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Object Oriented Data Analysis

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University of North Carolina

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How does Statistics relate to Data Science?

From My Elementary Courses:

- Gaining Insight from Numbers

  Similar to “Data Science” Definitions

- The Science of Managing Uncertainty

  Where Probability Modeling Is Vital

This is Why Statistics is Fundamental

More Currently Popular Terminology

Big Data

- Isn't It Just Statistics?
- Yes, But More Needed Too
- Maybe <u>Bigger</u> Challenge:

Optimization:
Machine Learning

Complex Data

An Idea Worth Spreading?

Well Understood Concept:

Great science now done by teams
with complementary skill sets

- Biology
- Chemistry
- Engineering
- Quantitative Work

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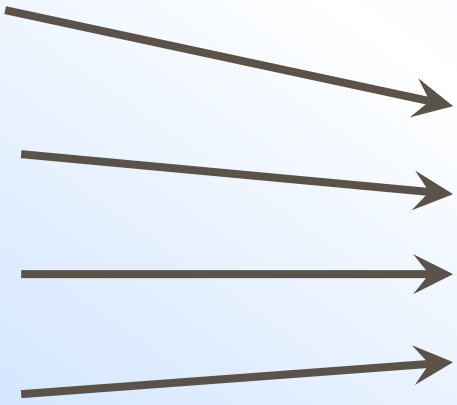
Common Current Idea:
1 Team member

An Idea Worth Spreading?

Extension of this:

Great *Quantitative Work* needs teams with complementary skill sets

- Statistics
- Imaging
- Optimization
- Data Base
- …



Big Data

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An Idea Worth Spreading?

Proposed New Approach:

Team Data Science

- Teams with Complimentary Skillsets
- Education of Team Members:
  - Bring Valued (Deep) Skill
  - Know Enough to Communicate
  - Give Opportunities to Practice

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Object Oriented Data Analysis

What is the "atom" of a statistical analysis?

- 1st Course: Numbers
- Multivariate Analysis Course : Vectors
- Functional Data Analysis: Curves
- More generally: Data Objects

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Object Oriented Data Analysis

Original Thought:

OODA = Mathematical Framework

(containing wide variety
of interesting cases)

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Object Oriented Data Analysis

Original Thought:

OODA = Mathematical Framework

Current View:

OODA = Focal Point

{For discussions (interdisciplinary)
about tackling serious analyses}

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Object Oriented Data Analysis

Original Thought:

OODA = Mathematical Framework

Current View:

OODA = Focal Point

What should be the Data Objects?

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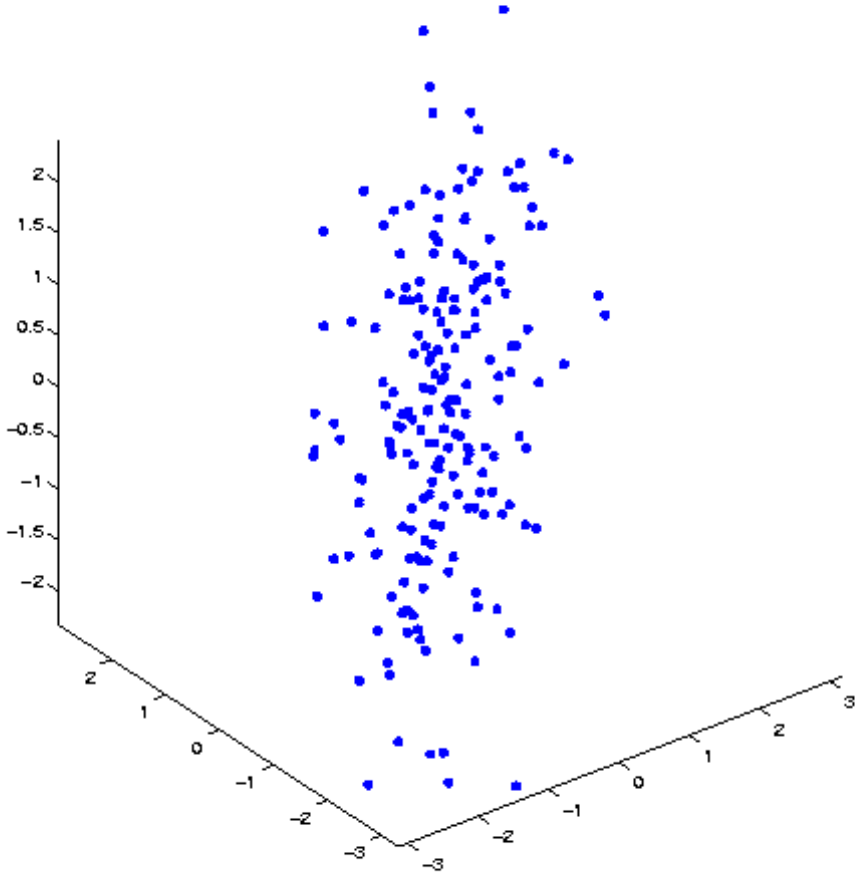
Principal Component Analysis

More Than *Dimensionality Reduction*:

- Visualization
  - Relationships Between Objects (Scores)

Demo PCA in $\mathbb{R}^3$

Raw Toy Data Set in $\mathbb{R}^3$



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Demo PCA in $\mathbb{R}^3$

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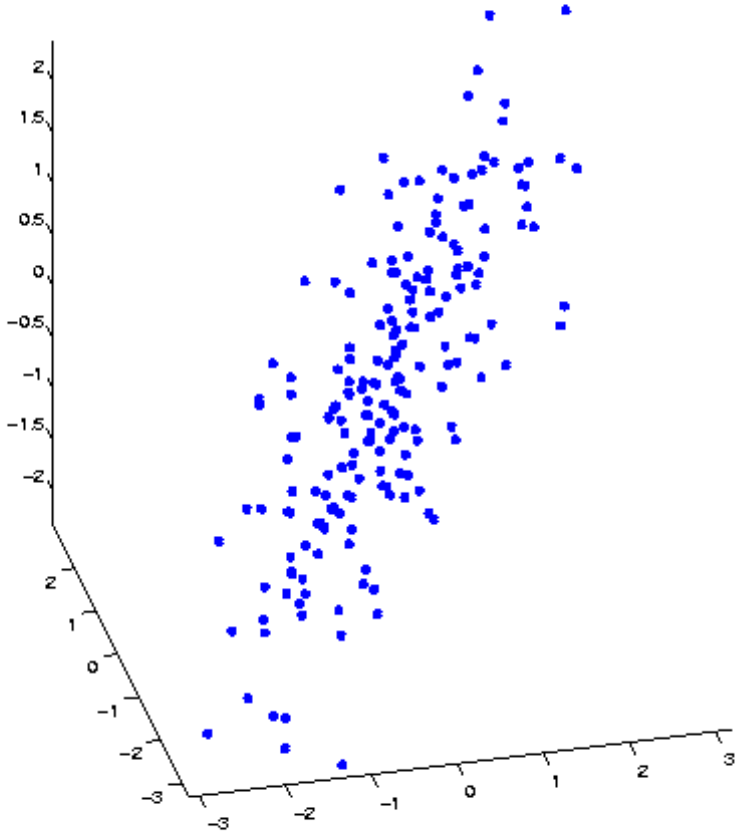

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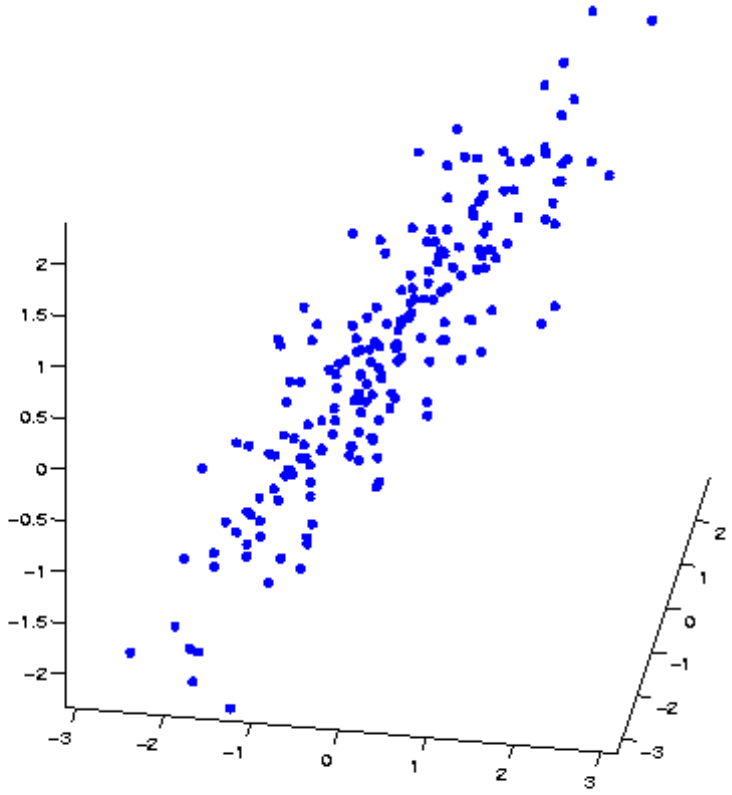

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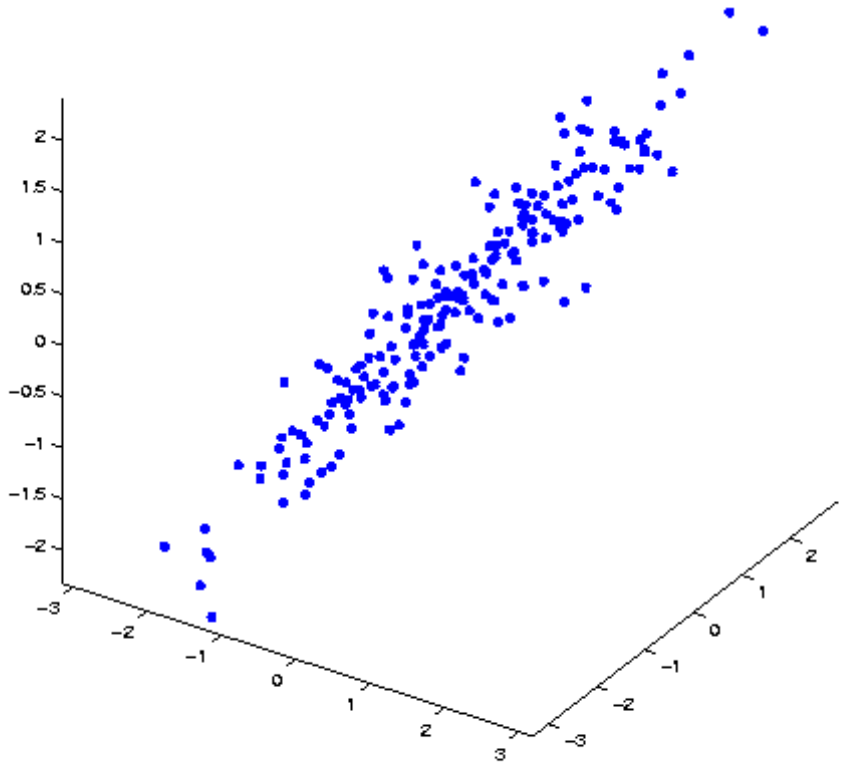

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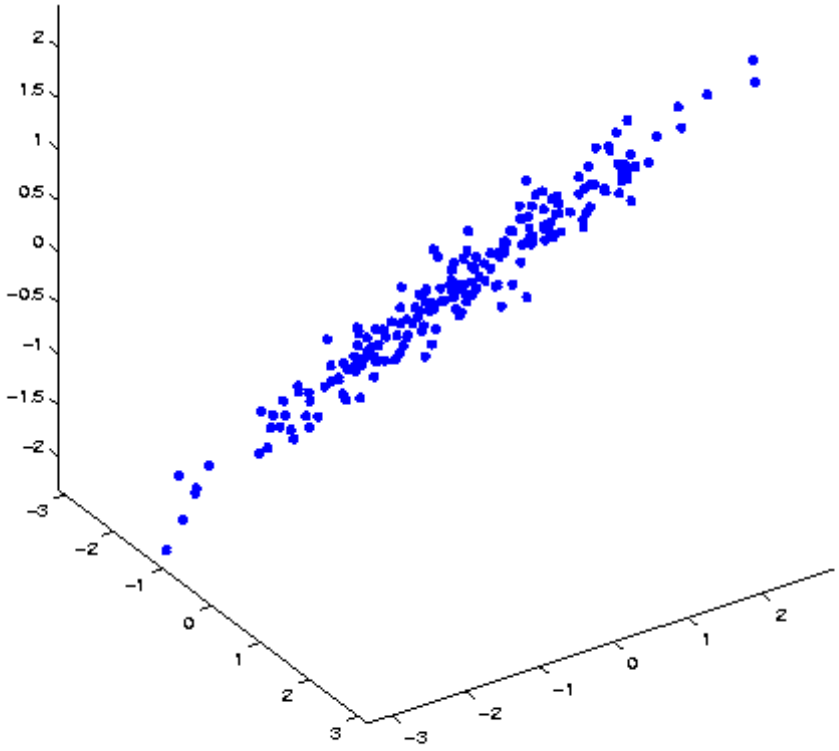

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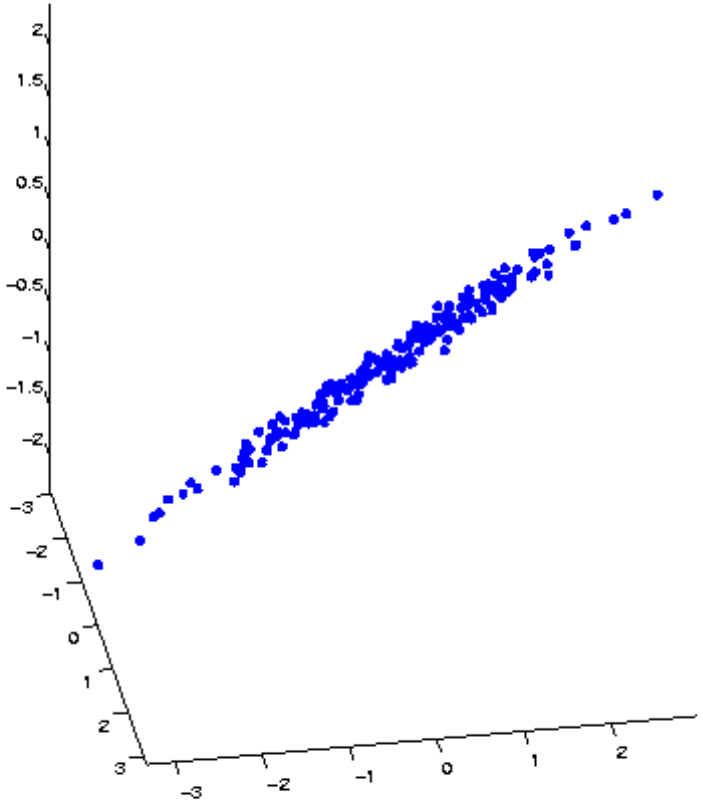
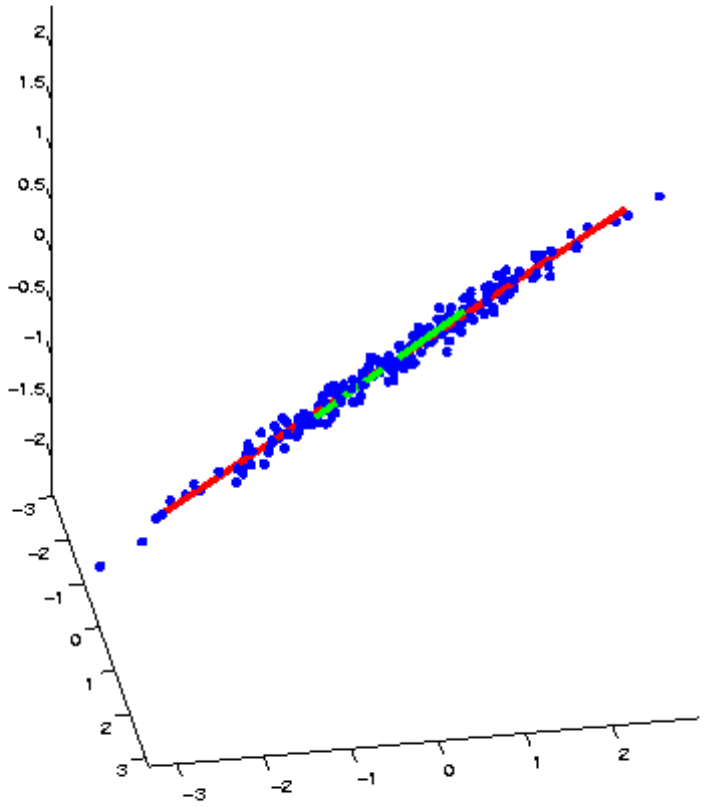


Demo PCA in $\mathbb{R}^3$

PCA Eigenvectors Give Useful Coordinates



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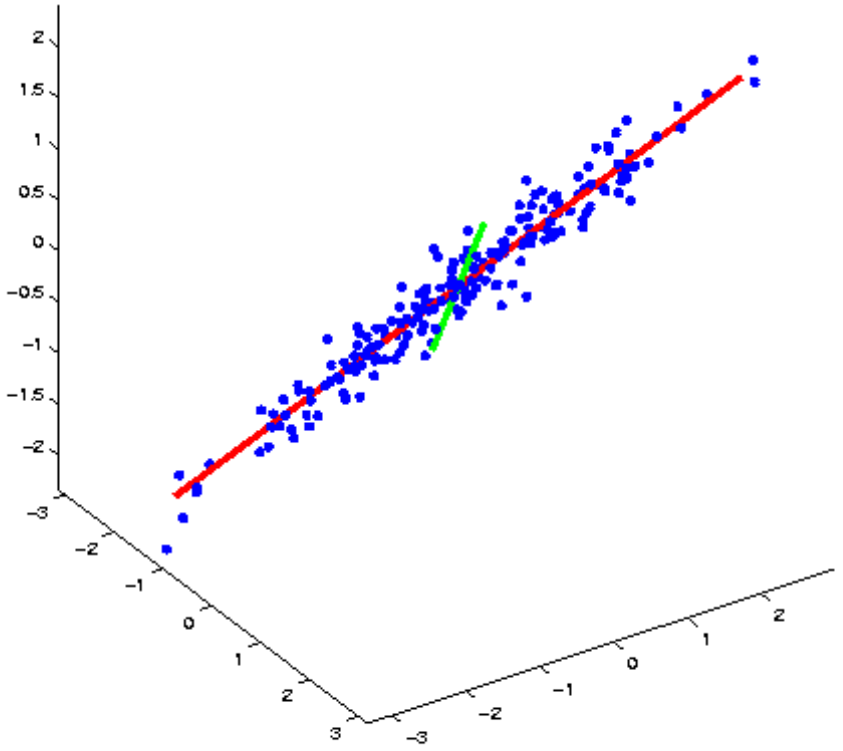

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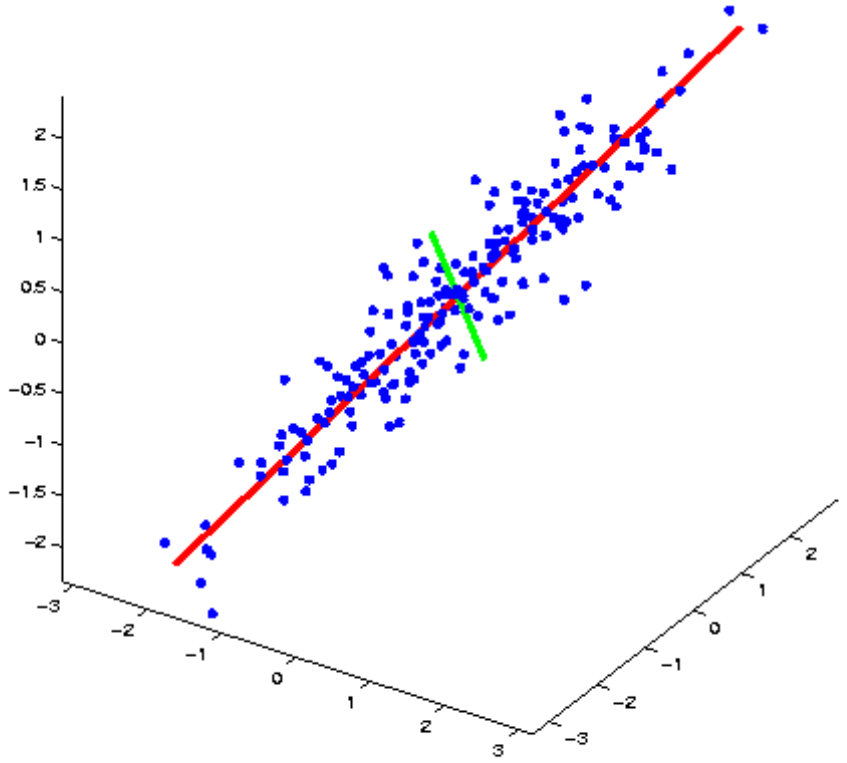

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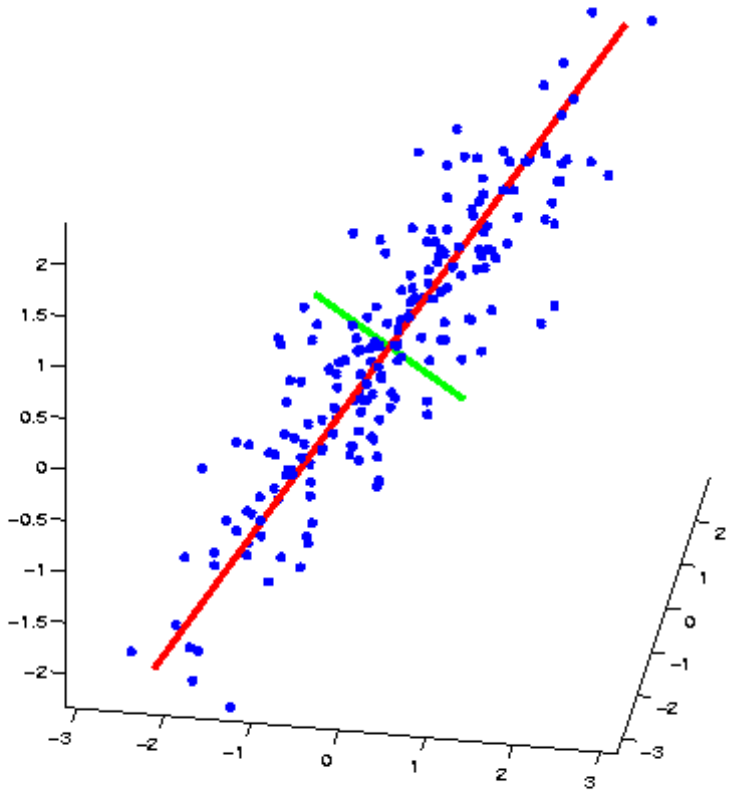

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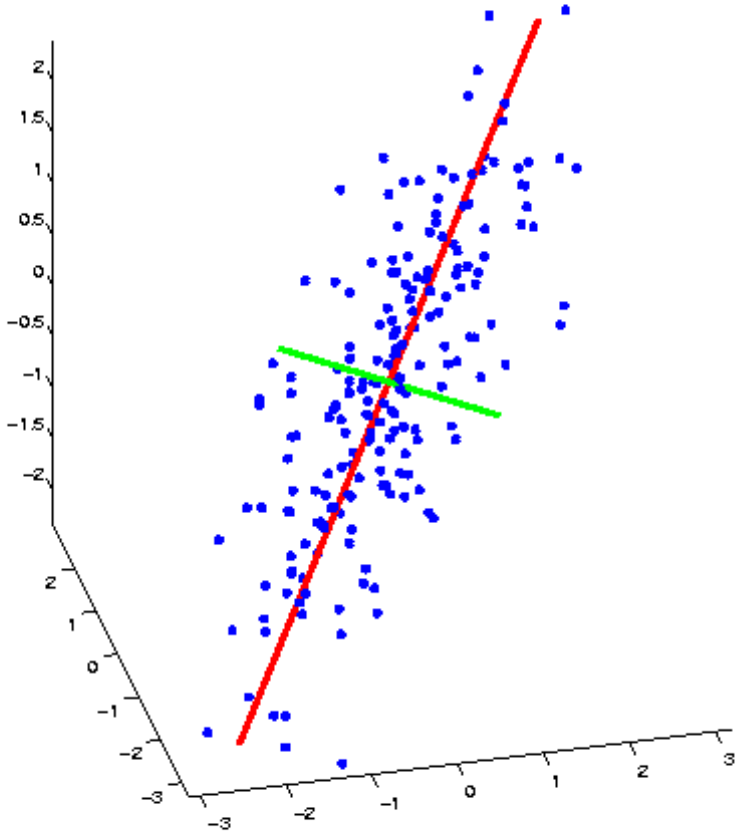

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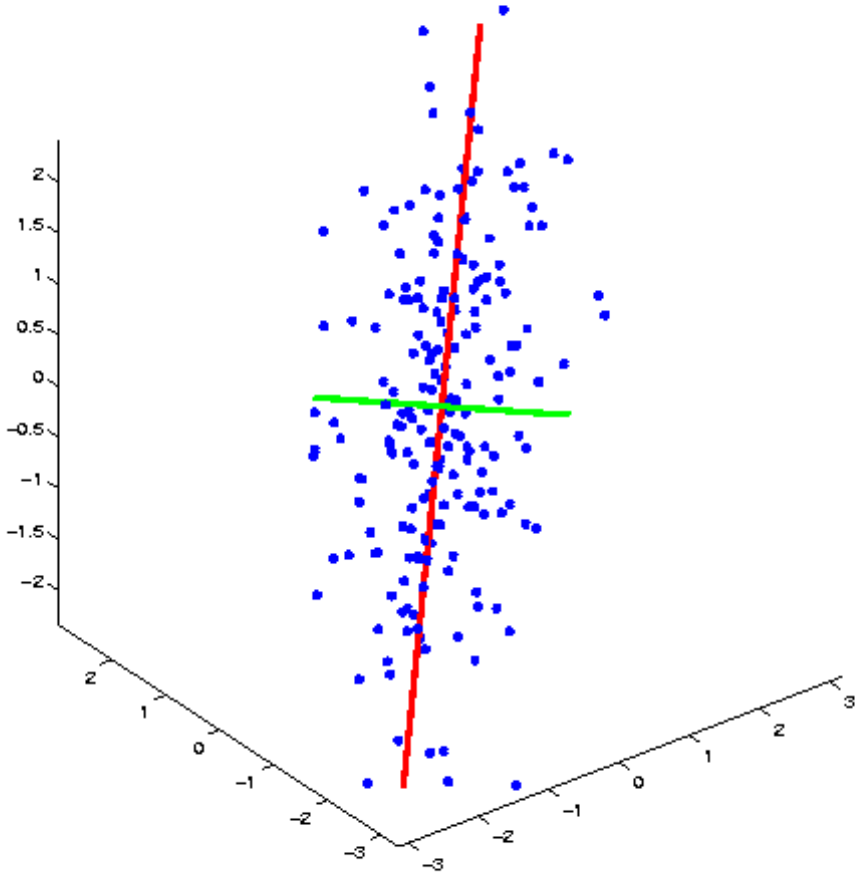
PCA Eigenvectors Give Useful Coordinates



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Functional Data Analysis

Interesting Real Data Example

- Genetics (Cancer Research)
- RNAseq (Next Gener'n Sequen'g)
- Deep look at "gene components"

Microarrays: Single number (per gene)

RNAseq: Thousands of measurements

Functional Data Analysis

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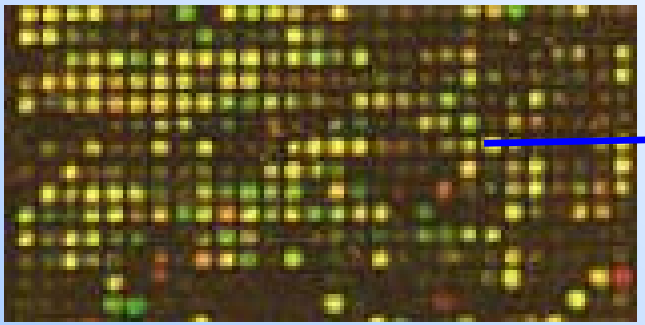

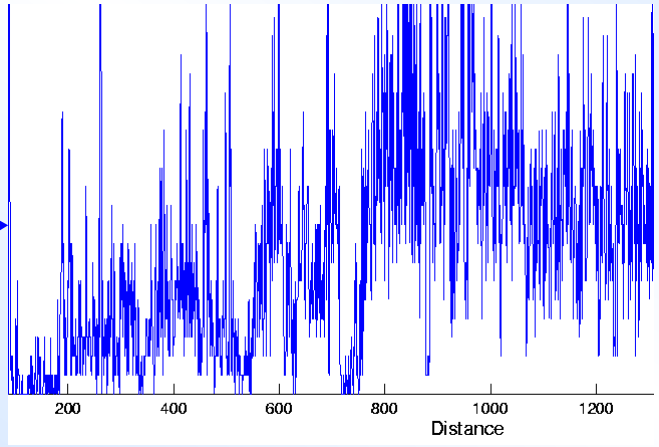

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Functional Data Analysis

Interesting Real Data Example

- Genetics (Cancer Research)
- RNAseq (Next Gener'n Sequen'g)
- Deep look at "gene components"

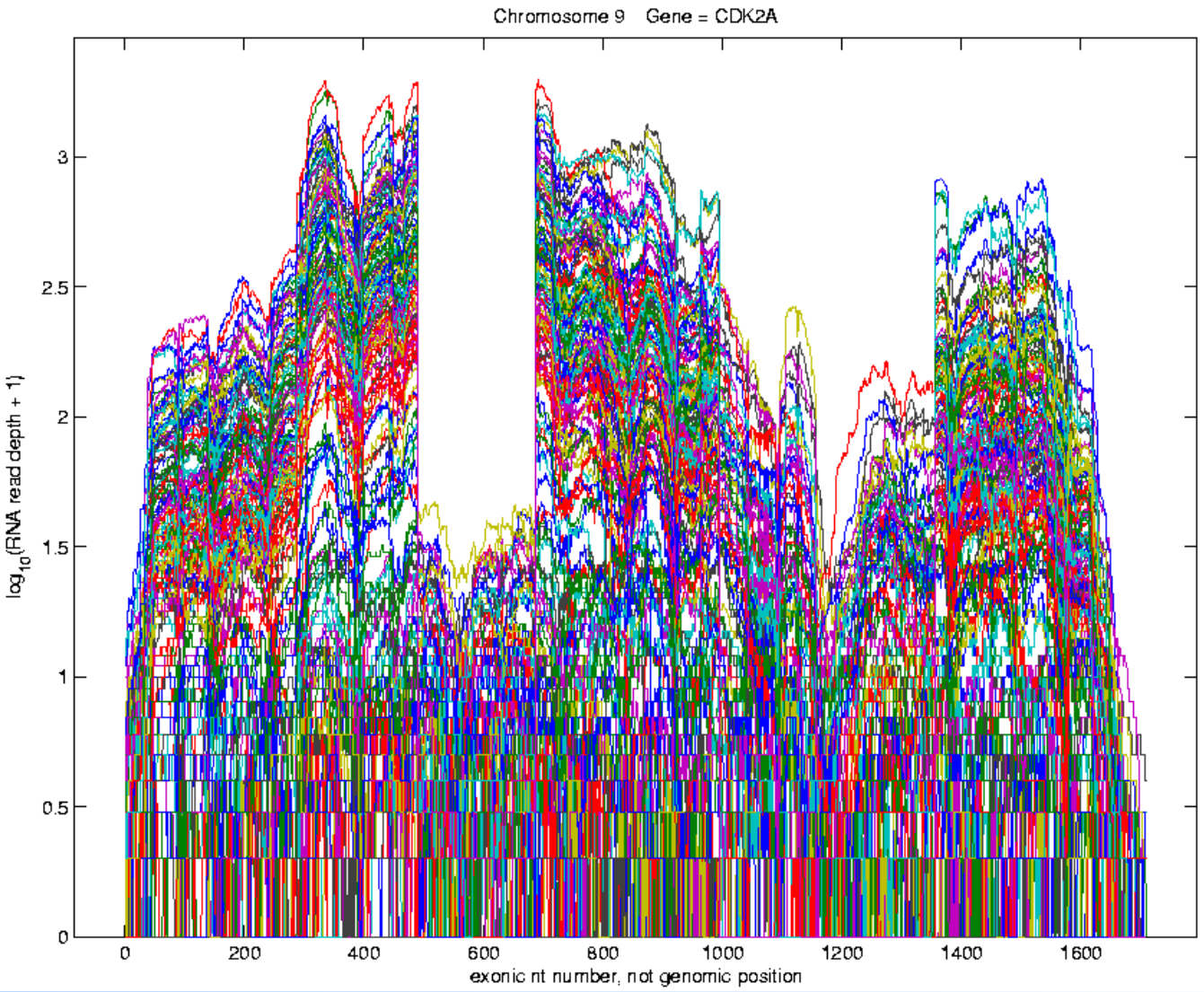
- Gene studied here: CDKN2A
- Goal: *Study Alternate Splicing*
- Sample Size, $n = 180$
- Dimension, $d = \sim 1700$

Functional Data Analysis

Simple 1st View: Curve Overlay

(log scale)

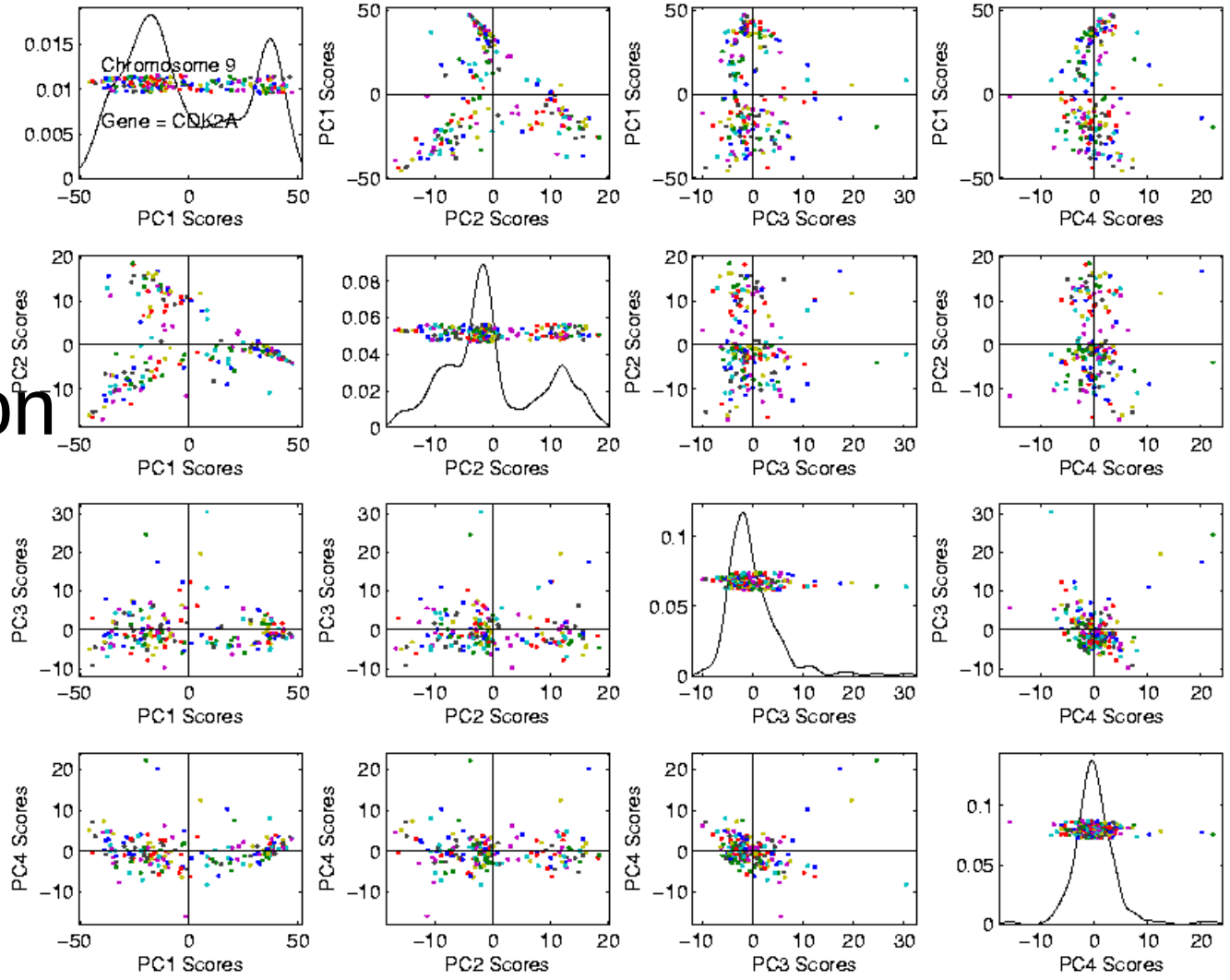
Thanks to Matt Wilkerson



Functional Data Analysis

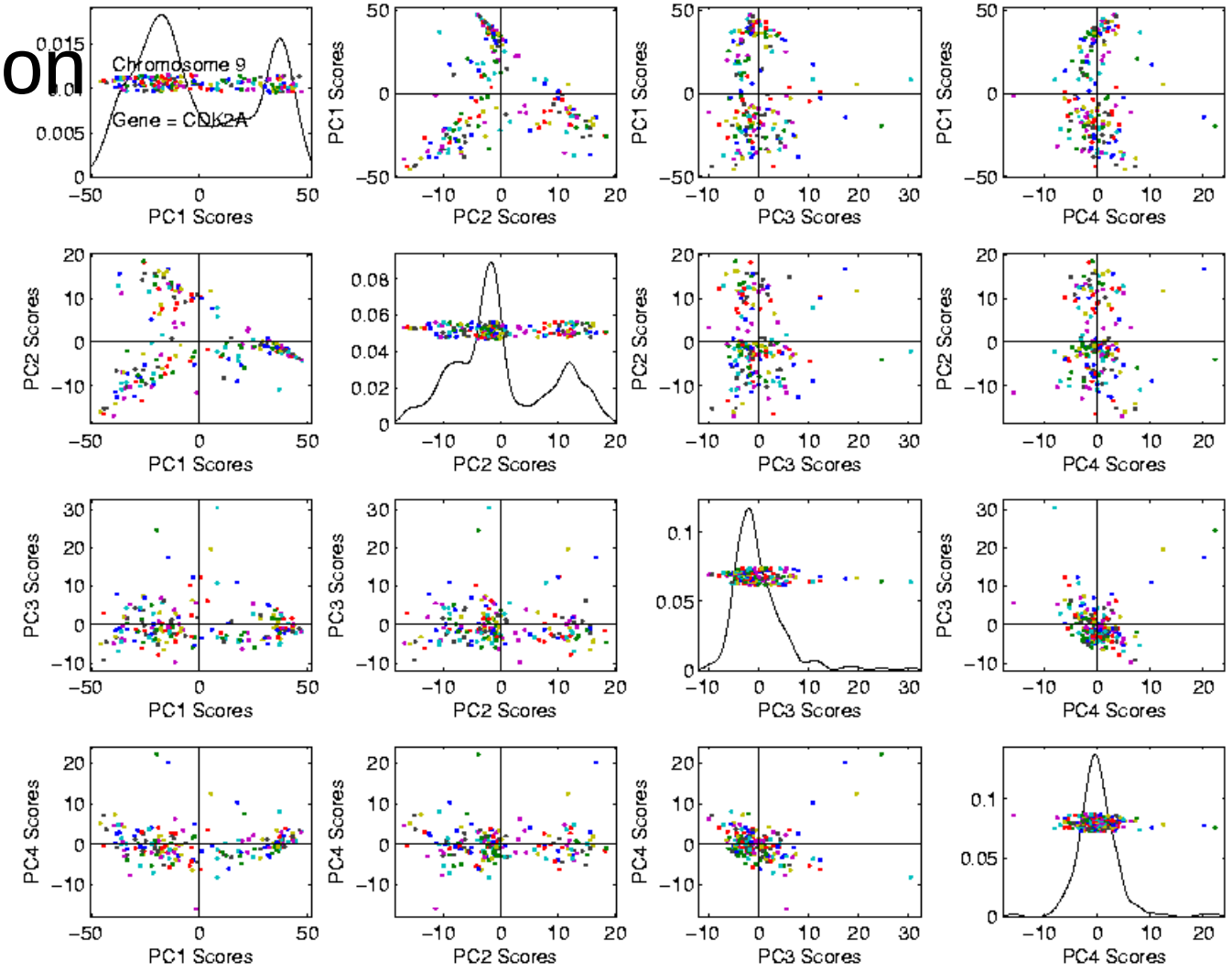
Often Useful Population View:

PCA Scores



Functional Data Analysis

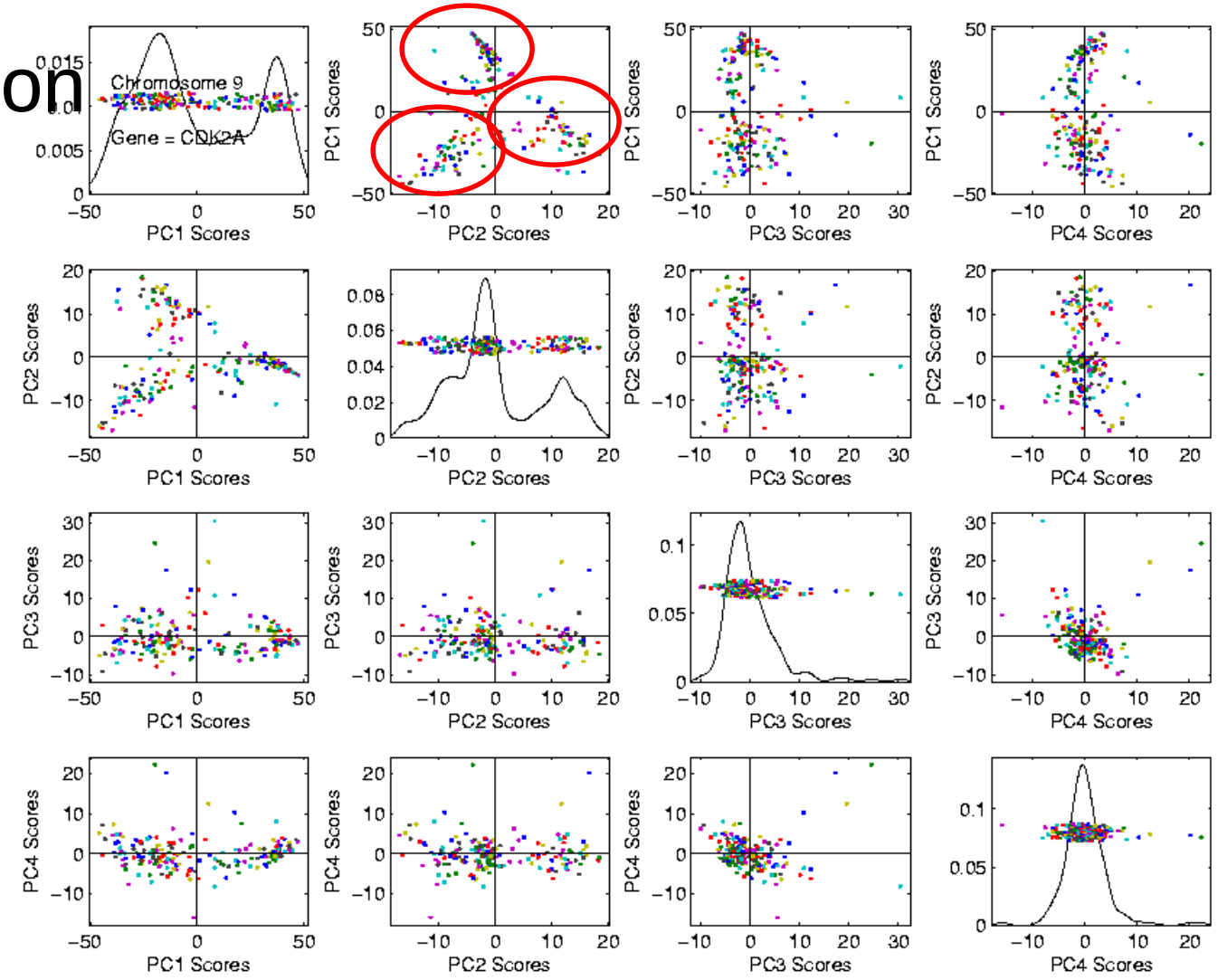
Suggestion Of Clusters ???



Functional Data Analysis

Suggestion Of Clusters

Which Are These?



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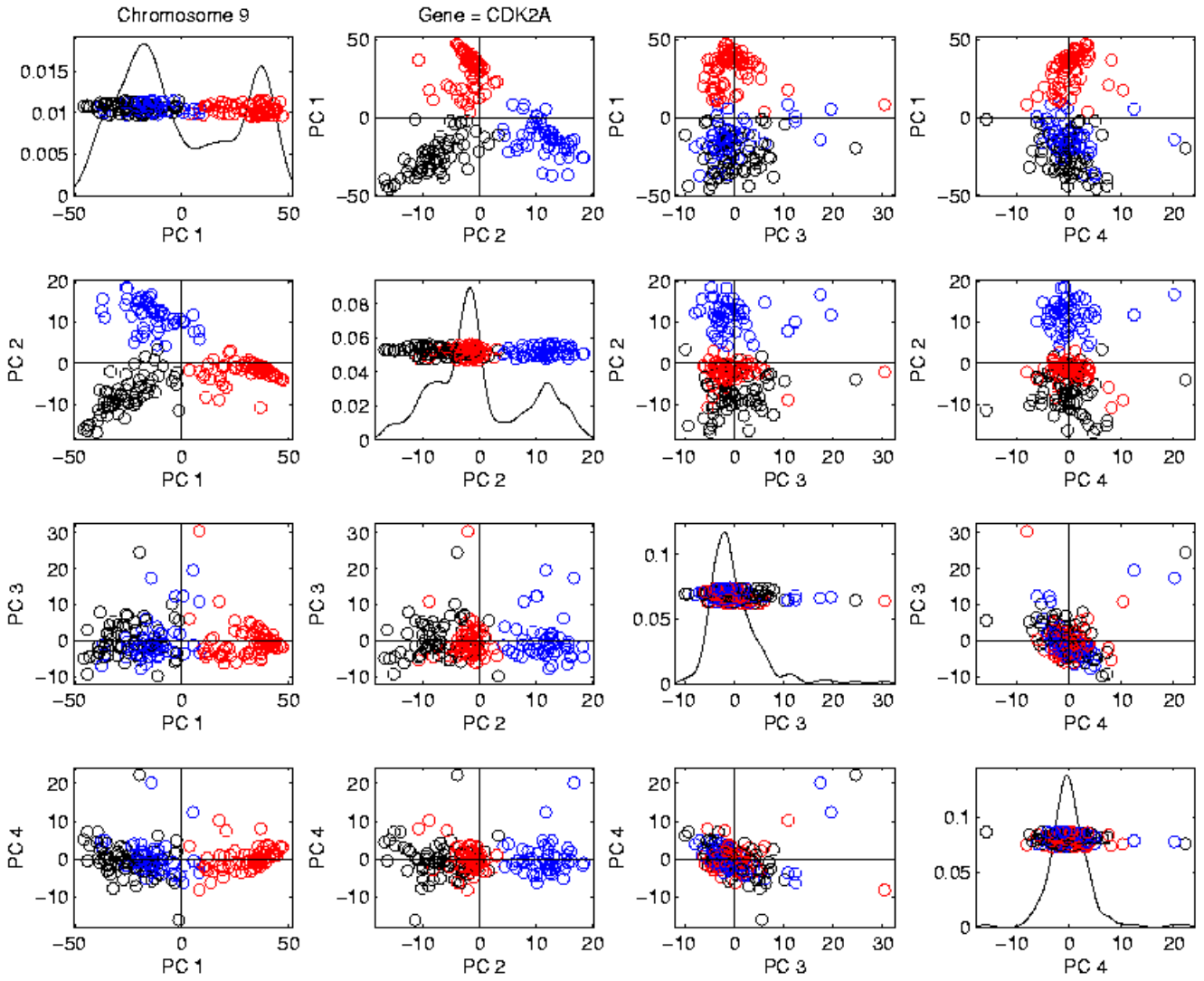
Functional Data Analysis

Manually Brush Clusters



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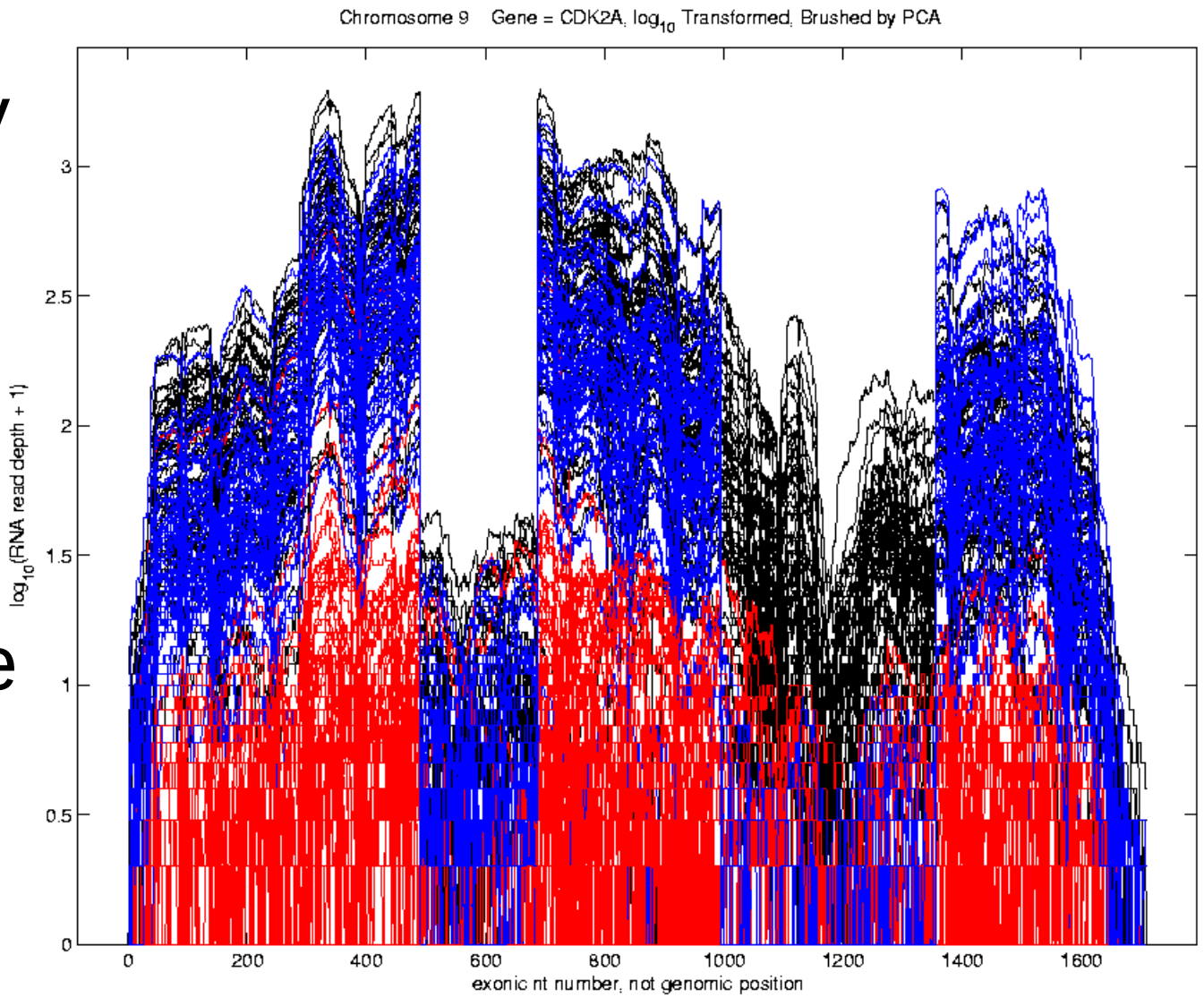
Functional Data Analysis

Manually Brush Clusters

Clear Alternate Splicing



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Functional Data Analysis

Consequences of this Visualization:

- ✓ Lead to Full Genome Screening Method
  SigFuge
- ✓ Important Component: SigClust
  (Which Clusters are *Really There*?)
- ✓ Found New Splices
  (Now Been Biologically Verified)

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Object Oriented Data Analysis

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- Functional Data Analysis: Curves
- More generally: Data Objects

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Personal Motivating Contexts

Interdisciplinary Areas:

- Cancer Genetics
- Medical Image Analysis
- Evolutionary Biology
- Drug Discovery

Some Special Cases of OODA

Data Object Types:

- Curves (Functional Data Analysis)
- Spectra (Non-Negative!)
- Images
- Shapes
- Trees
- Movies (Functional MRI)

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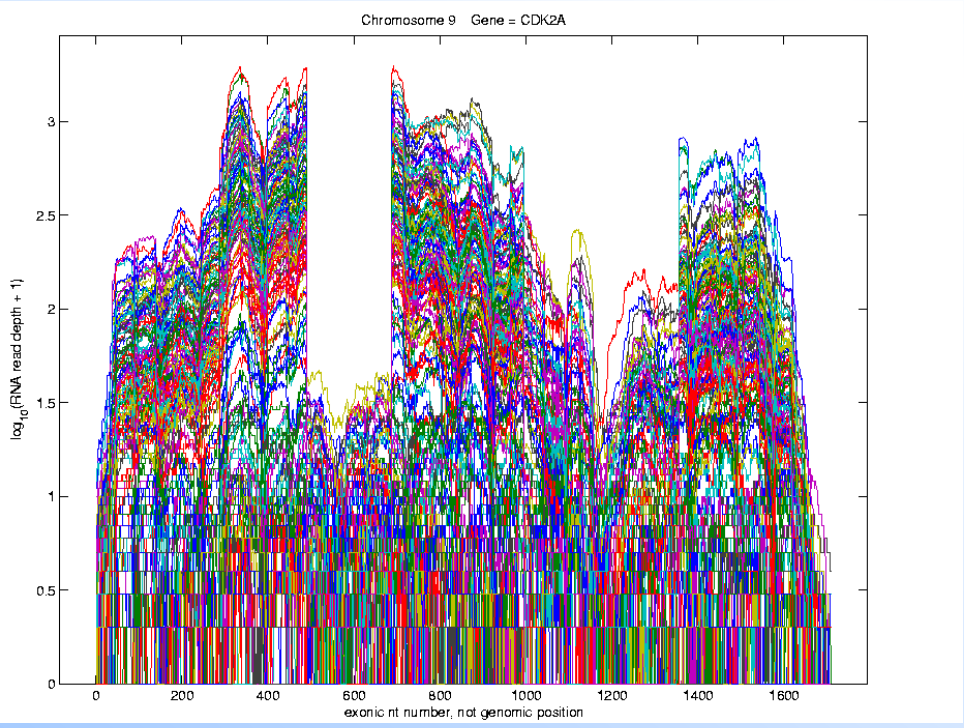
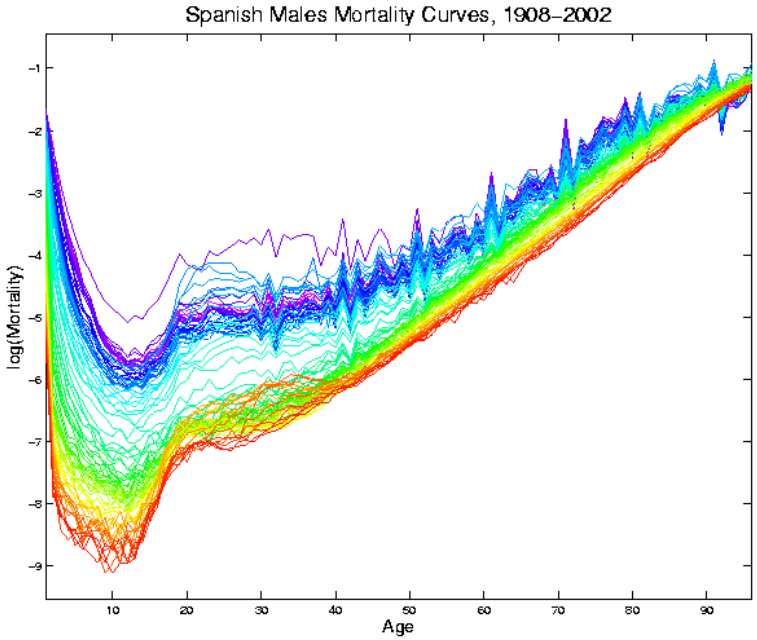
Curves as Data Objects (FDA)

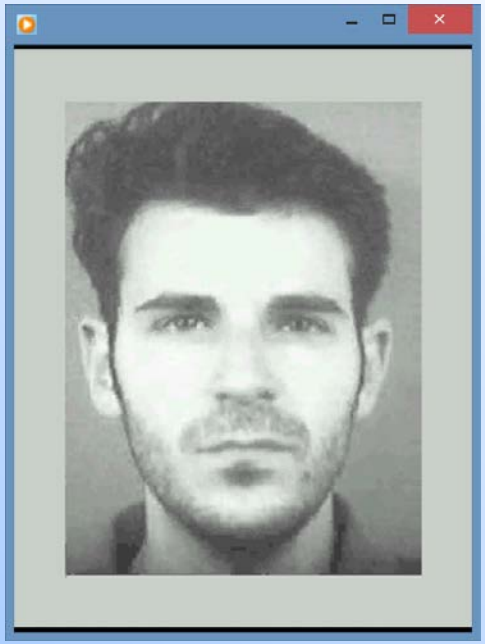
Generally Euclidean: Use standard methods

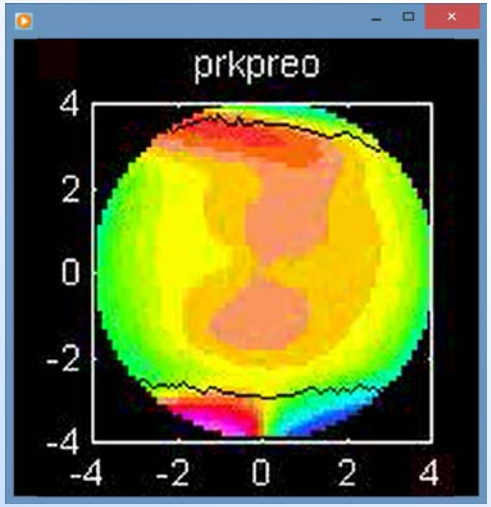


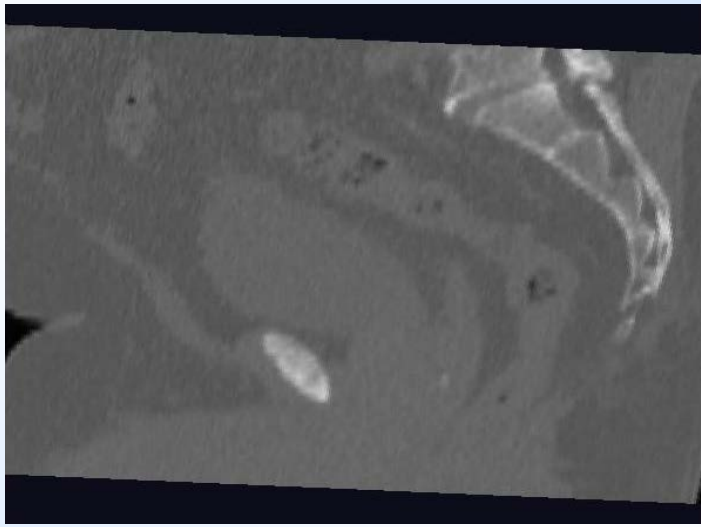


Images as Data Objects

Challenge: High Dimension, Low Sample Size

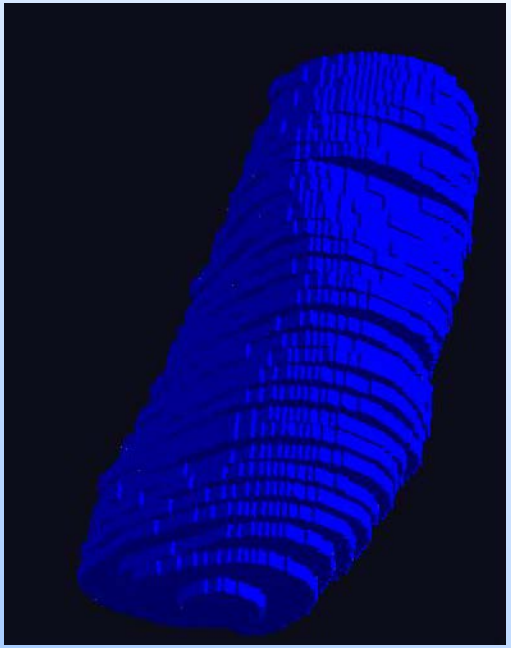


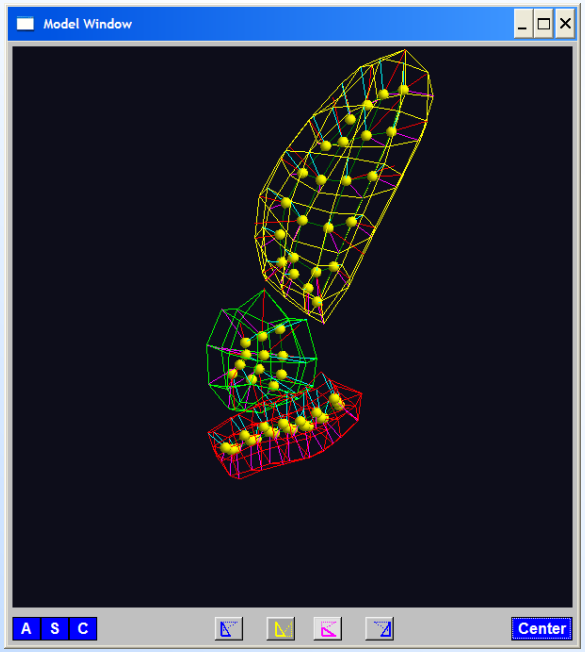




Shapes as Data Objects

Challenge: Data Lie in (Curved) Manifold





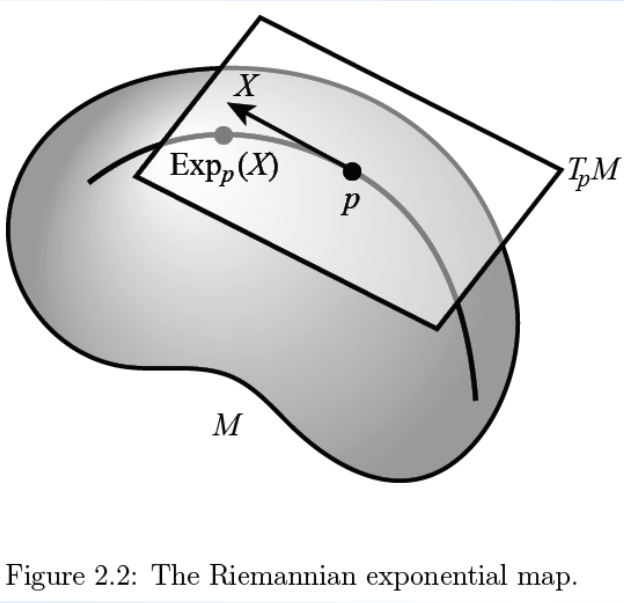


Figure 2.2: The Riemannian exponential map.

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Shapes as Data Objects

Challenge: Data Lie in (Curved) Manifold

{Tackle With Differential Geometry}

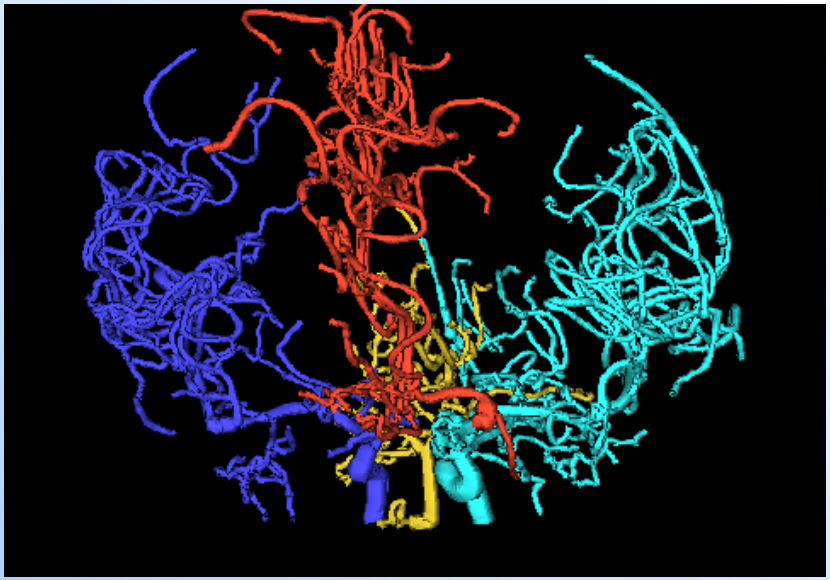
Important General Development:

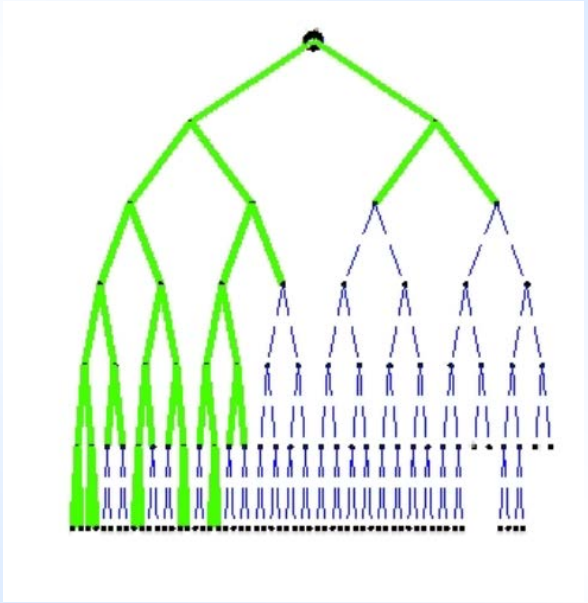
Backwards PCA

Trees as Data Objects

Challenge: More Complicated Data Space

Manifold Stratified Space





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Trees as Data Objects

Challenge: More Complicated Data Space

Manifold Stratified Space

Surprisingly (?!?) Useful Approach:

Topological Data Analysis

Persistent Homology

Advertisement

Short Course on OODA & TDA

International Biometrics Conference

Seoul July 2020

Moo K. Chung, U. Wisc.

Yuan Wang, U. S. C.

Carolina Breast Cancer Study

The Carolina Breast Cancer Study

Phase III: The Jeanne Hopkins Lucas Study

Thanks to: **Iain Carmichael** (Deep Learning, AJIVE)
Melissa Troester (Head, CBCS)
Joseph Geradts, Benjamin Calhoun (Pathology)
Katie Hoadley, Chuck Perou (Genomics)

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Carolina Breast Cancer Study

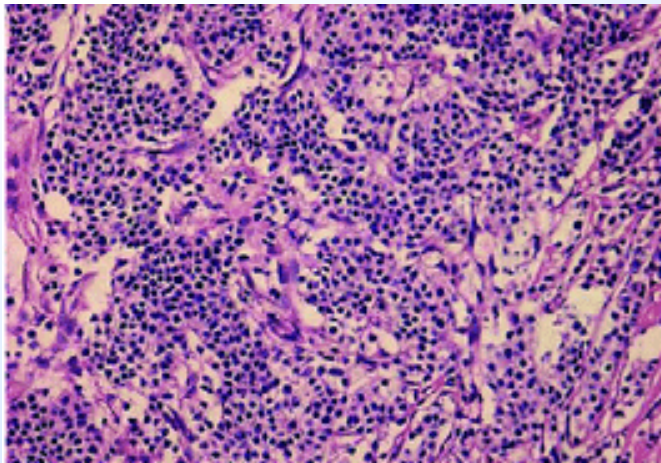
Clinical Diagnosis of Cancer:

Pathologist Views Tissue Under Microscope,

Tissue Stained with Hematoxylin & Eosin (H&E)

Thanks to BBC.CO.UK

and Reseachgate.net



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Carolina Breast Cancer Study

Analysis Goal:

Clinical Diagnostic Standard

Understand How Images & Genomics

Deep Insight & New Treatments

- Work Together
- Work Separately

Approach: JIVE

As of Jan. 2020: ~70 Drugs Approved for Breast Cancer Therapy

JIVE

Joint & Individual Variation Explained

(Angle Based)

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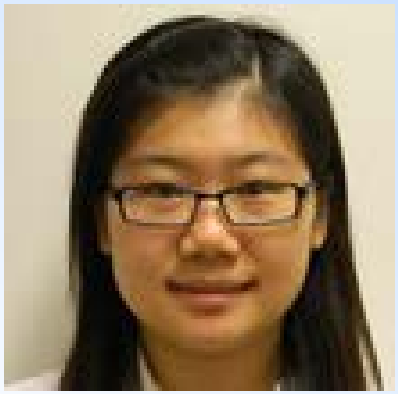
JIVE Collaborators

Eric Lock



Qing Feng

Andrew Nobel

Jan Hannig

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JIVE Data Structure

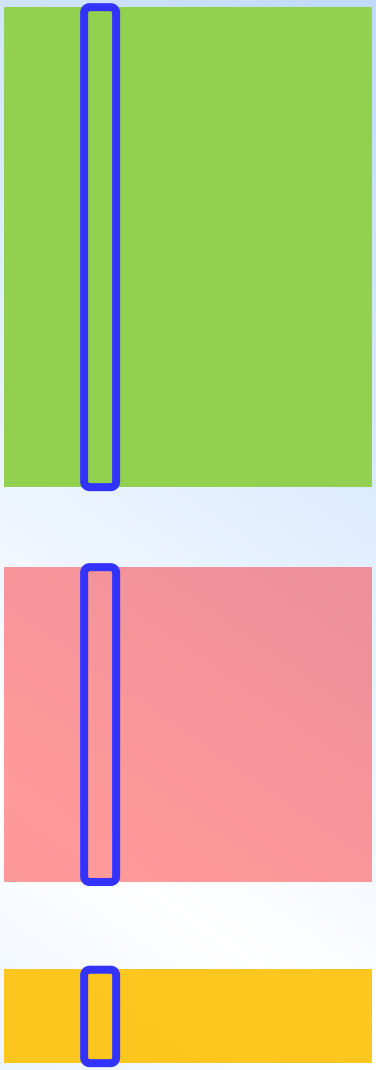
JIVE Organizational Model:

Multiple Matrices

(Data Types, i.e. “Blocks”)

With common

Columns as Data Objects



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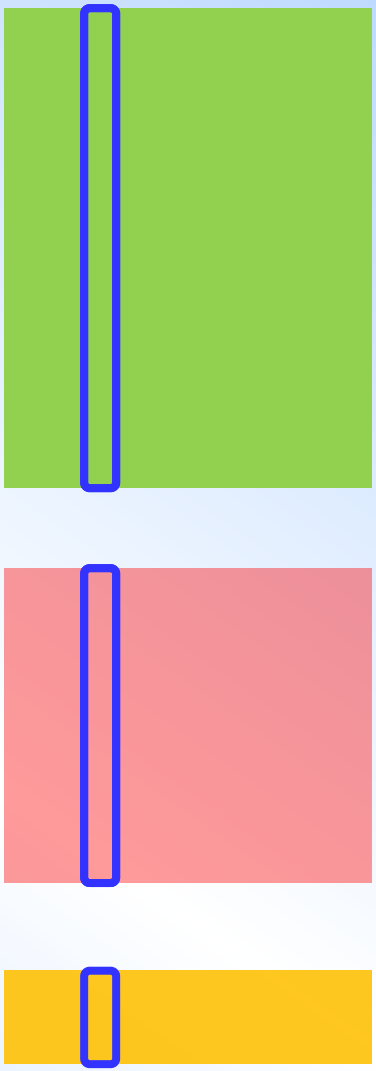
JIVE Analytic Goals

Explore & Quantify Variation

In spirit of PCA

(Principal Component Analysis)



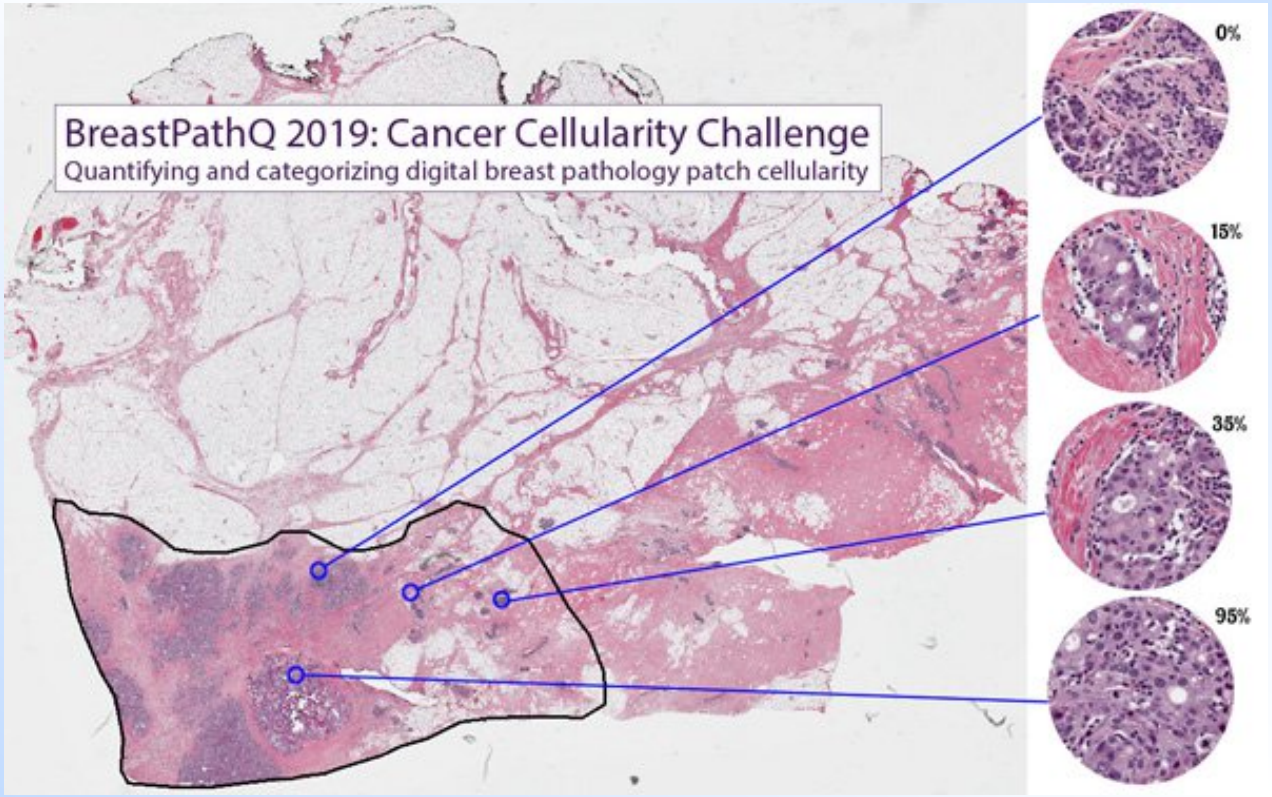
Carolina Breast Cancer Study

Tissue Micro Array Data:

Extract Small

(1mm diam.)

“Cores”

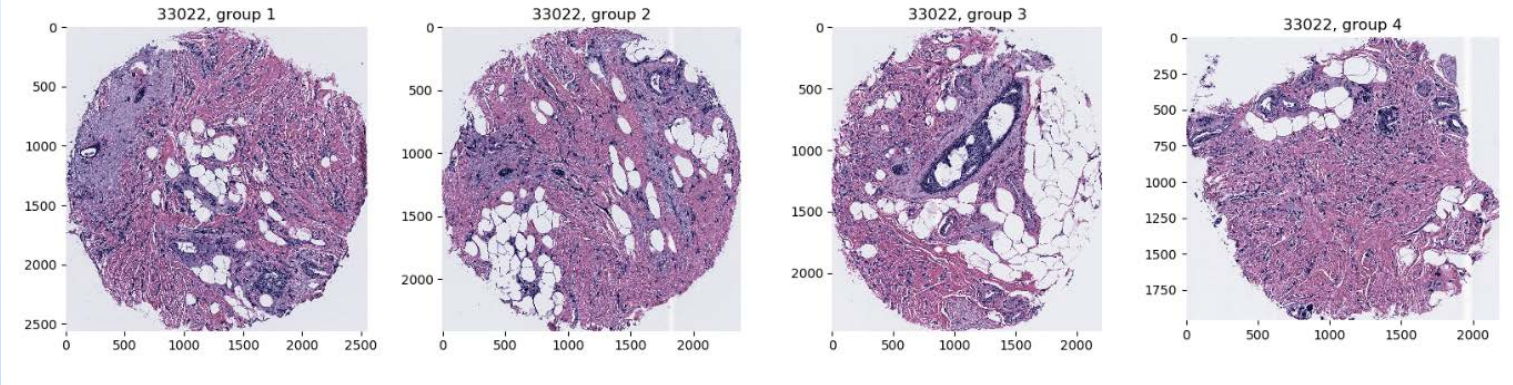


Thanks to SPIE.ORG

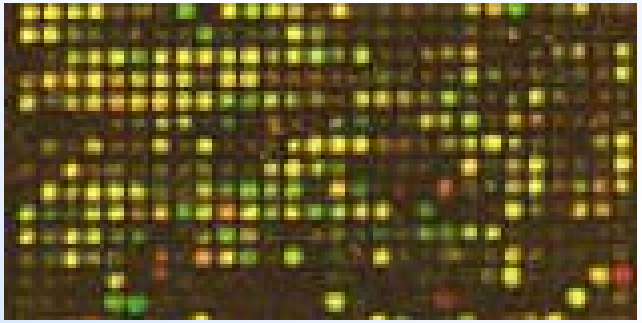
Carolina Breast Cancer Study

Experimental Design: $n = 1191$ people

For Each: 1 – 4 TMA Cores



PAM 50 Gene Expression:



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PAM 50 Gene Expression:

- Set of 50 Genes
- Measured mRNA Expression Level
- Good at Separating SubTypes
  - Basal
  - Her2
  - Luminal A
  - Luminal B

Early Technology, More Recent
RNAseq → 10,000s Genes

Perou Discovery:
No Benefit From
Chemo-Therapy

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Carolina Breast Cancer Study

Deep Learning Image Representation

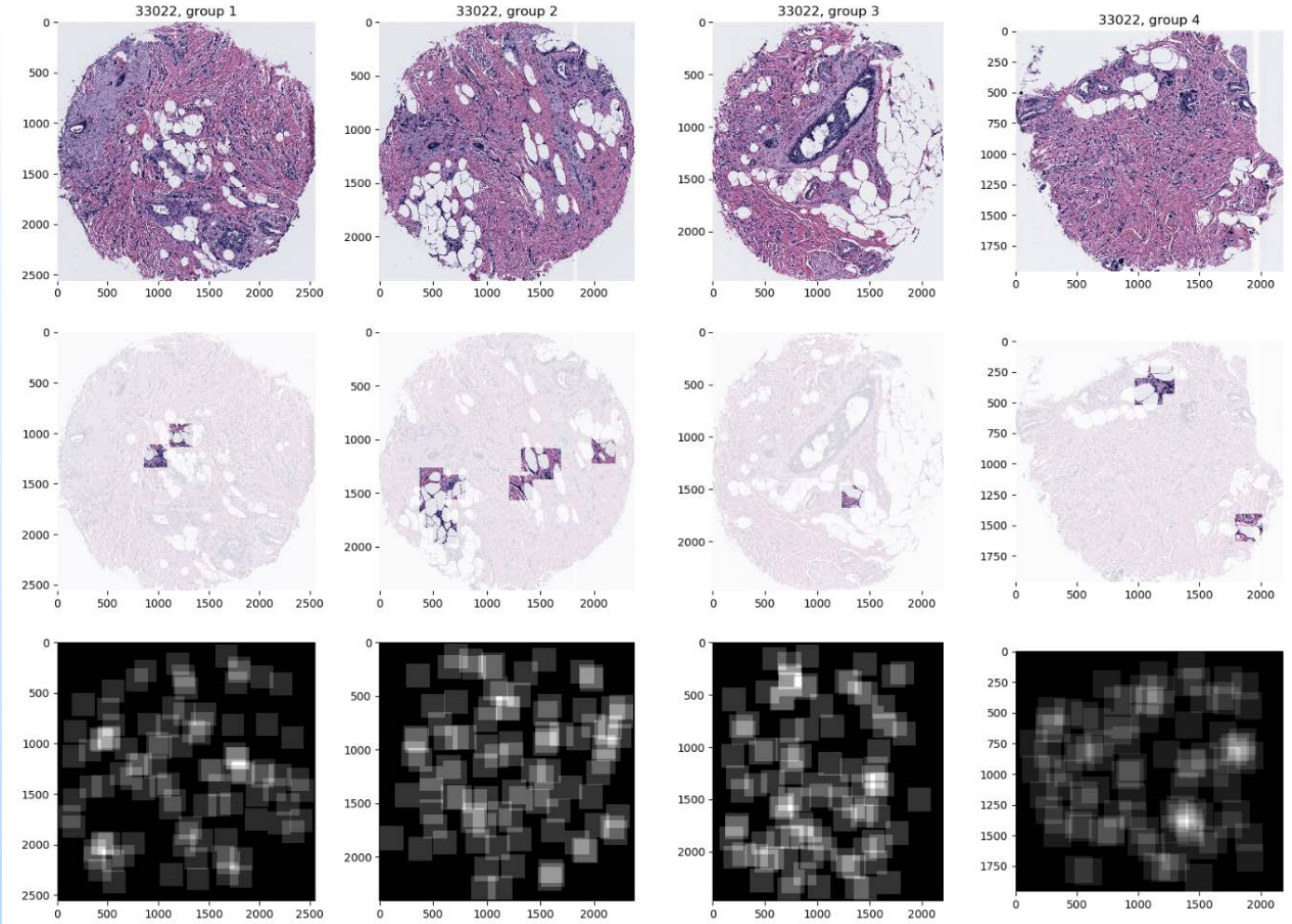
Each Core:

Randomly

Select 100

224×224

Patches



Carolina Breast Cancer Study

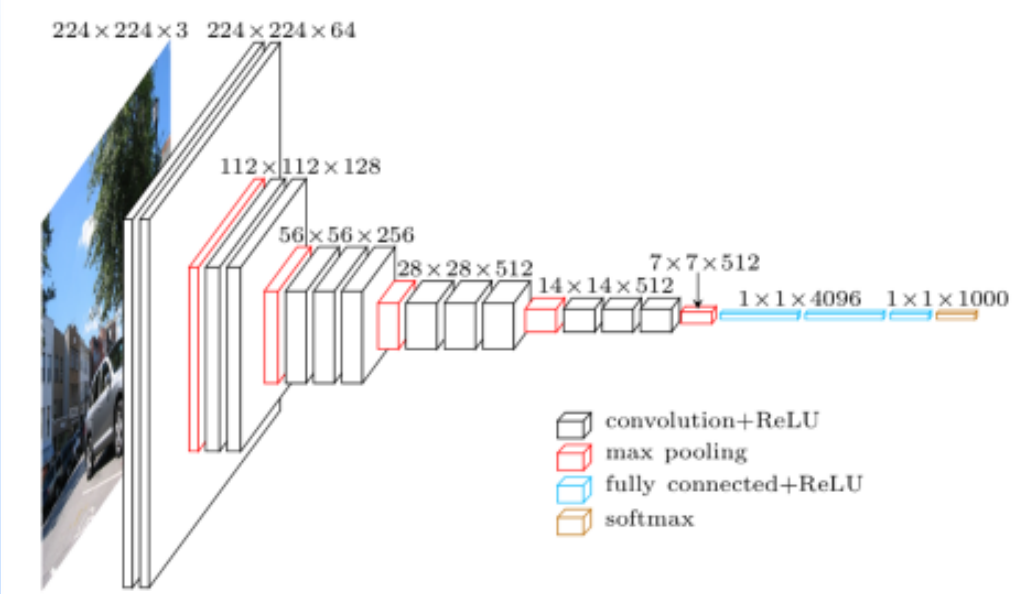
Deep Learning Image Representation

Reduce Each Patch to 512 Features

Using Transfer Learning From VGG16:

(Trained on Many

Natural Images)



Thanks to pyimagesearch.com

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Deep Learning Image Representation

For Each Core:

Aggregate Patches by Averaging

(Damps Out “Location” Information)

Then Average Cores For Each Person

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Carolina Breast C

JIVE: Common Nor

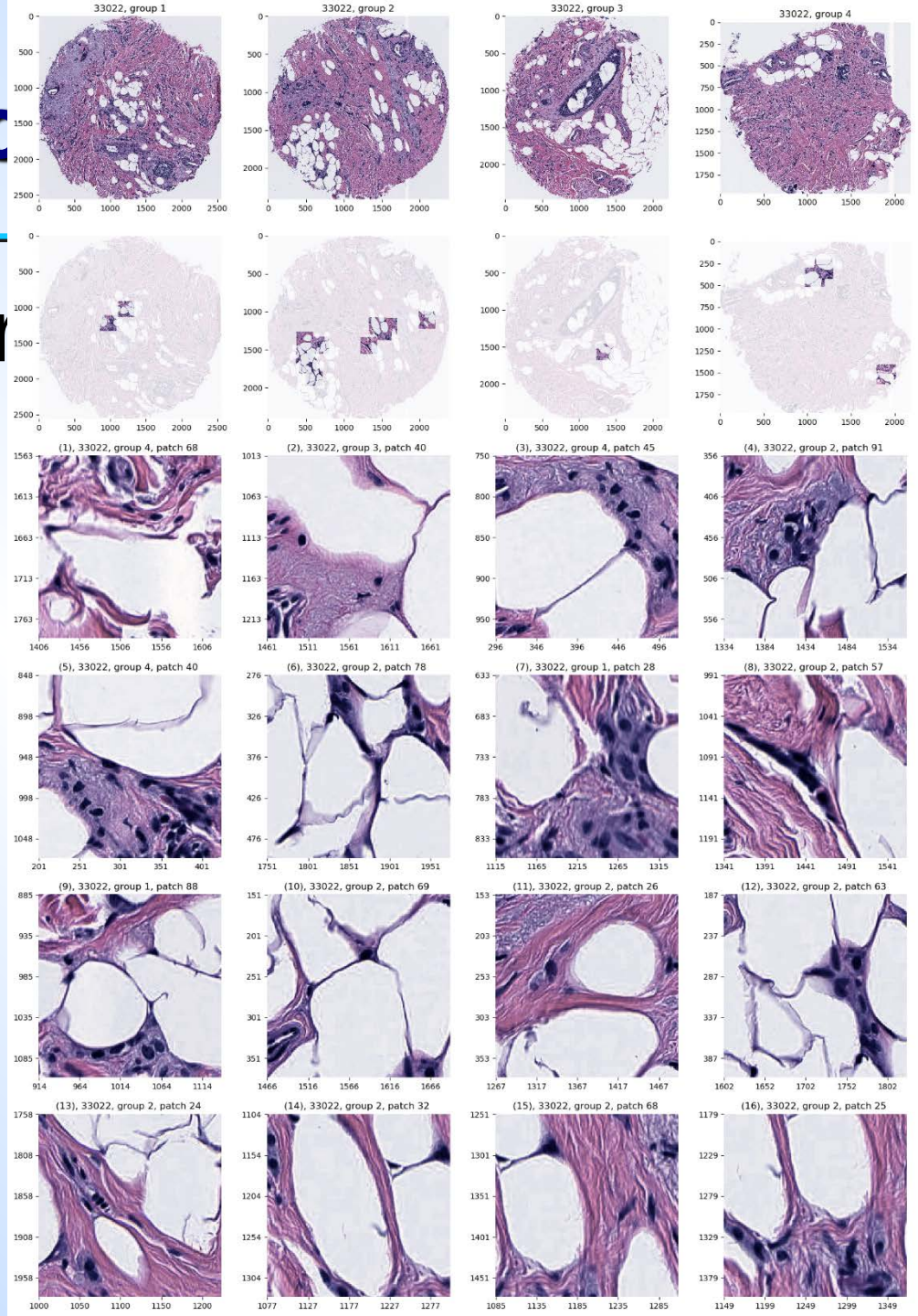
Look at Extremes

Negative End

Top Person

Top 16 Patches

Fat Cells & Stroma



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Carolina Breast C

JIVE: Common Nor

Look at Extremes

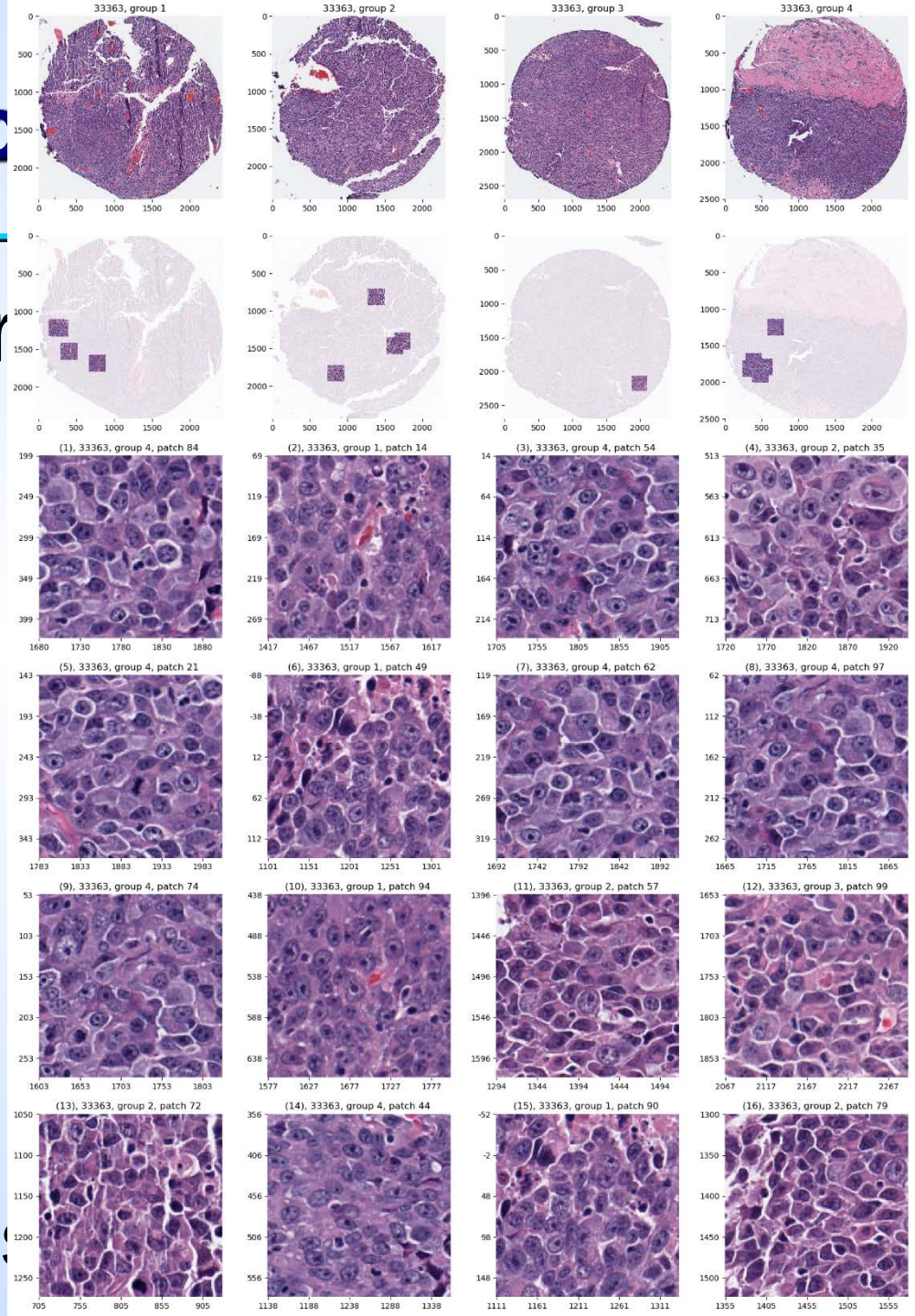
Positive End

Top Person

Top 16 Patches

Highly “Cellular”

Markedly Atypical Cells



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JIVE: Gene Expression

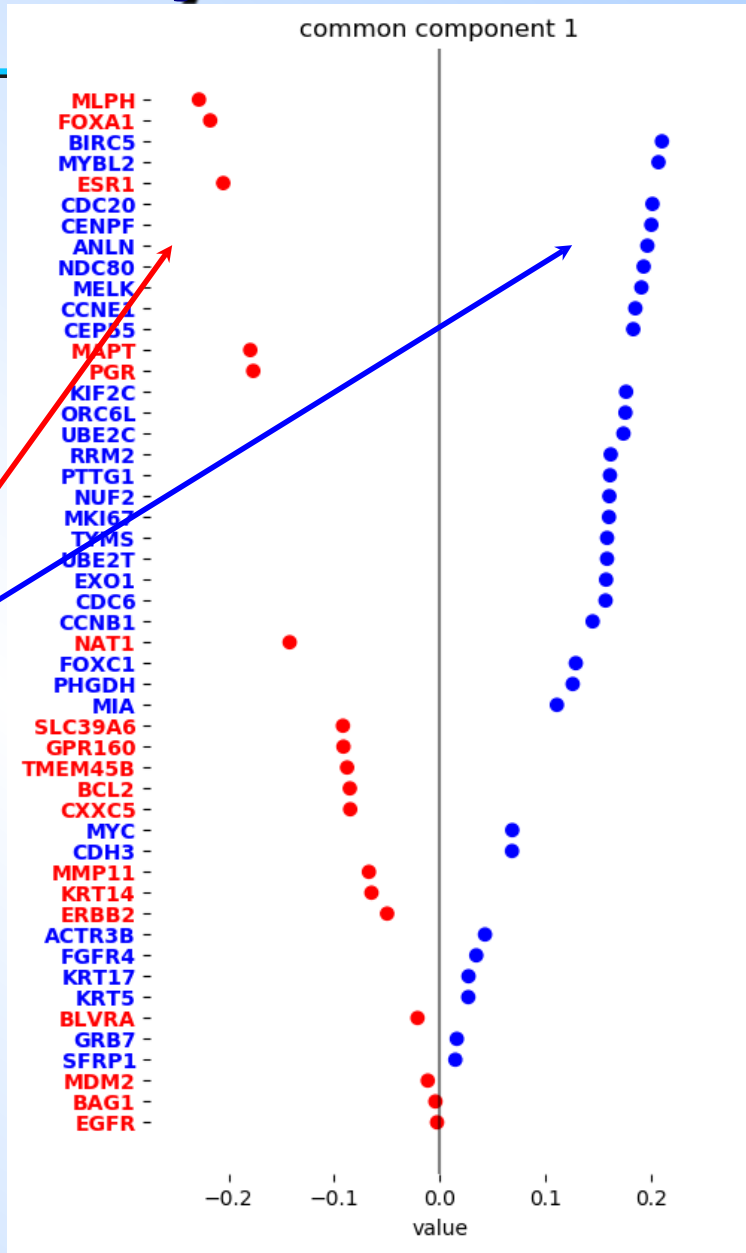
Common Normalized

Loadings 1

"High Proliferation" Genes

"Low Prolif." – Lum A Genes

Very Consistent w/ Image



UNC, Stat & OR

Carolina Breast C

JIVE: Common Nor

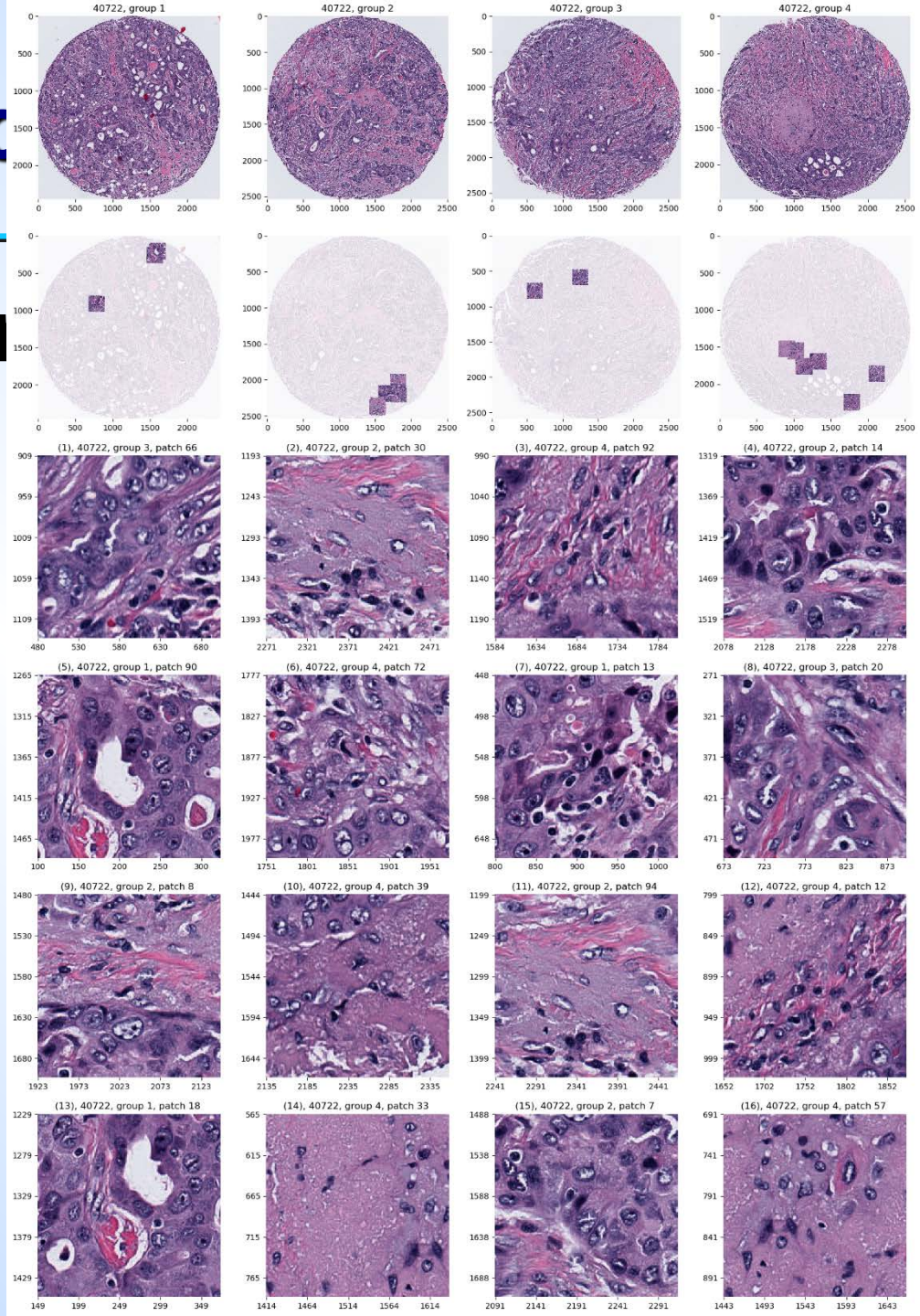
Look at Extremes

Negative, Top

Top 16 Patches

High Nuclear Grade

Atypical Cells



UNC, Stat & OR

Carolina Breast C

JIVE: Common Nor

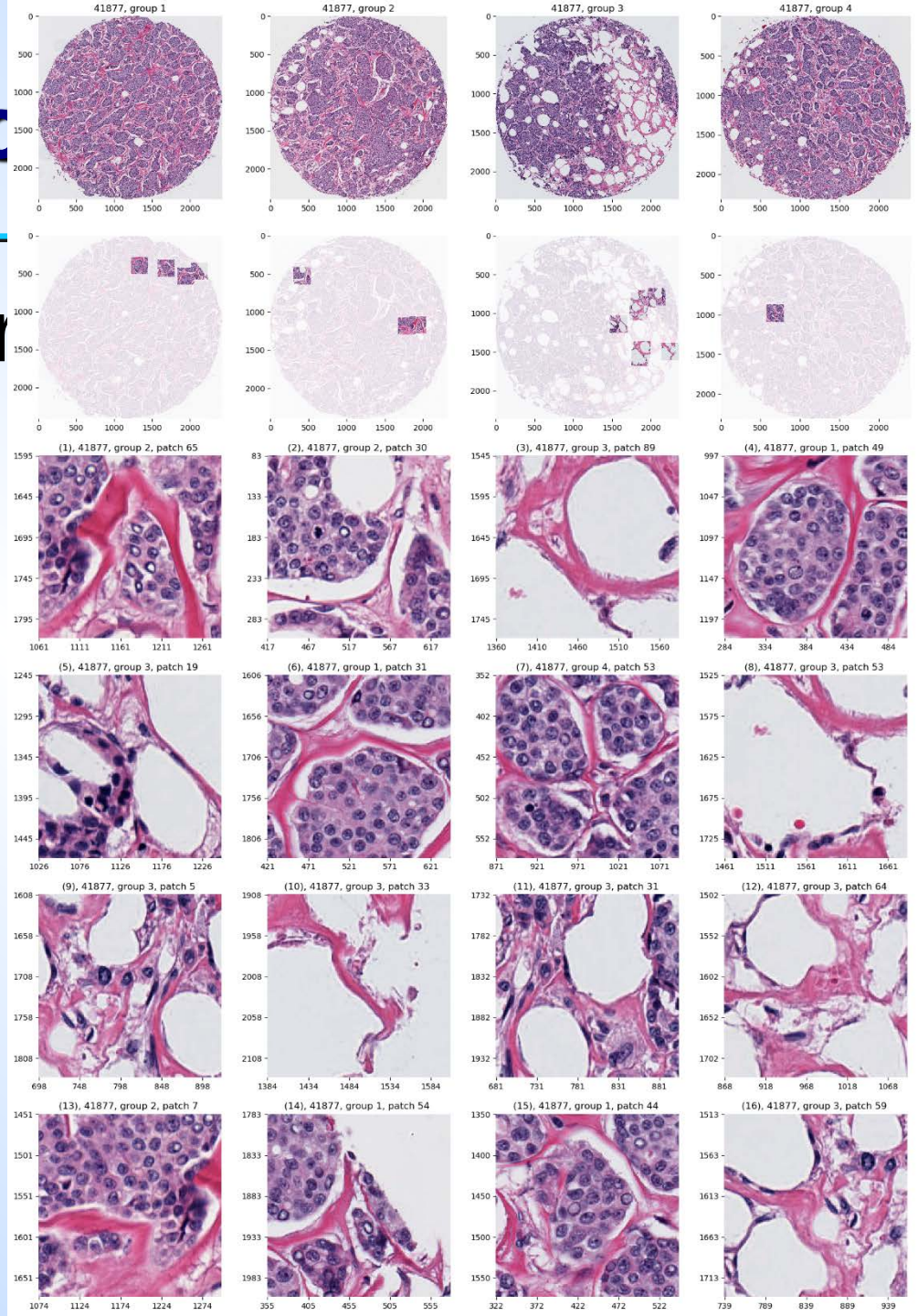
Look at Extremes

Positive, Top

Top 16 Patches

Lower Nuclear Grade

Stroma, Sclerosis



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Carolina Breast Canc

JIVE: Gene Expression

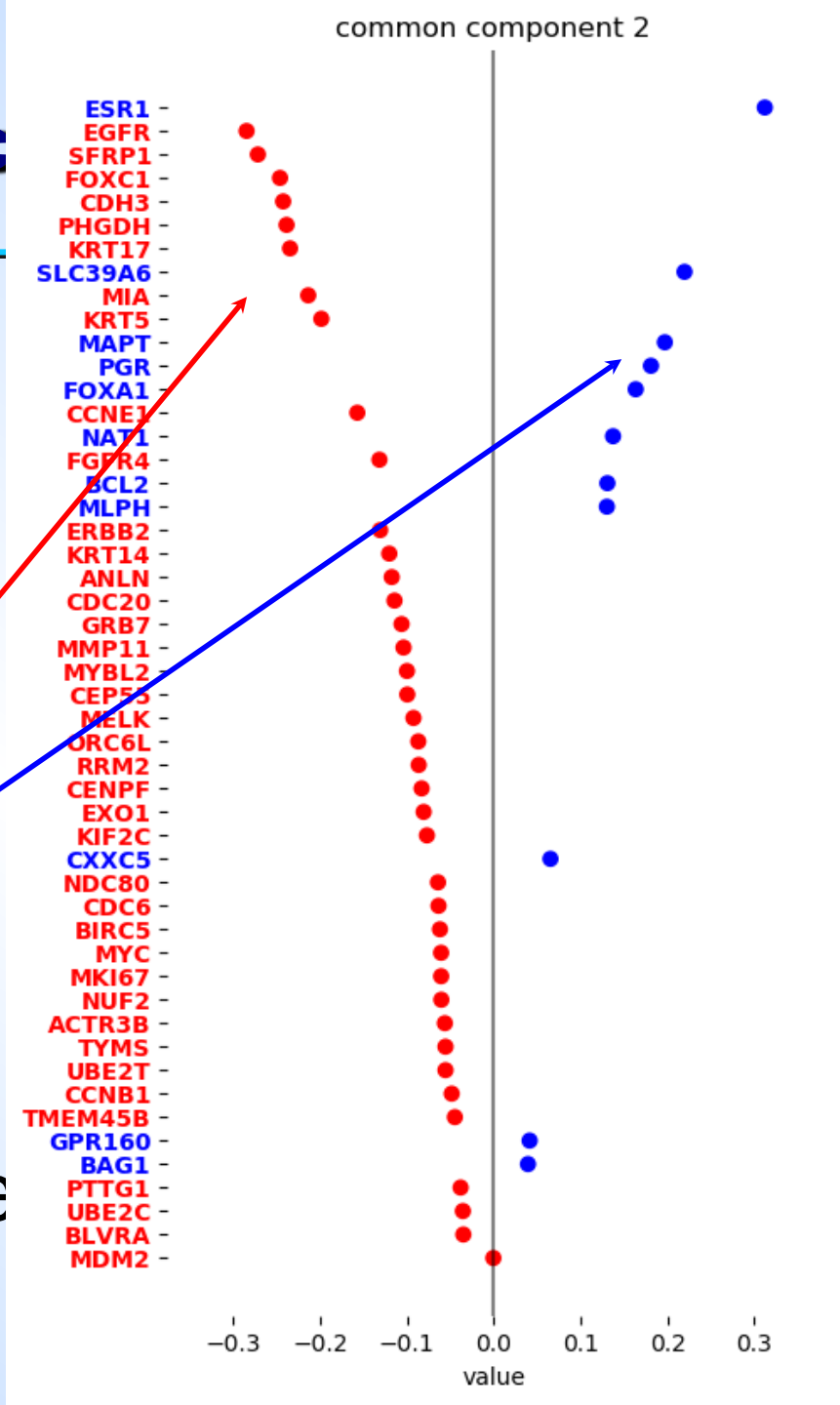
Common Normalized

Loadings 2

Luminal Subtype Genes

Basal Subtype Genes

Very Consistent w/ Image



UNC, Stat & OR

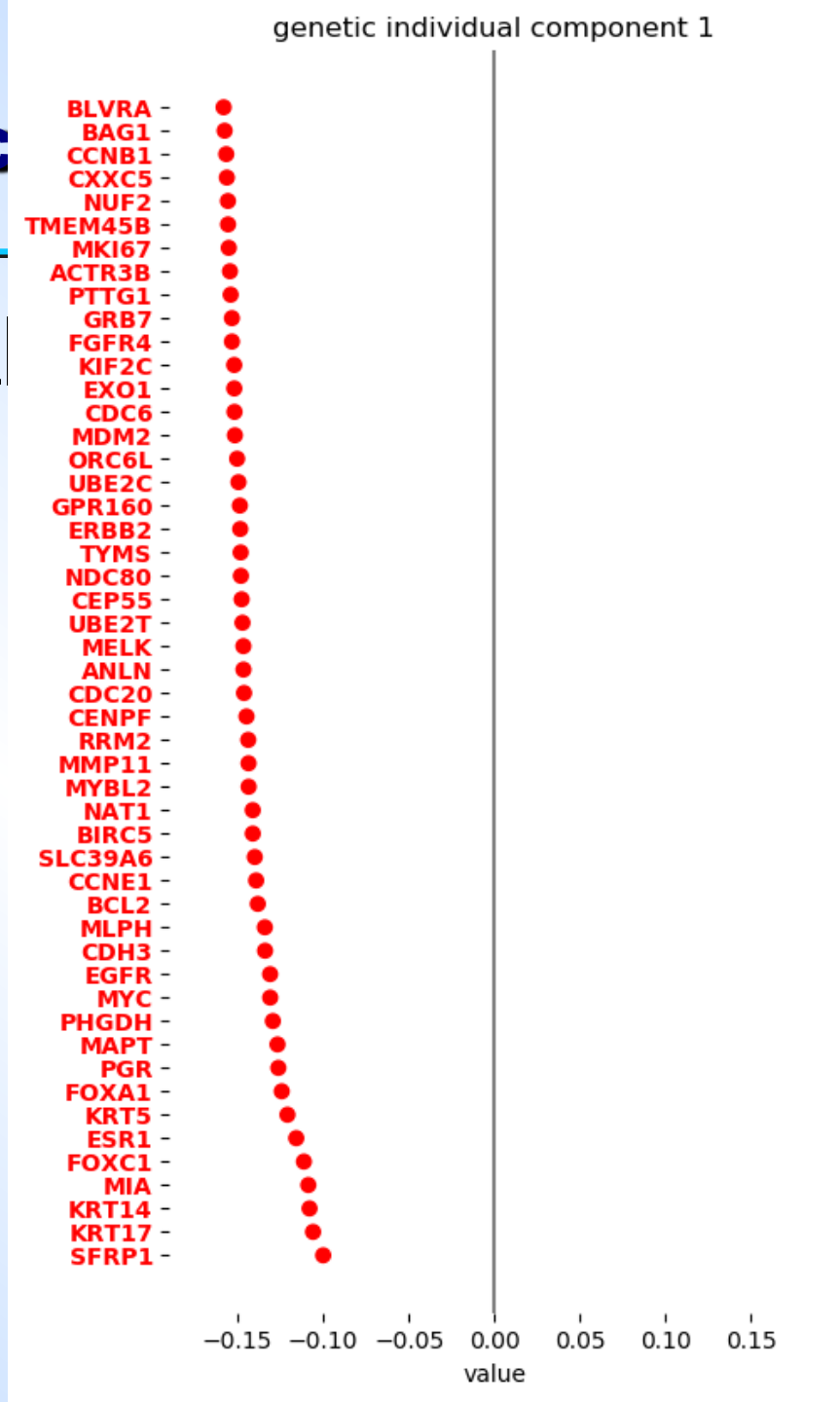
Carolina Breast Canc

JIVE, Genes, Individua

Overall Up & Down

Together

Not Subtype Related!



UNC, Stat & OR

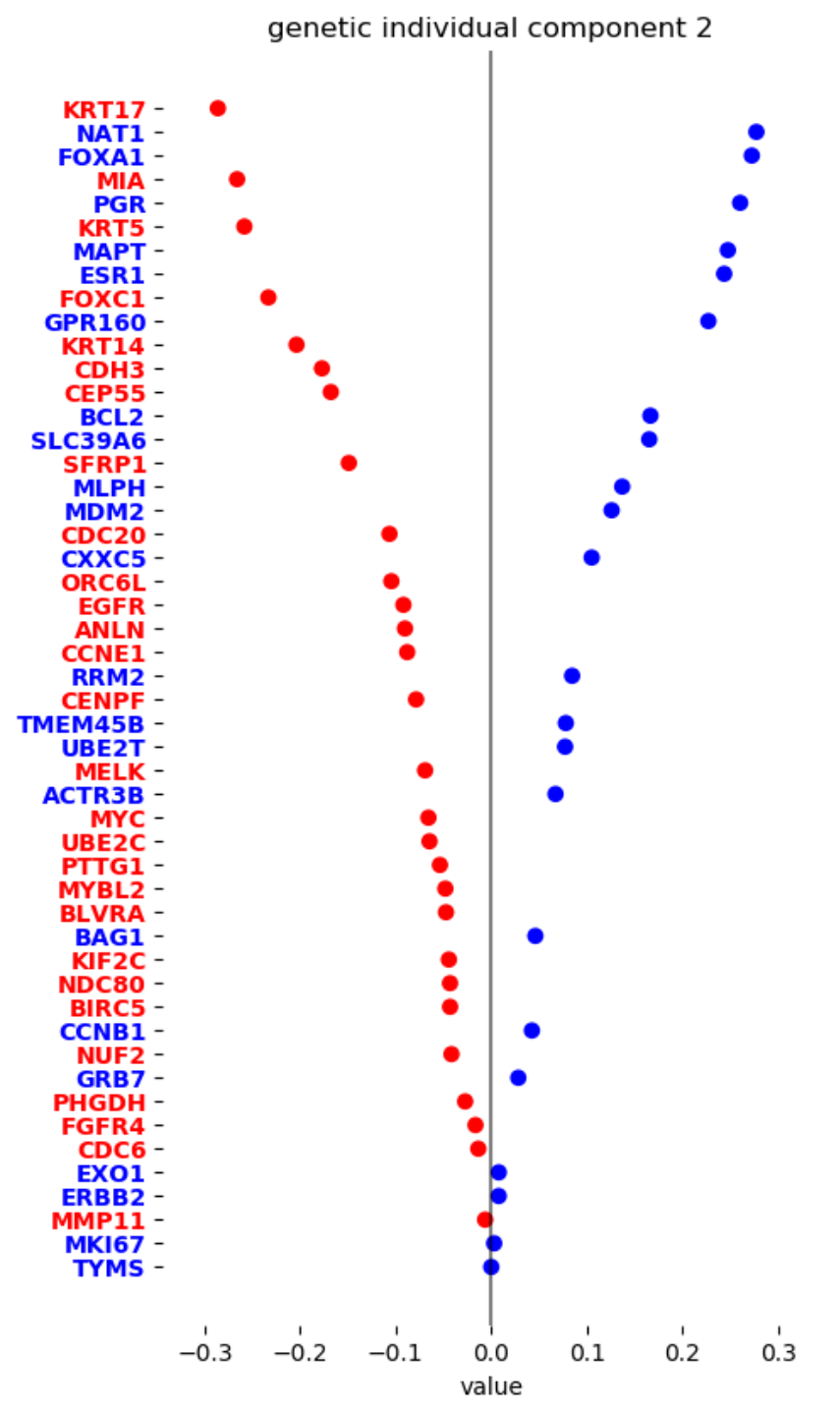
Carolina Breast Canc

JIVE, Genes, Individua

Luminal vs. Basal

“Contrast”?

“Unbalanced Types”?



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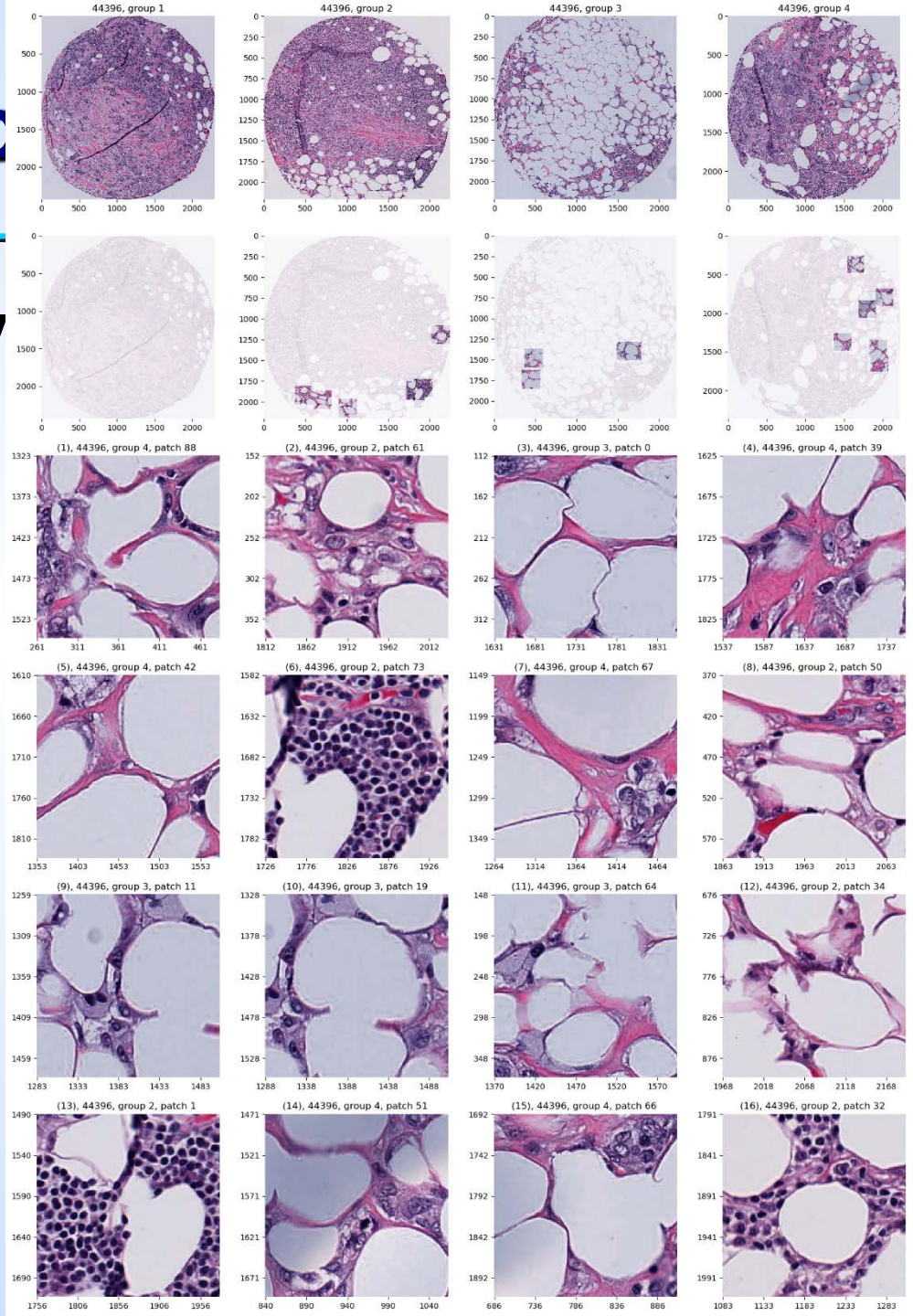
Carolina Breast C

JIVE, Images, Indiv

Negative

Mostly Fat Cells

Few Nuclei



UNC, Stat & OR

Carolina Breast C

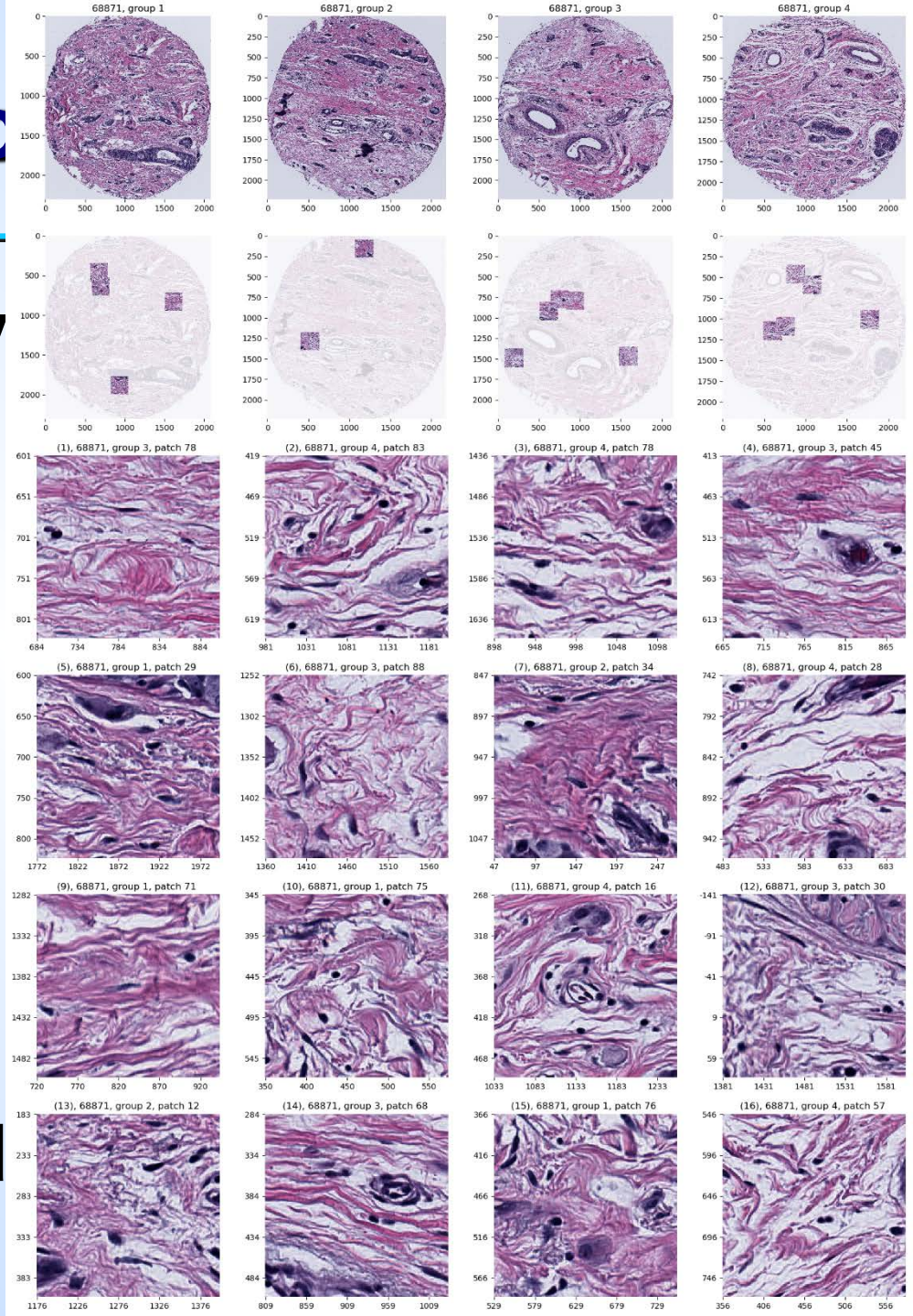
JIVE, Images, Indiv

Positive

Reactive Stroma,

Few Nuclei

Little Gene Connected



UNC, Stat & OR

Carolina Breast C

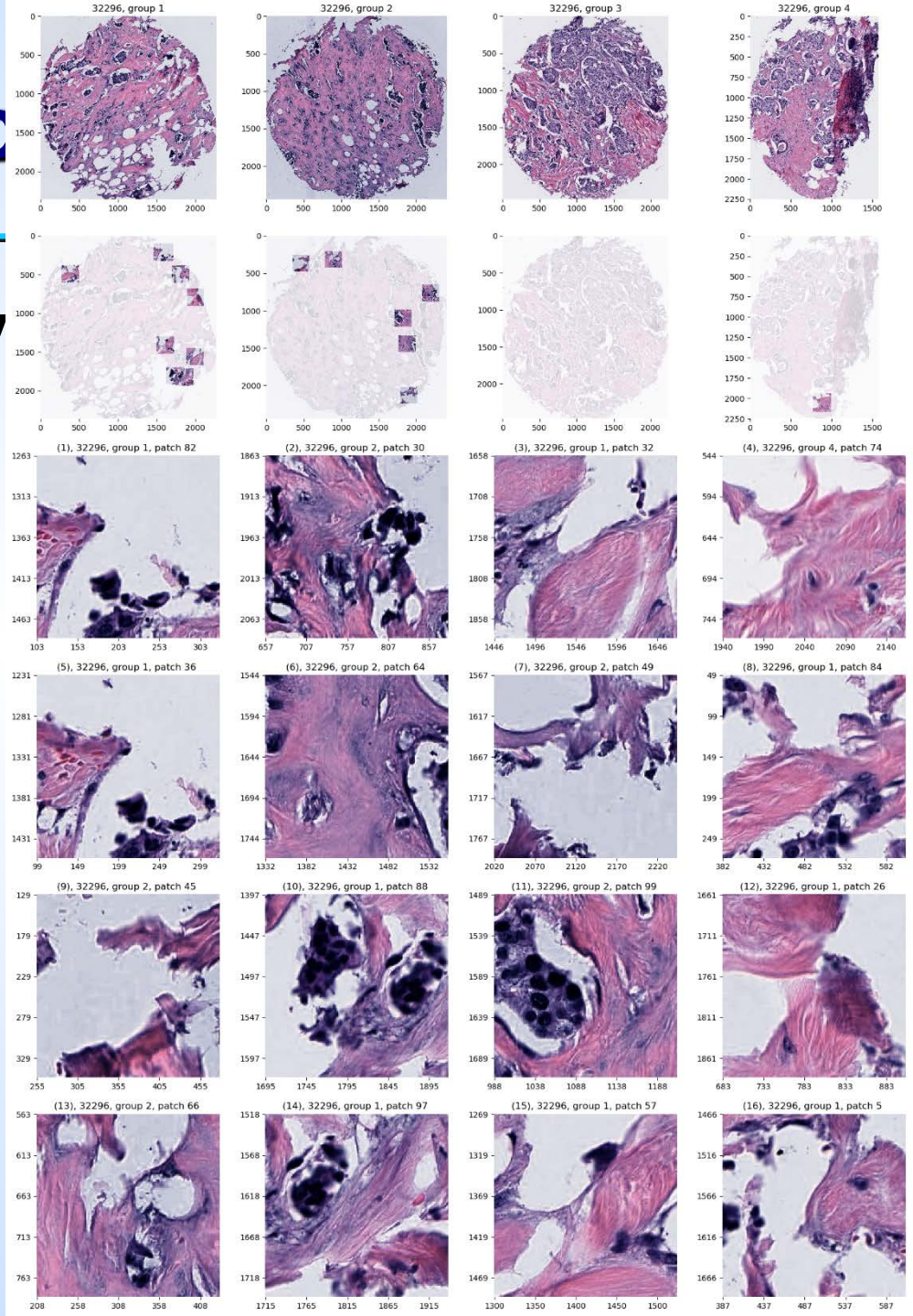
JIVE, Images, Indiv

Negative

Mucinous & Micro-

Papillary Carcinoma

Not PAM50 Related



UNC, Stat & OR

Carolina Breast C

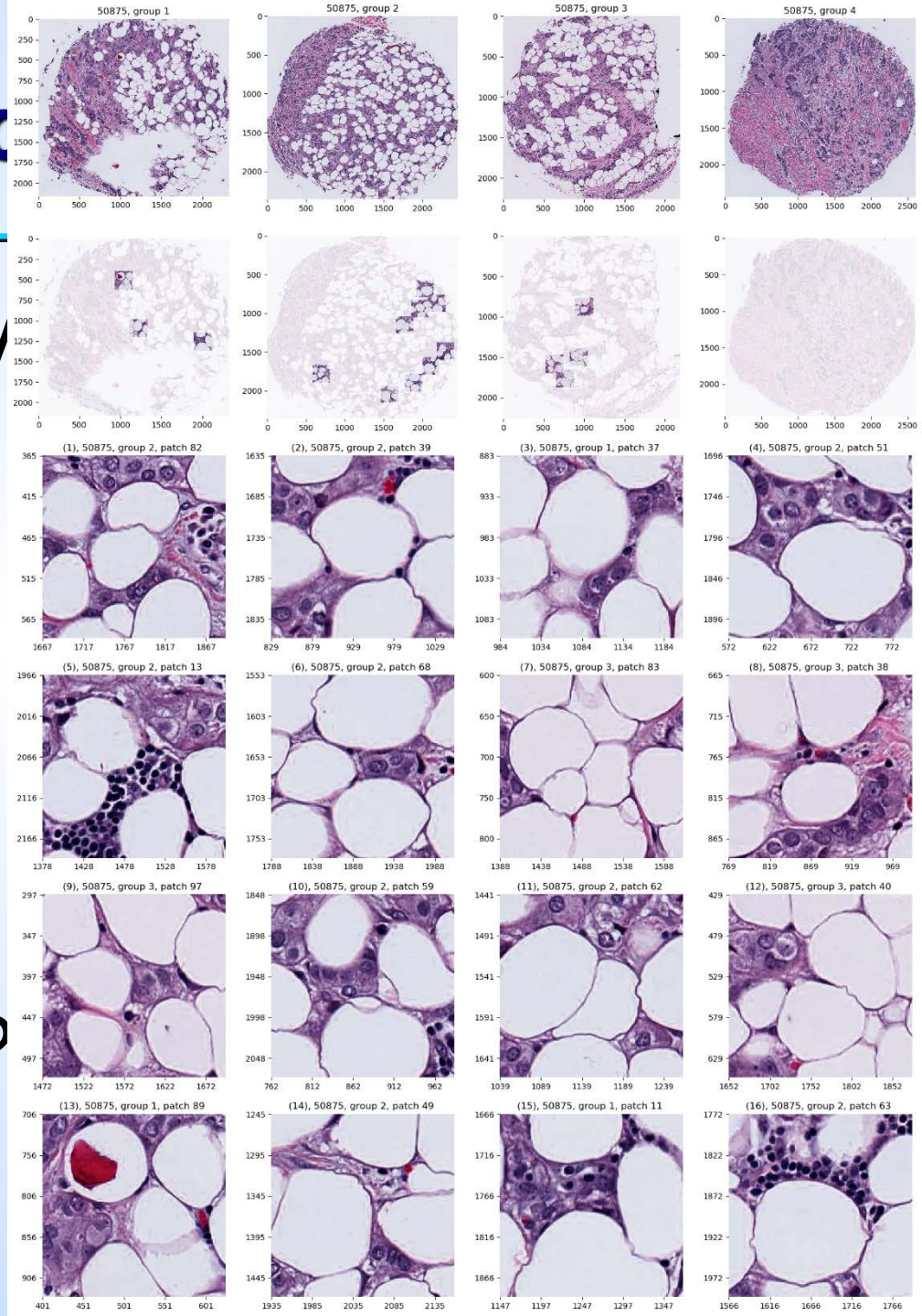
JIVE, Images, Indiv

Positive

Fat Cells

Common Endpoint?

“Center”?



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Next Generation Data Integration

Data Integration Via Subspace Analysis

(DIVAS)

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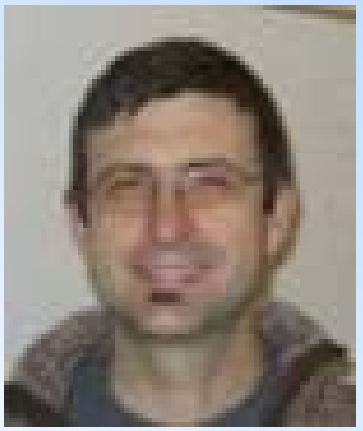
DIVAS / JIVE Collaborators

Jan Hannig



Meilei Jiang

Xi Yang

Iain Carmichael

Jack Prothero

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DIVAS Improves JIVE

1. Partially Shared Blocks

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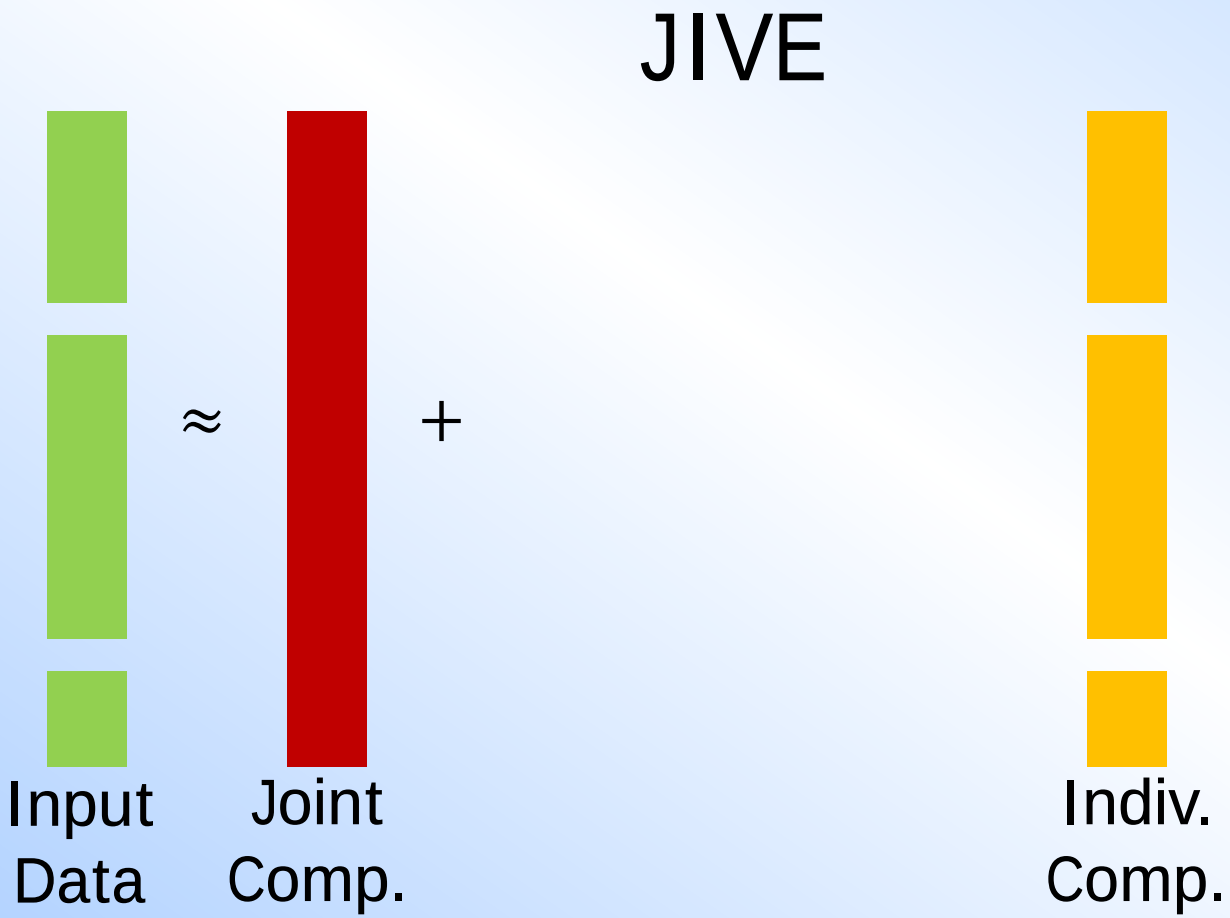
DIVAS Improves JIVE

1. Partially Shared Blocks



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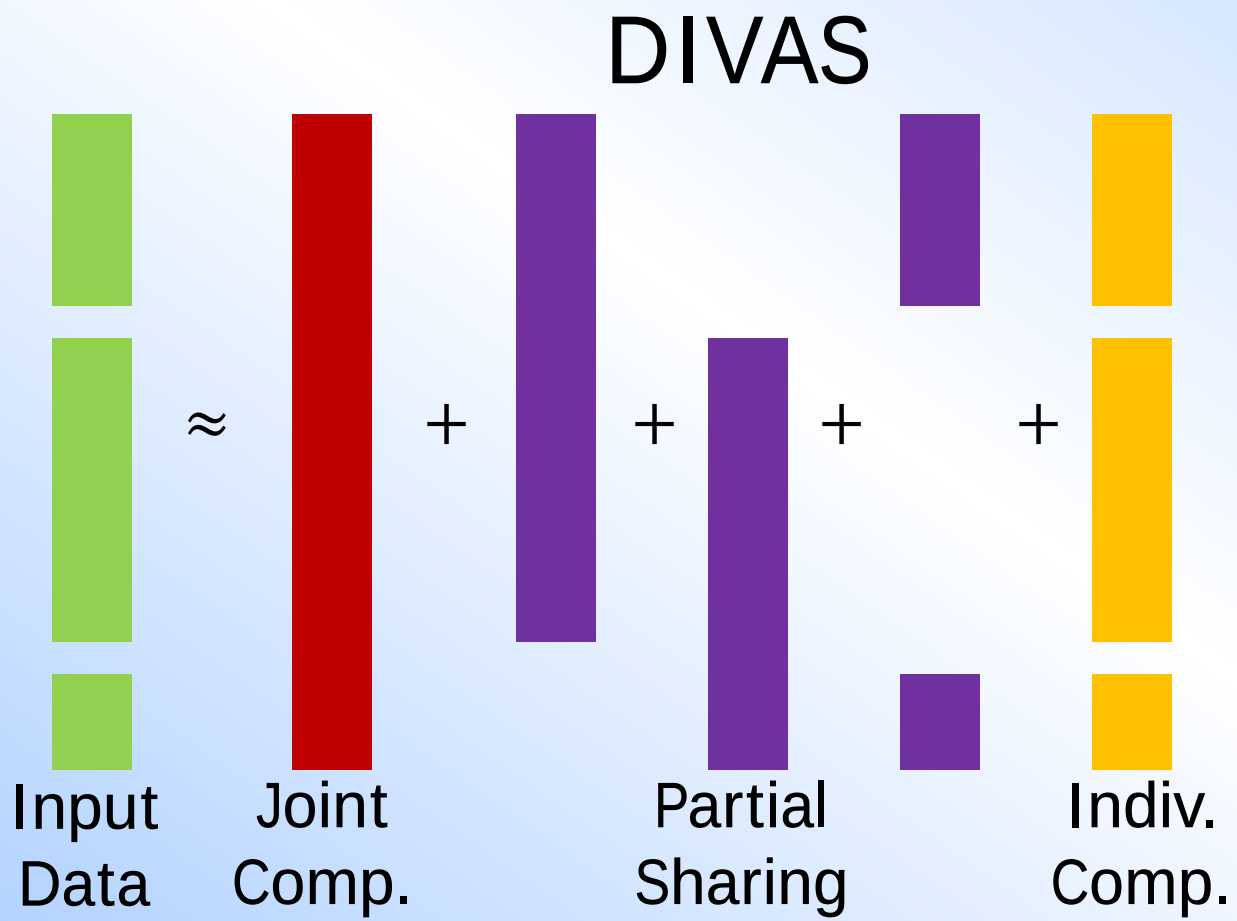
DIVAS Improves JIVE

1. Partially Shared Blocks



DIVAS Motivation

The Cancer Genome Atlas

Multiple Blocks

People <u>Common</u> Across Blocks

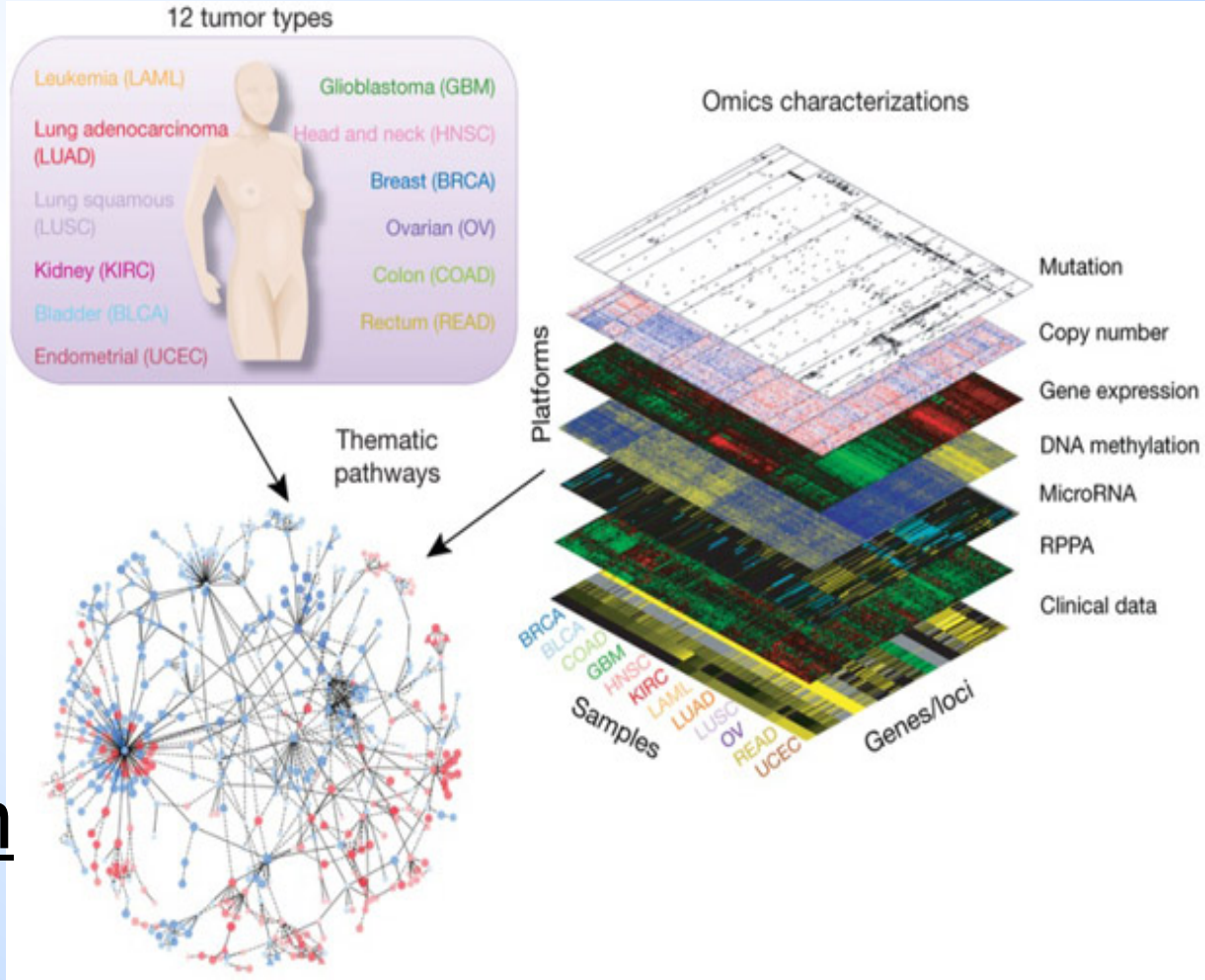


Figure : The Cancer Genome Atlas Research Network, Weinstein, J.N., Collisson, E.A., Mills, G.B., Shaw, K.M., Ozenberger, B.A., Ellrott, K., Shmulevich, I., Sander, C., and Stuart, J.M. (2013)
The Cancer Genome Atlas Pan-Cancer analysis project.

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DIVAS on TCGA Data

Breast Cancer

- Gene Expression (GE) [16615 x 616]
- Copy Number (CN) [24174 x 616]
- Protein Exp. (RPPA) [187 x 616]
- Mutation Status (MU) [18256 x 616]

DIVAS on TCGA Data

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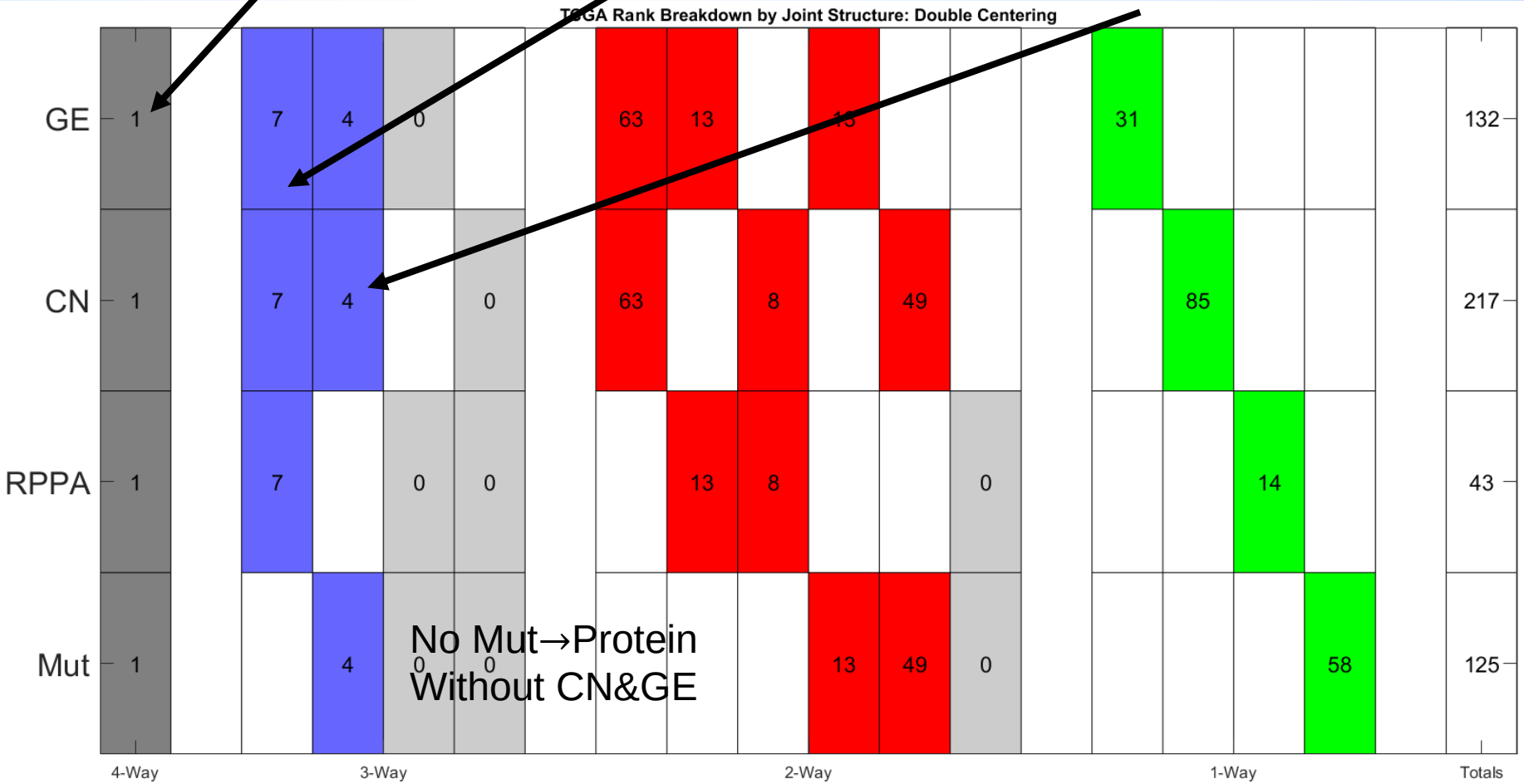
Single 4-way mode, as in AJIVE Analysis

CN→GE→Protein Common

Statistical Significance Summary

Mut→CN→GE Sensible



DIVAS on TCGA Data

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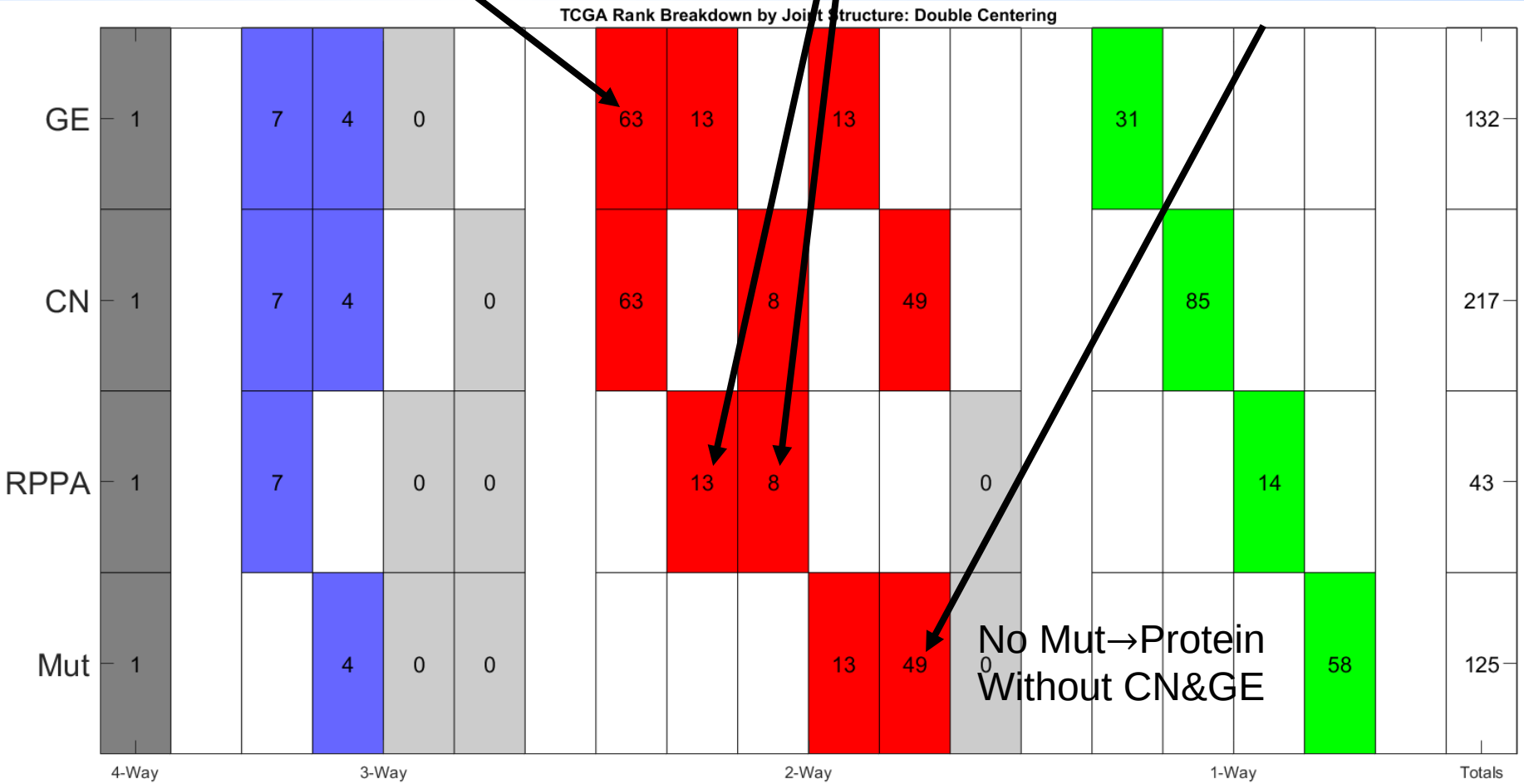
Major CN→GE Variation

GE or CN→ Proteins

Statistical Significance Summary

Lots of Mut&CN Variation



Carry Away Concept

OODA is more than a “framework”

It Provides a Focal Point

Highlights Pivotal Choices:

What should be the Data Objects?

How should they be Represented?