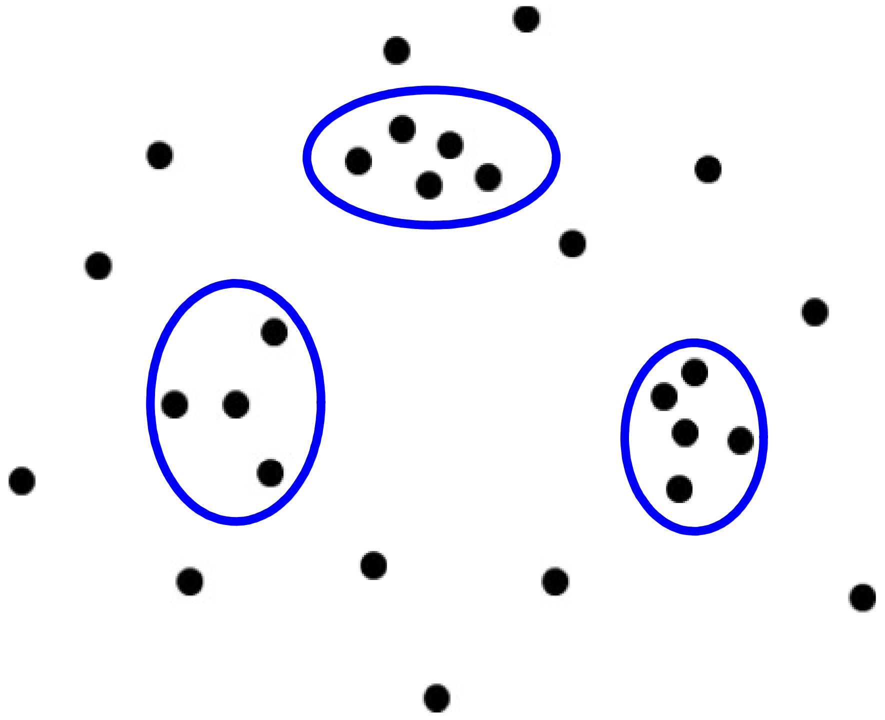
- 2D illustration



HIGHER-ORDER STRUCTURES

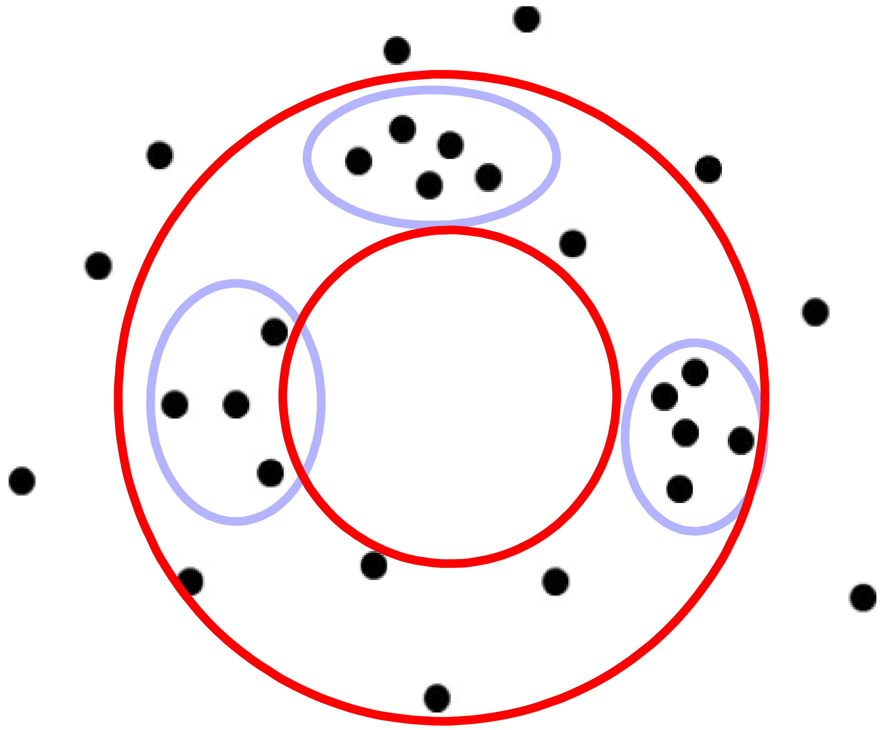
- 2D illustration

- traditional approach
  e.g., clustering
  - local structure



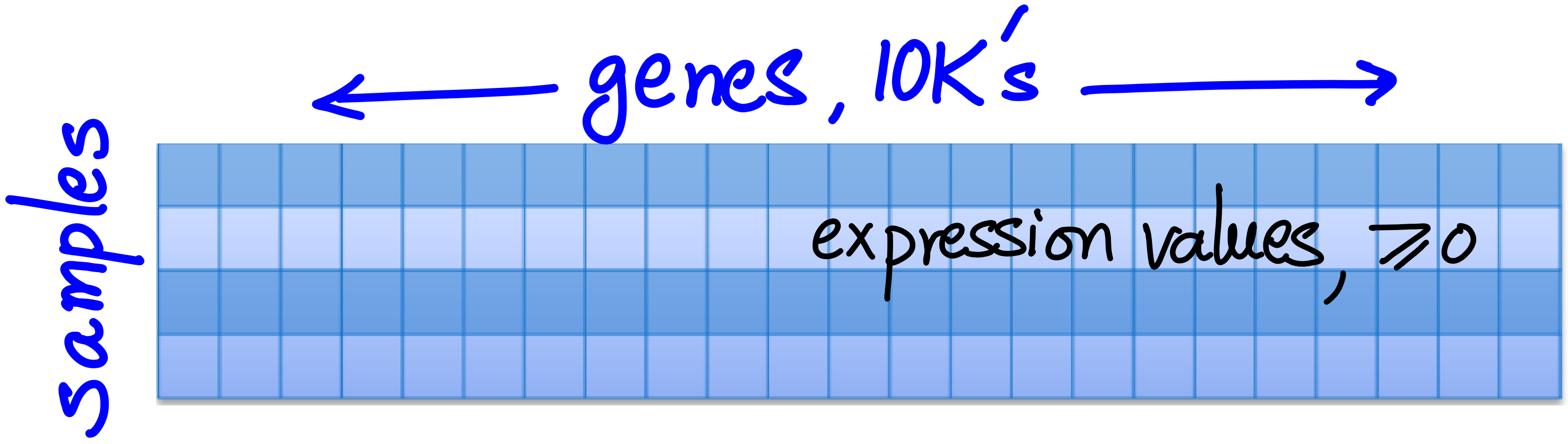
HIGHER-ORDER STRUCTURES

- 2D illustration
- traditional approach
  e.g., clustering
  – local structure
- miss higher order structure (loop)



HI-DIM: DUAL SPACE

- instead of



HI-DIM: DUAL SPACE

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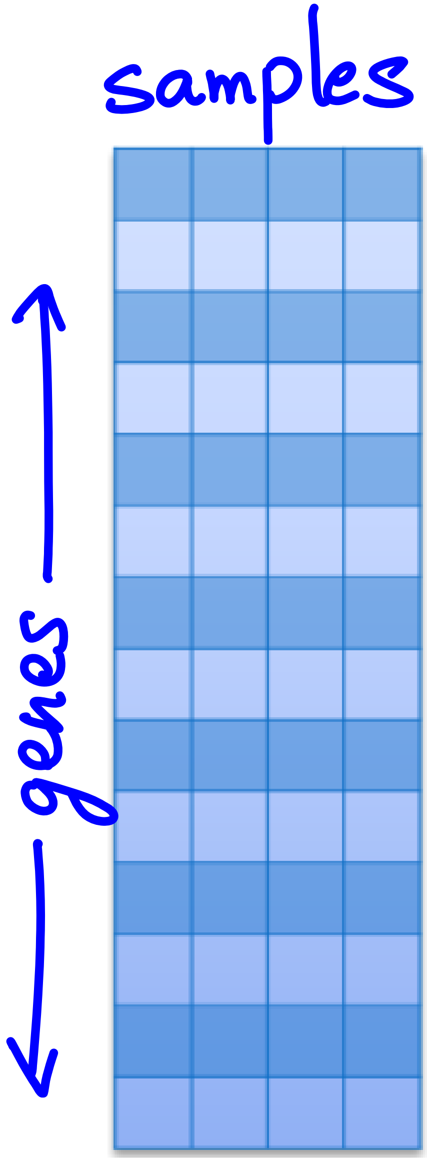
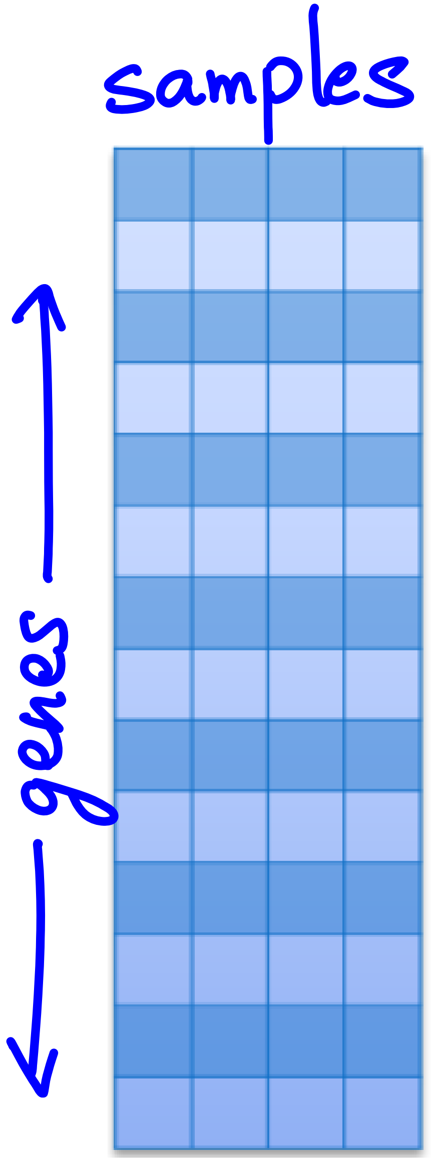


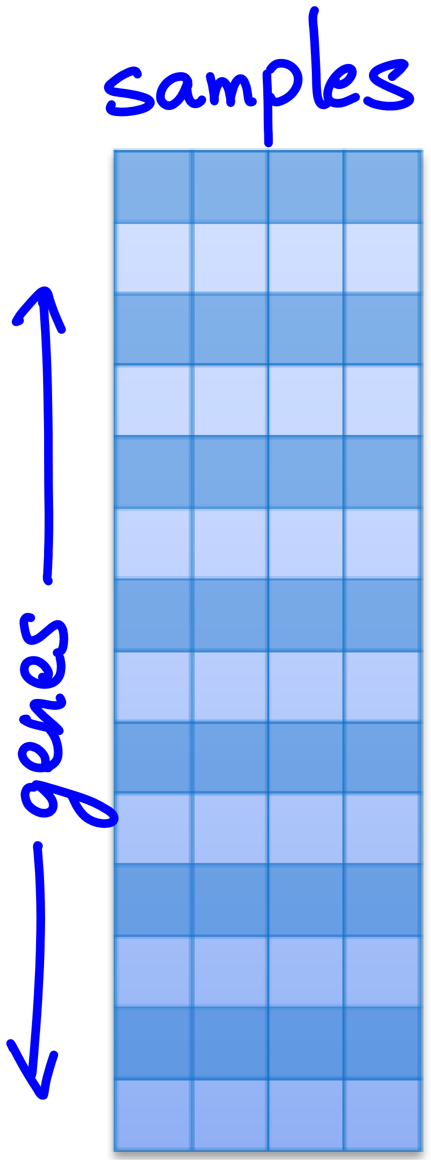
HI-DIM: DUAL SPACE

- use
- gene expressions considered across patients



HI-DIM: DUAL SPACE

- use
- gene expressions considered across patients
- pairwise distances are much more meaningful



PERSISTENT HOMOLOGY

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  - dim 0: connected components
  - dim 1: loops (around holes)
  - dim 2: enclosed voids

    ⋮

PERSISTENT HOMOLOGY

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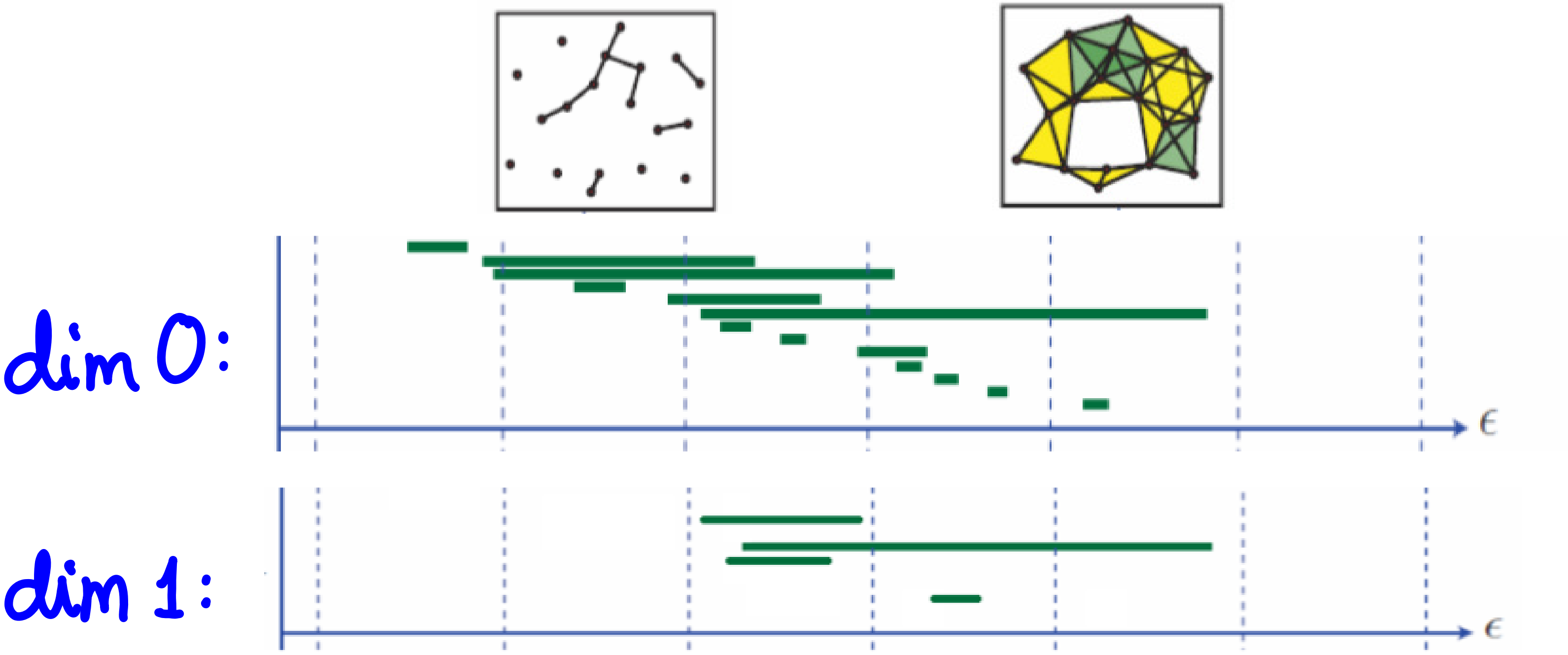

(image adapted from Ghrist, 2008)

WITNESS COMPLEX

de Silva & Carlsson, 2004

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  - v is the witness for the p-simplex

METHOD

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  dim-1 barcode

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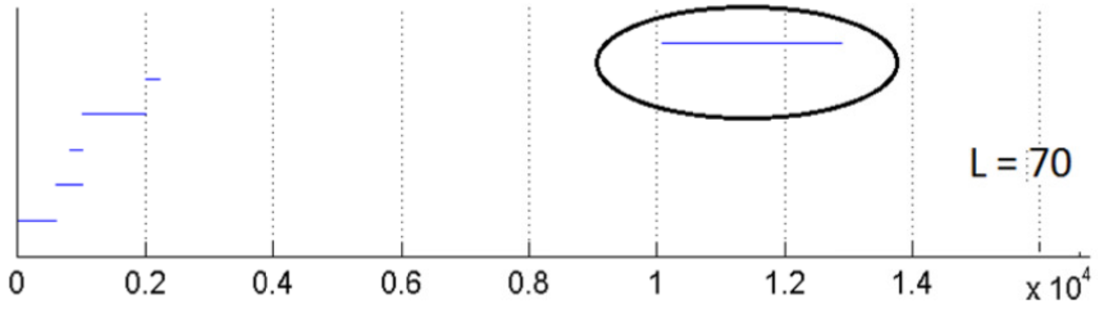

genes = 70

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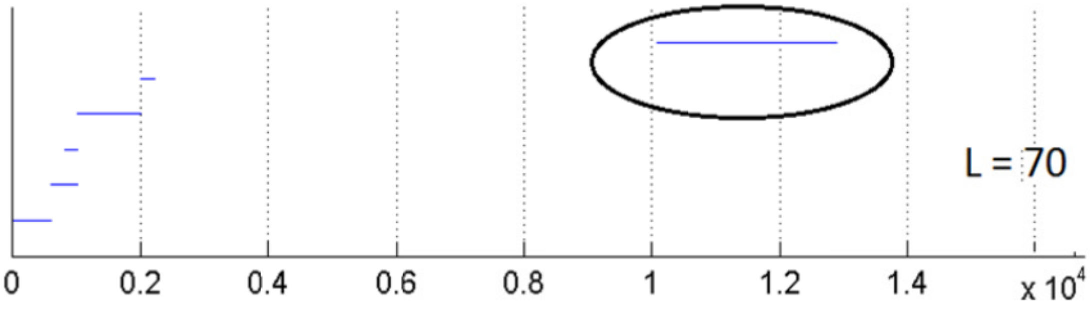

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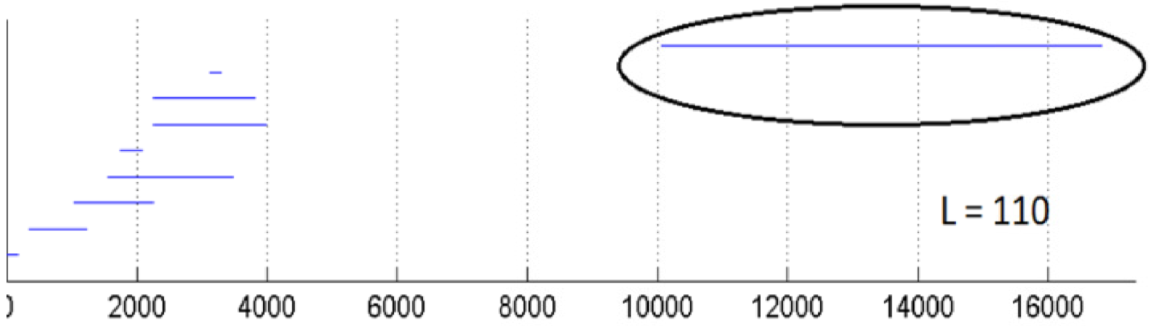

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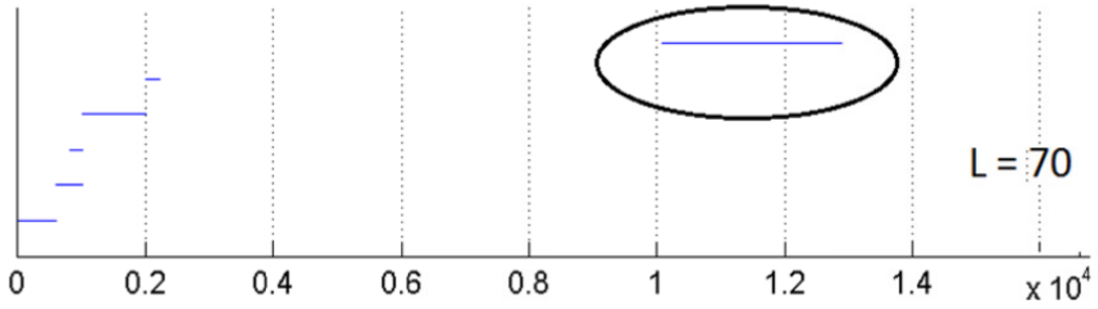

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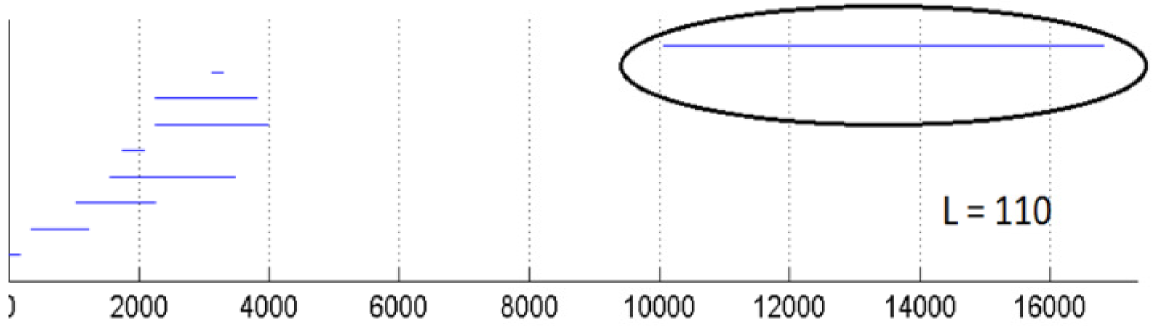

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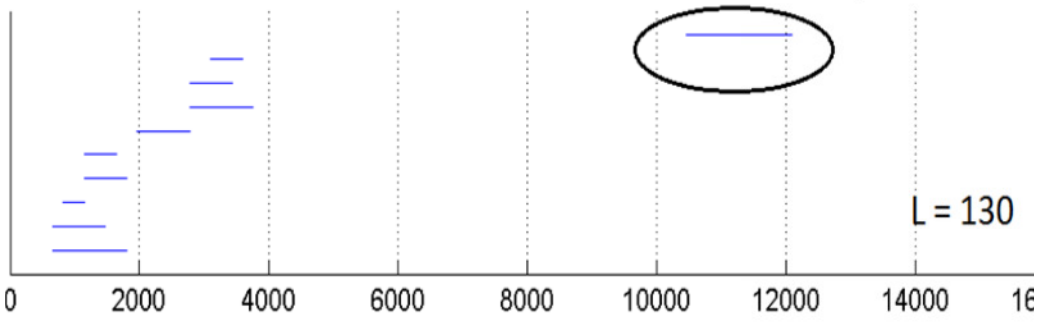

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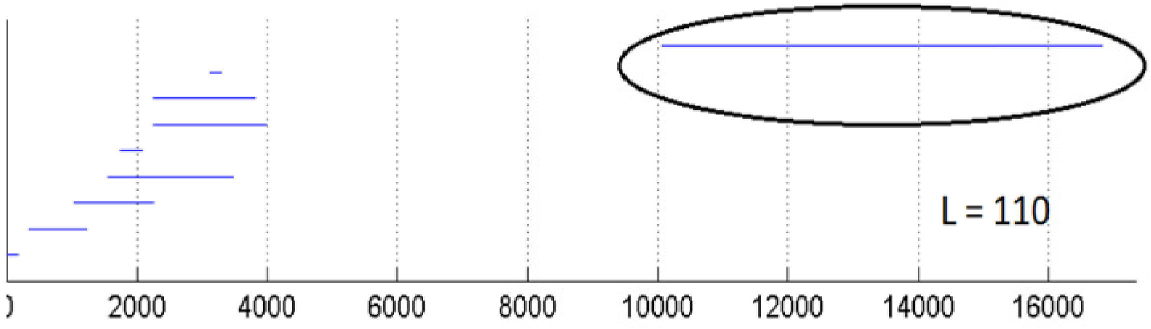
- pick the longest loop(s)



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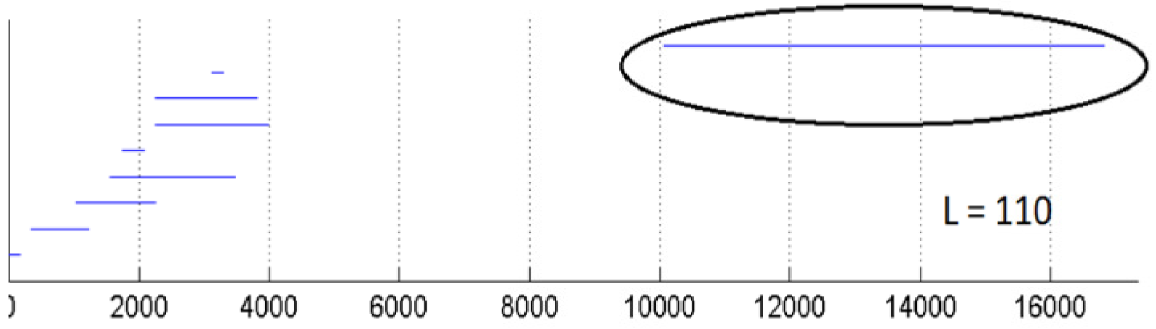

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- Are genes in loop(s) relevant for cancer?

METHOD

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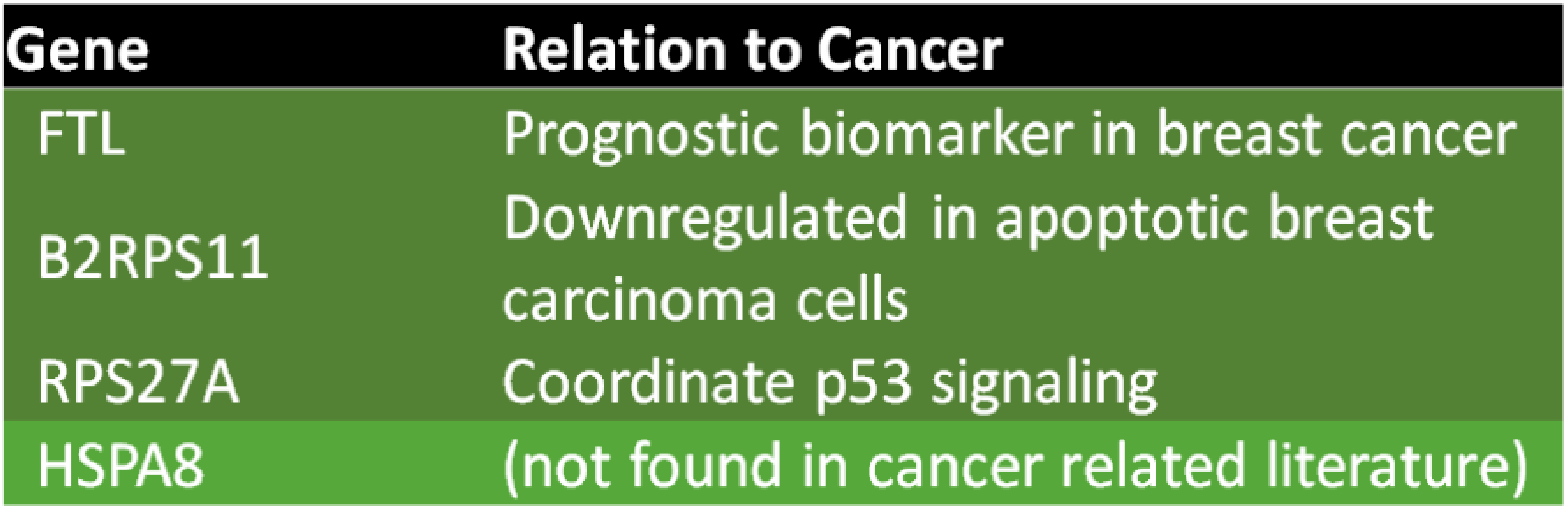
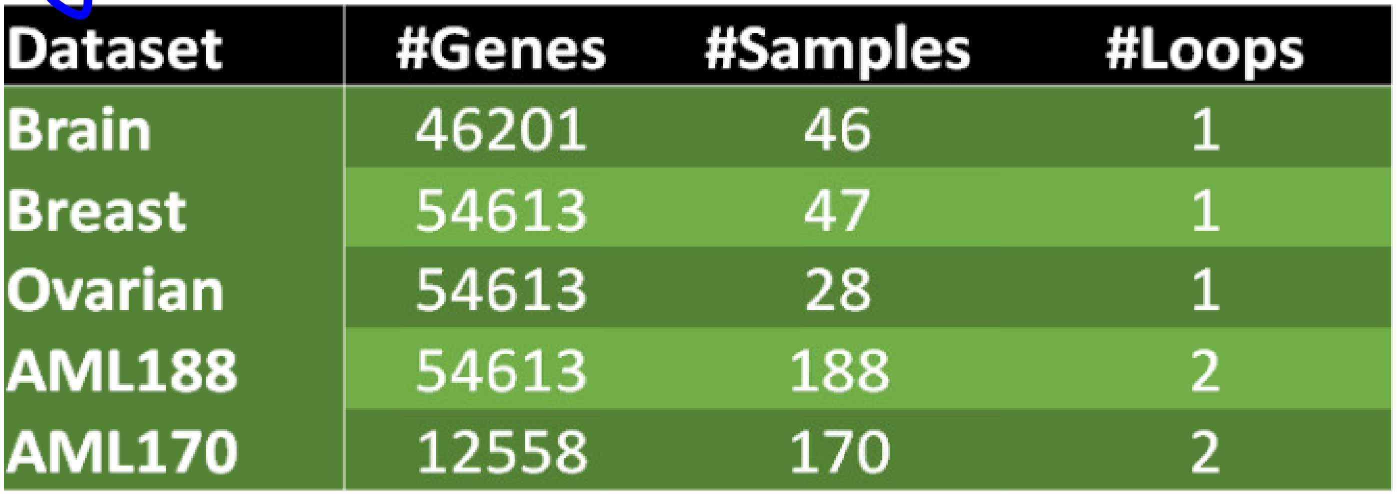
- genes in the breast cancer loop:



Gene	Relation to Cancer
FTL	Prognostic biomarker in breast cancer
B2RPS11	Downregulated in apoptotic breast carcinoma cells
RPS27A	Coordinate p53 signaling
HSPA8	(not found in cancer related literature)

RESULTS

* analyzed five different cancer datasets



Dataset	#Genes	#Samples	#Loops
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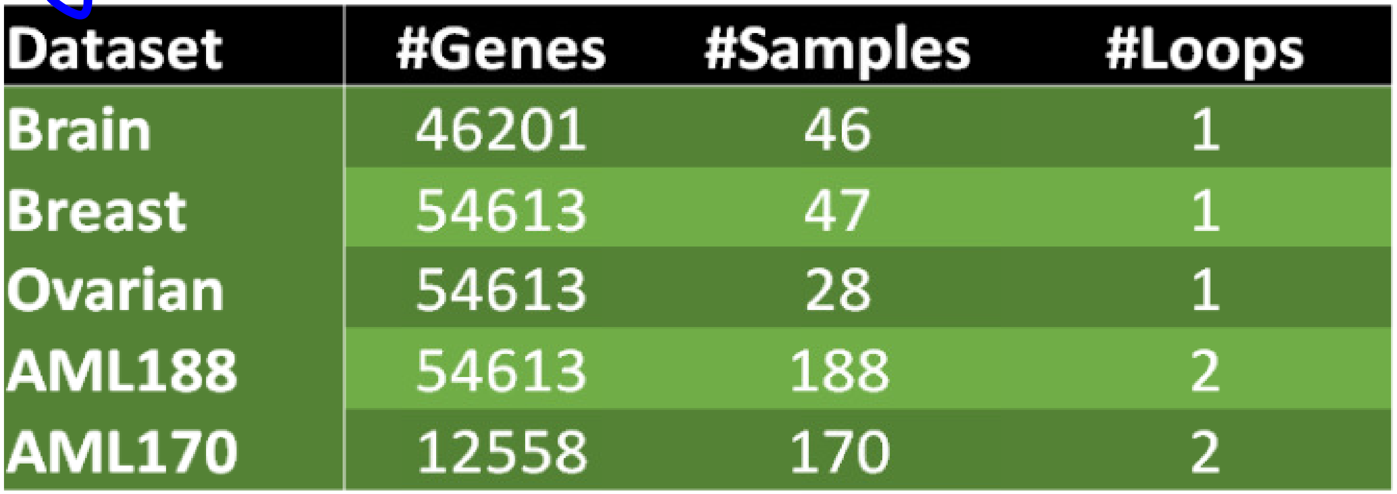

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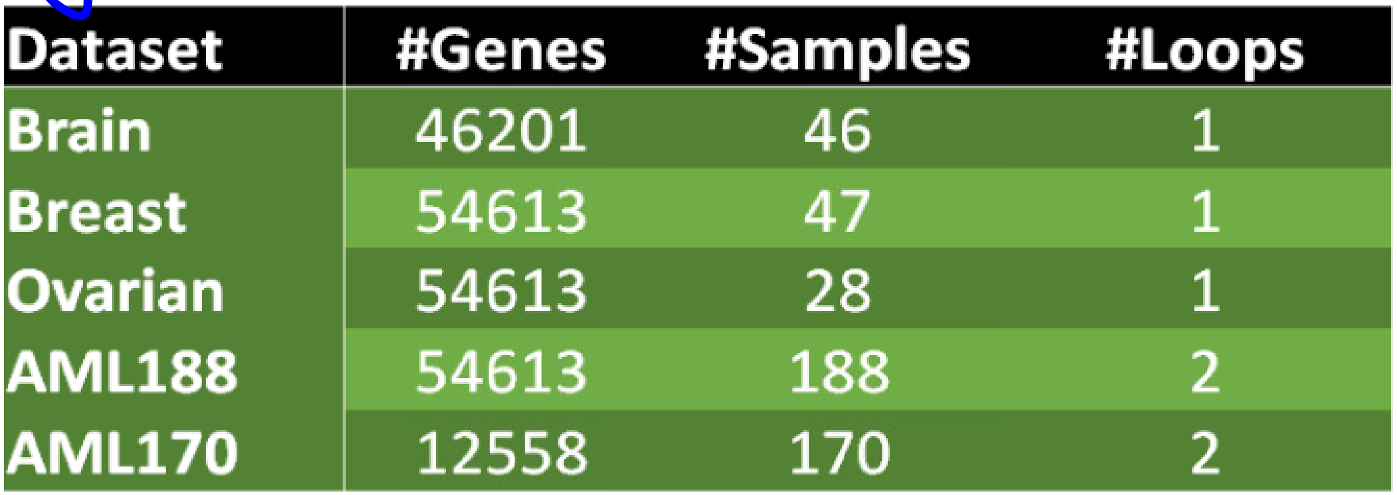

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* selected landmarks (L), as well as loop genes do <u>not</u> have extreme expression values

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- ✱ Does dualization affect ability to prove results on structure/stability of data?

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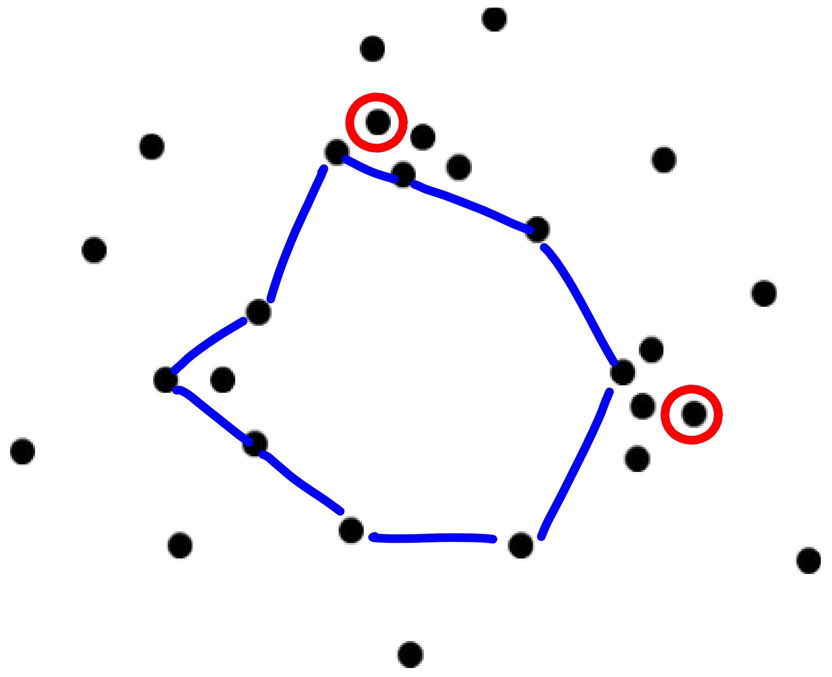

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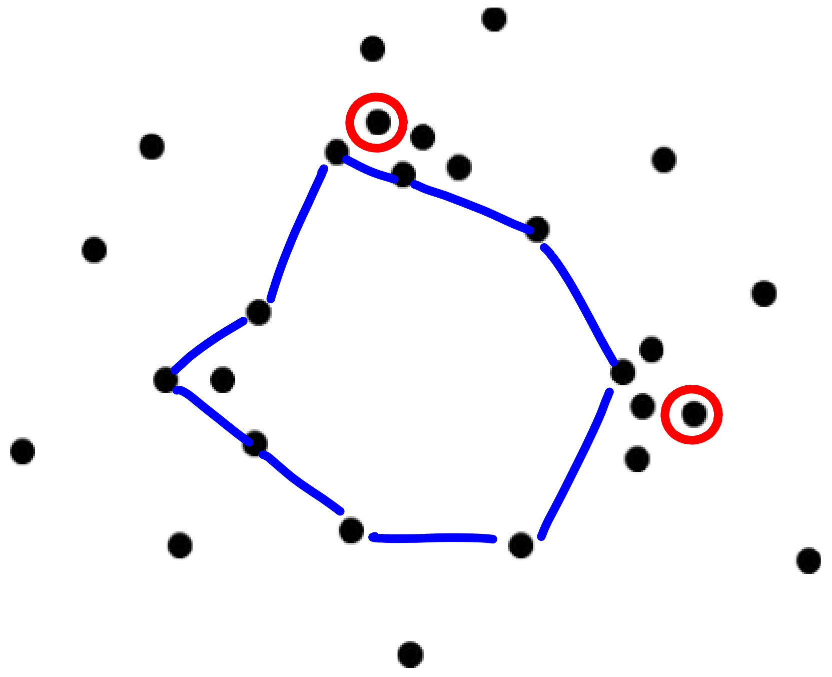

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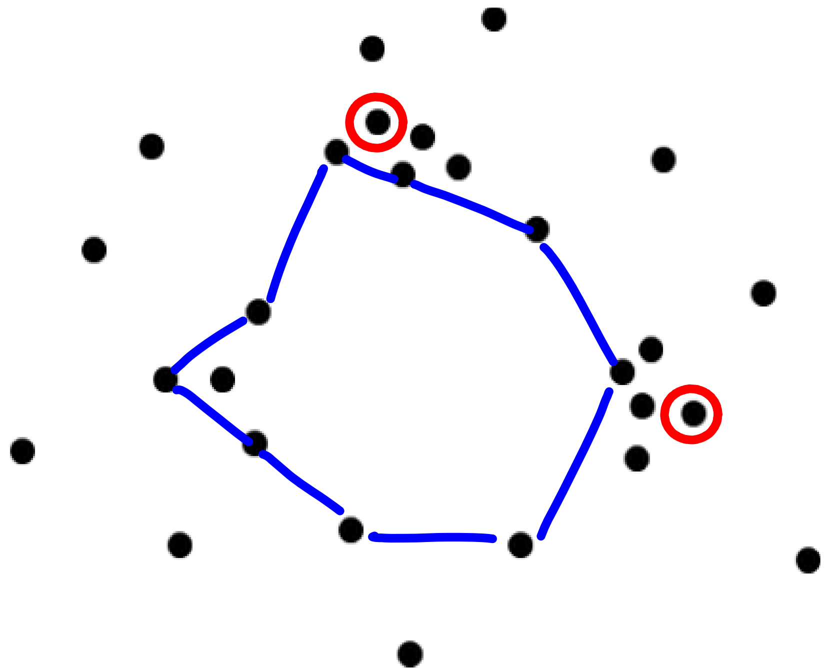

- Can we identify loop(s) with "all critical genes"?
- Apply to other classes of data sets?