BGGN 213

Unsupervised Learning II

Lecture 10

Barry Grant

UC San Diego

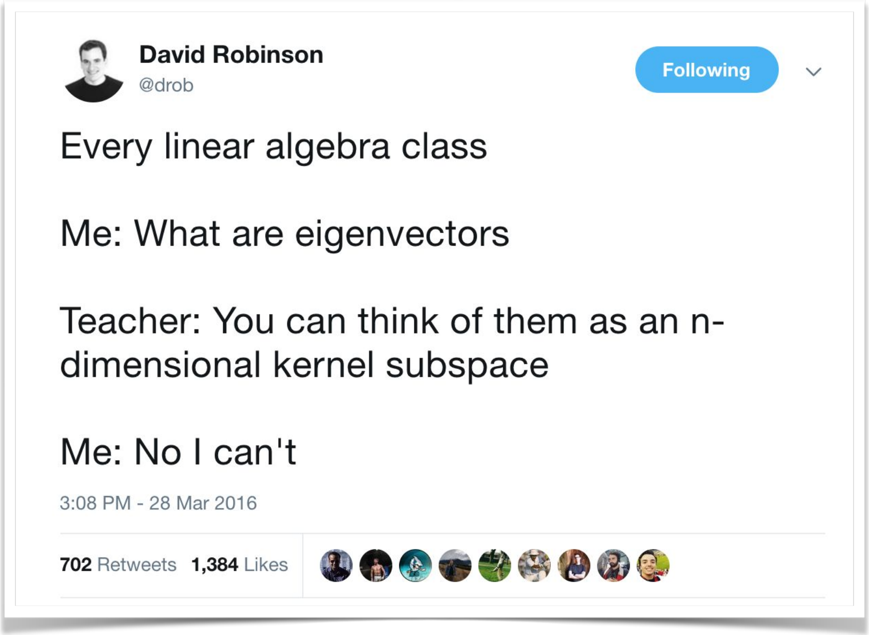
http://thegrantlab.org/bggn213

Recap of Lecture 8

- Introduction to machine learning
  - Unsupervised, supervised and reinforcement learning
- Clustering
  - K-means clustering
  - Hierarchical clustering
- Dimensionality reduction, visualization and 'structure' analysis
  - Principal Component Analysis (PCA)

[Muddy Point Feedback Link]

A long time ago in a galaxy far, far away....



David Robinson
@drob

Every linear algebra class

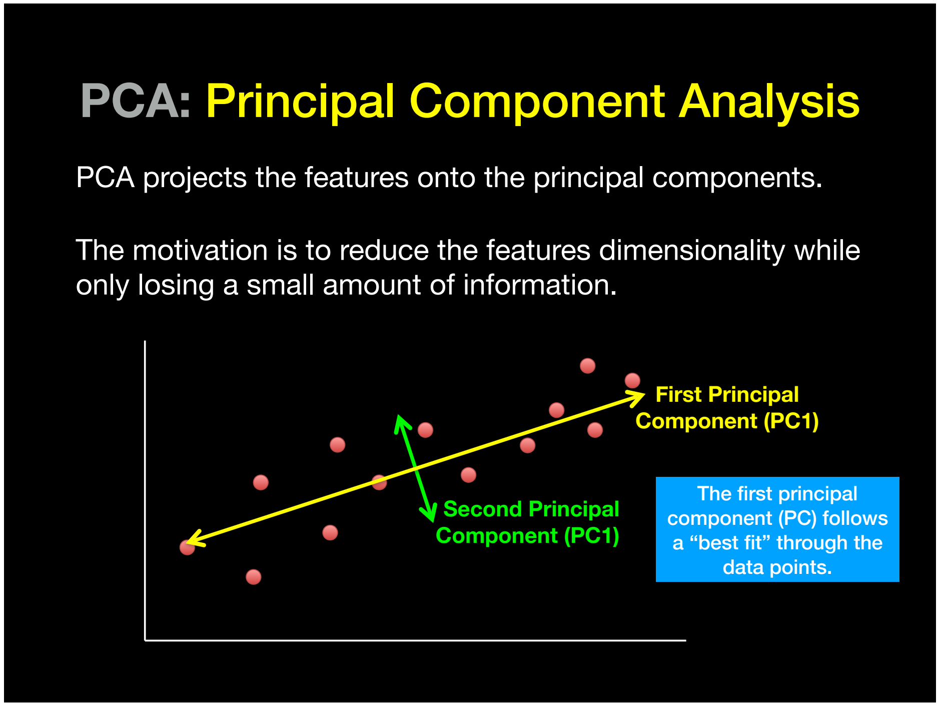
Me: What are eigenvectors

Teacher: You can think of them as an n-dimensional kernel subspace

Me: No I can't

3:08 PM - 28 Mar 2016

702 Retweets 1,384 Likes



PCA: Principal Component Analysis

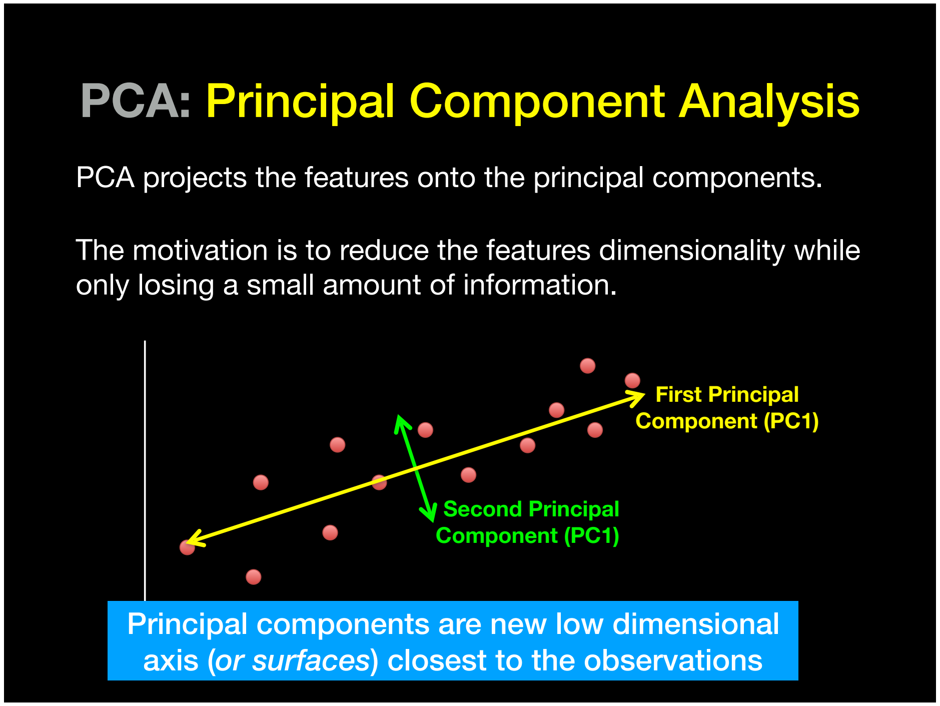
PCA projects the features onto the principal components.

The motivation is to reduce the features dimensionality while only losing a small amount of information.

First Principal Component (PC1)

Second Principal Component (PC1)

The first principal component (PC) follows a “best fit” through the data points.



PCA: Principal Component Analysis

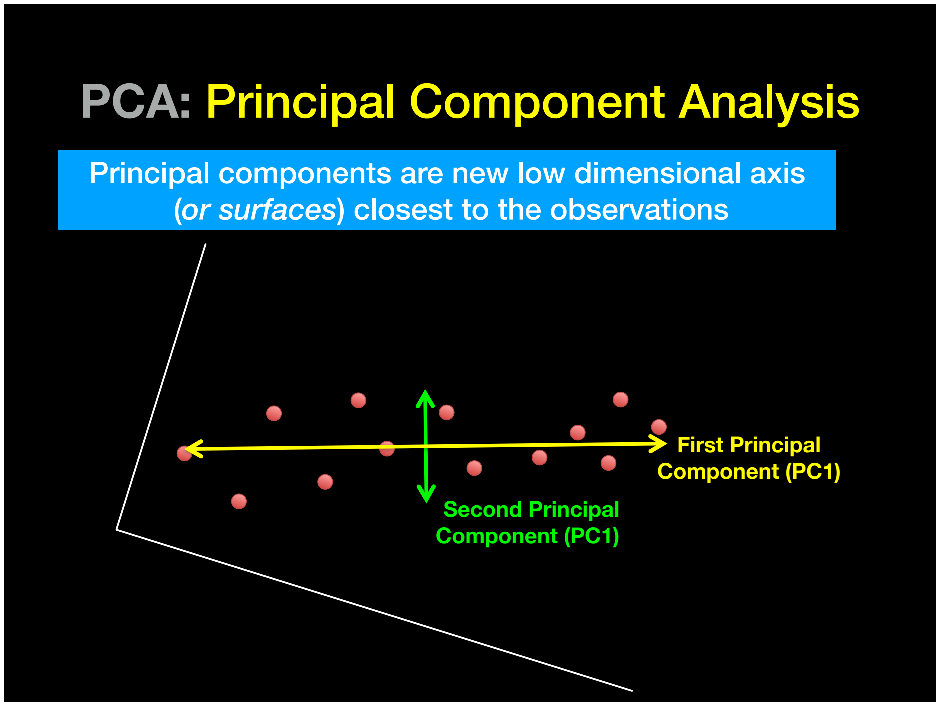
PCA projects the features onto the principal components.

The motivation is to reduce the features dimensionality while only losing a small amount of information.

First Principal Component (PC1)

Second Principal Component (PC1)

Principal components are new low dimensional axis (*or surfaces*) closest to the observations

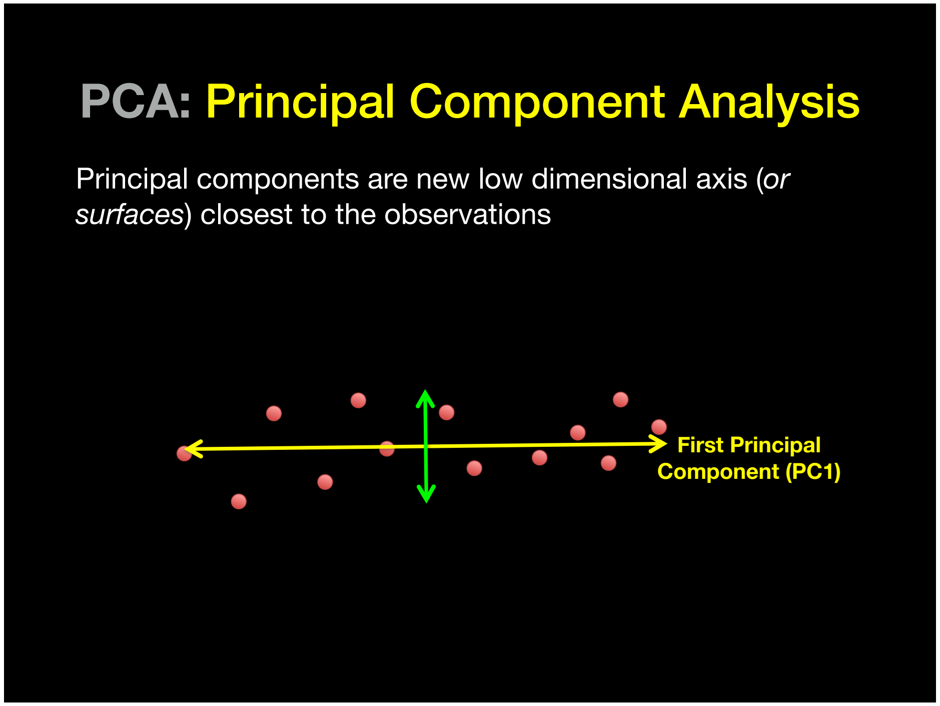


PCA: Principal Component Analysis

Principal components are new low dimensional axis (*or surfaces*) closest to the observations

First Principal Component (PC1)

Second Principal Component (PC1)



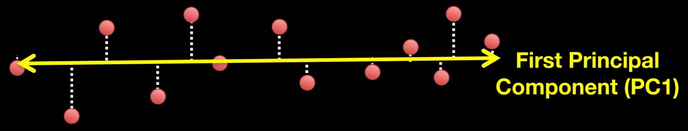
PCA: Principal Component Analysis

Principal components are new low dimensional axis (*or surfaces*) closest to the observations

First Principal Component (PC1)

PCA: Principal Component Analysis

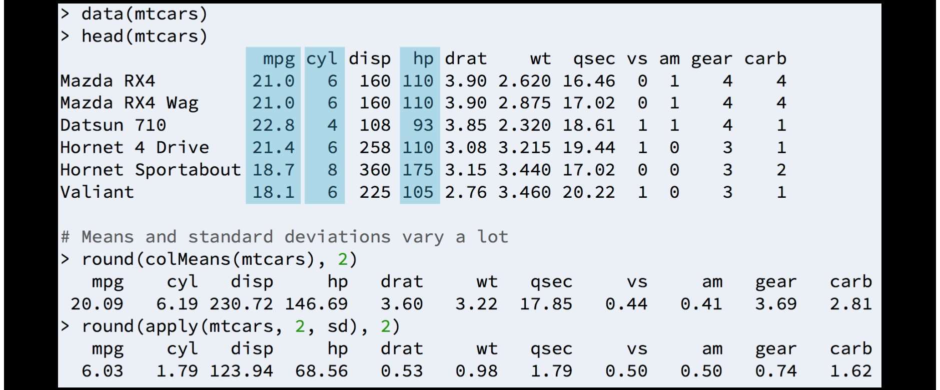
The data have maximum variance along PC1 (then PC2 etc.) which makes the first few PCs useful for visualizing our data and as a basis for further analysis



Recap: PCA objectives

- To reduce dimensionality
- To visualize multidimensional data
- To choose the most useful variables (features)
- To identify groupings of objects (e.g. genes/samples)
- To identify outliers

Practical PCA issue: Scaling



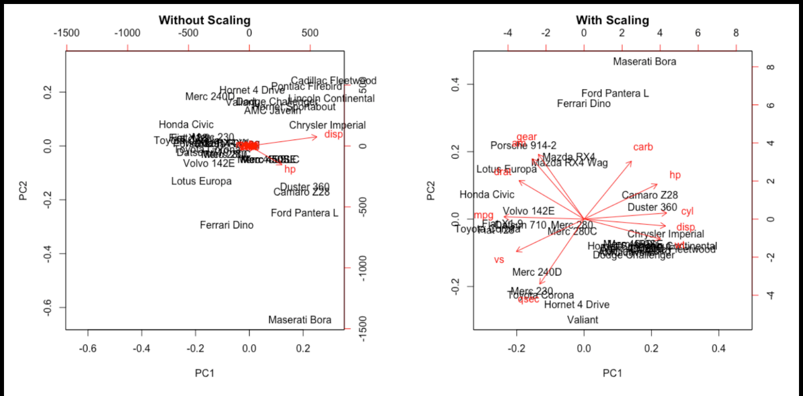
```
> data(mtcars)
> head(mtcars)
                   mpg cyl disp  hp drat    wt  qsec vs am gear carb
Mazda RX4         21.0   6  160 110 3.90 2.620 16.46  0  1    4    4
Mazda RX4 Wag     21.0   6  160 110 3.90 2.875 17.02  0  1    4    4
Datsun 710        22.8   4  108  93 3.85 2.320 18.61  1  1    4    1
Hornet 4 Drive    21.4   6  258 110 3.08 3.215 19.44  1  0    3    1
Hornet Sportabout 18.7   8  360 175 3.15 3.440 17.02  0  0    3    2
Valiant           18.1   6  225 105 2.76 3.460 20.22  1  0    3    1

# Means and standard deviations vary a lot
> round(colMeans(mtcars), 2)
   mpg     cyl    disp      hp    drat      wt    qsec      vs      am    gear    carb
 20.09    6.19  230.72  146.69    3.60    3.22   17.85    0.44    0.41    3.69    2.81
> round(apply(mtcars, 2, sd), 2)
   mpg     cyl    disp      hp    drat      wt    qsec      vs      am    gear    carb
  6.03    1.79  123.94   68.56    0.53    0.98    1.79    0.50    0.50    0.74    1.62
```

Practical PCA issue: Scaling

`prcomp(x, scale=FALSE)`

`prcomp(x, scale=TRUE)`



Do it Yourself!

Your turn!

Unsupervised Learning Mini-Project

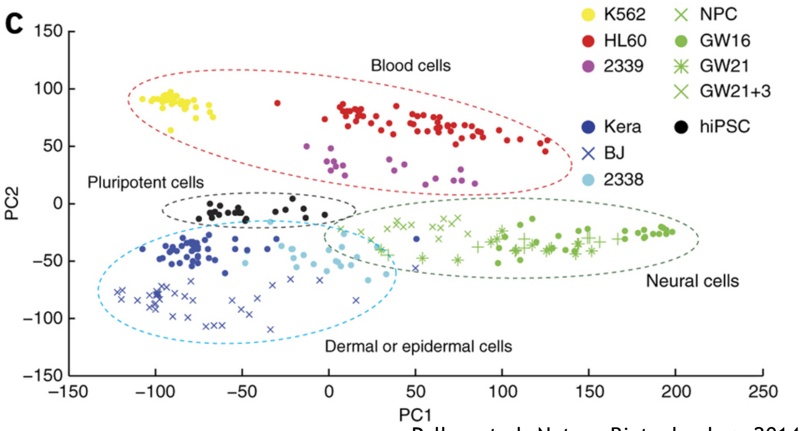
Sections 1 & 2 only please

Input: read, View/head,
PCA: prcomp,
Cluster: kmeans, hclust
Compare: plot, table, etc.

Reference Slides

This PCA plot shows clusters of cell types.

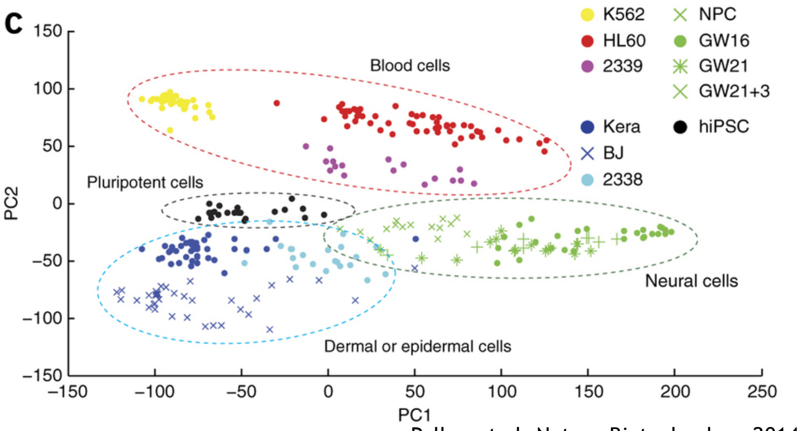
This graph was drawn from single-cell RNA-seq.
There were about 10,000 transcribed genes in each cell.



Pollen et al. Nature Biotechnology 2014

This PCA plot shows clusters of cell types.

Each dot represents a single-cell and its transcription profile
The general idea is that cells with similar transcription should cluster.

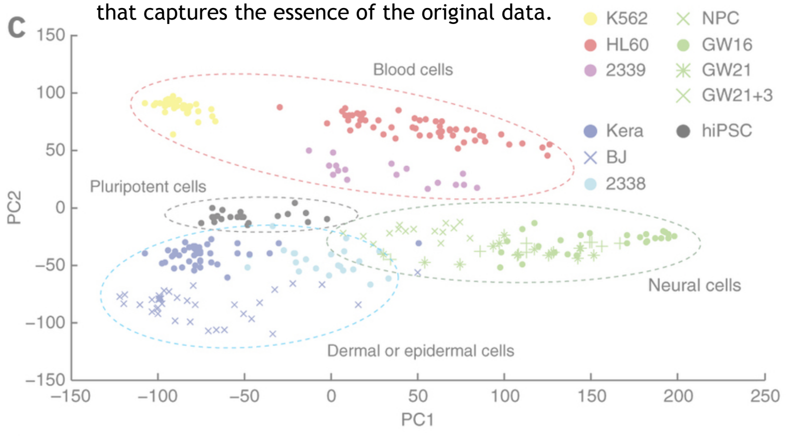


Pollen et al. Nature Biotechnology 2014

This PCA plot shows clusters of cell types.

How does transcription from 10,000 genes get compressed to a single dot on a graph?

PCA is a method for compressing a lot of data into something that captures the essence of the original data.



What does PCA aim to do?

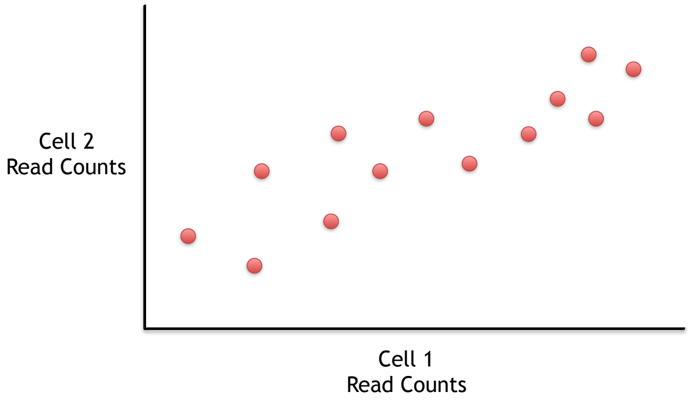
- PCA takes a dataset with a lot of dimensions (i.e. lots of cells) and flattens it to 2 or 3 dimensions so we can look at it.
  - It tries to find a meaningful way to flatten the data by focusing on the things that are different between cells. (much, much more on this later)

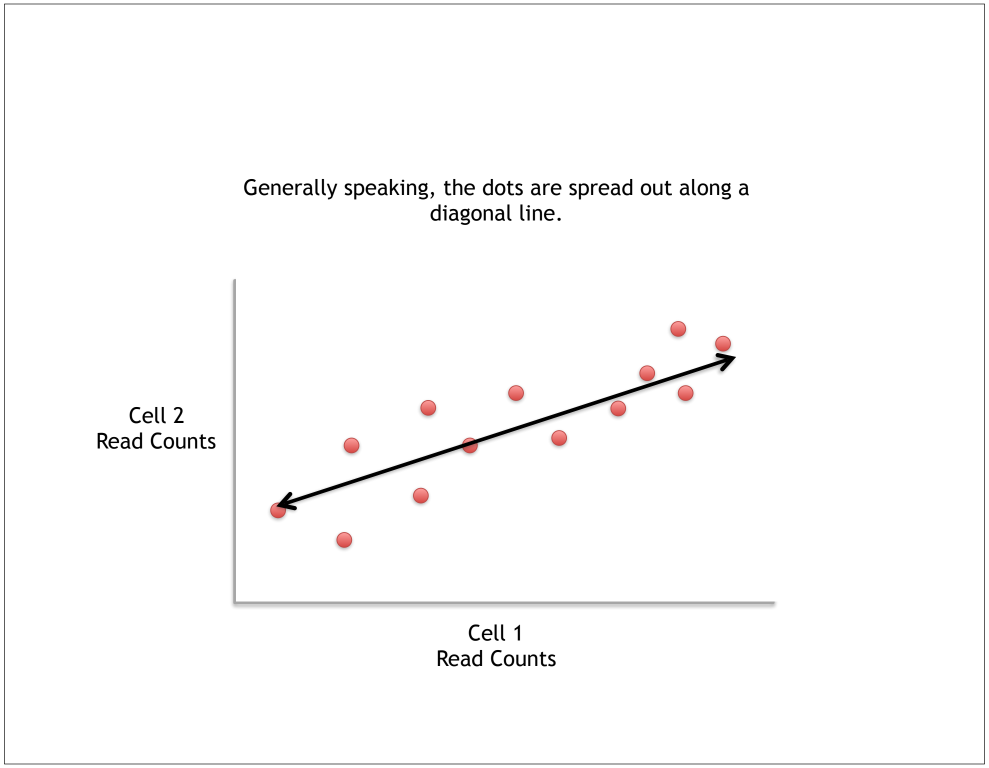
A PCA example

Again, we'll start with just two cells
Here's the data:

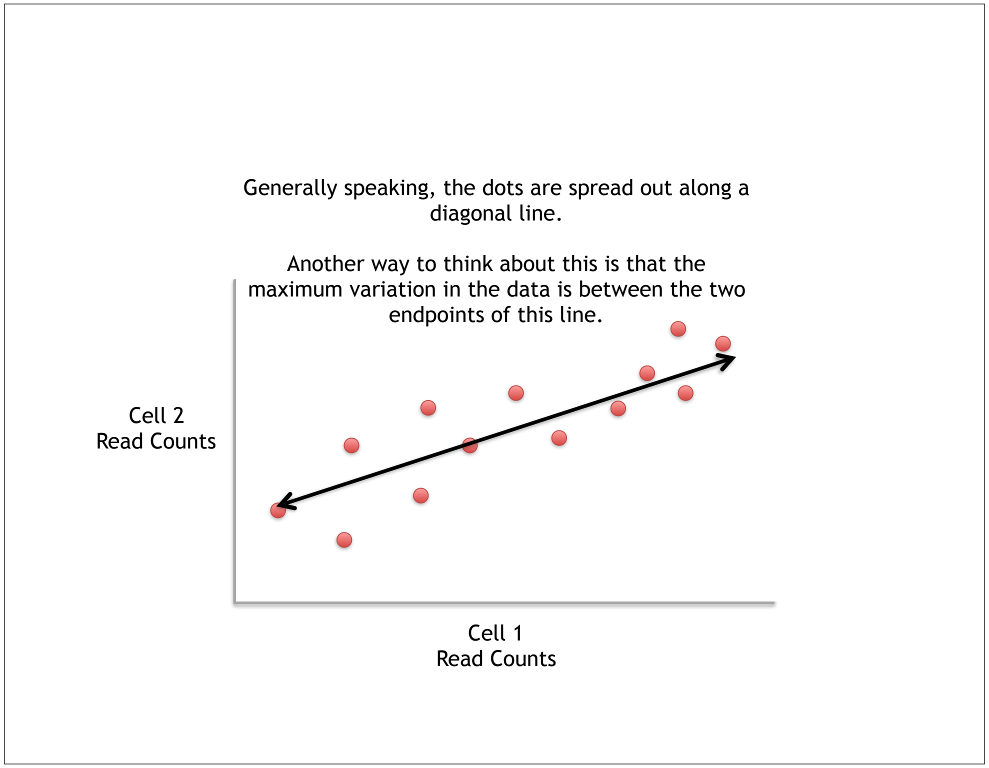
Gene	Cell1 reads	Cell2 reads
a	10	8
b	0	2
c	14	10
d	33	45
e	50	42
f	80	72
g	95	90
h	44	50
i	60	50
… (etc)	… (etc)	… (etc)

Here is a 2-D plot of the data from 2 cells.



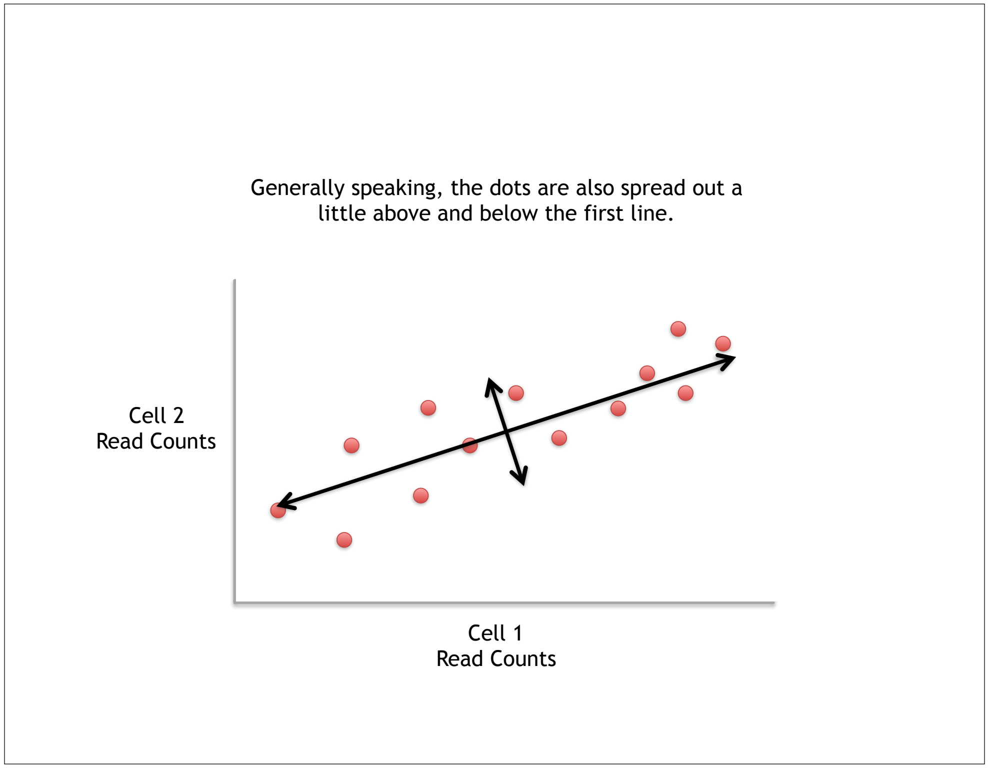


Generally speaking, the dots are spread out along a diagonal line.

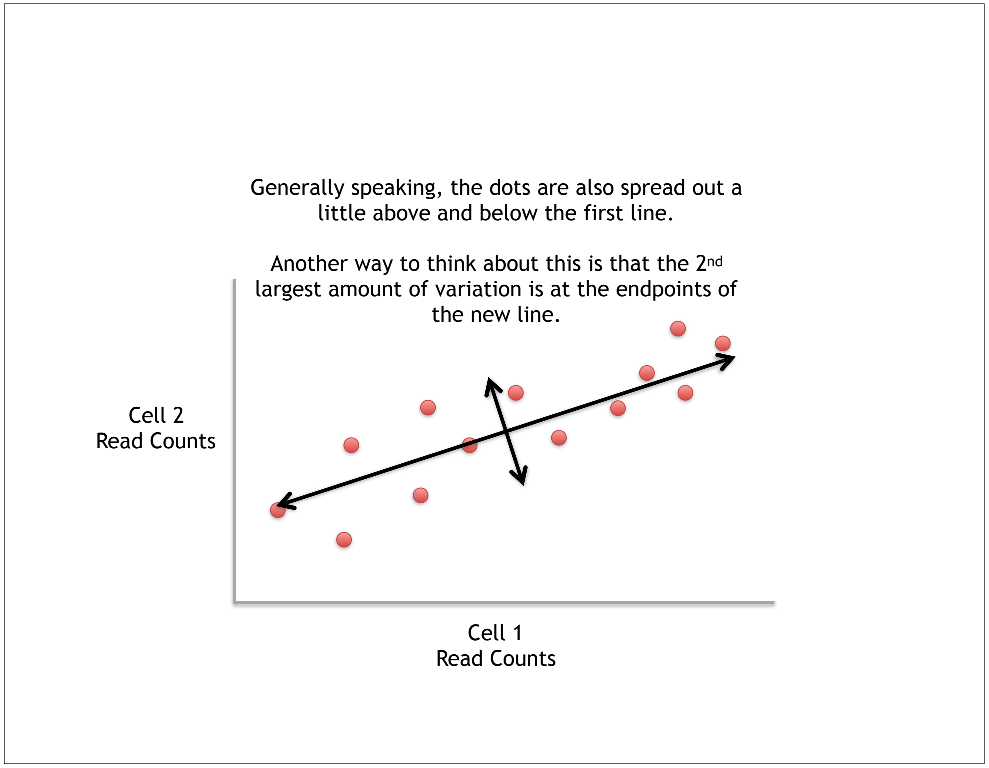


Generally speaking, the dots are spread out along a diagonal line.

Another way to think about this is that the maximum variation in the data is between the two endpoints of this line.



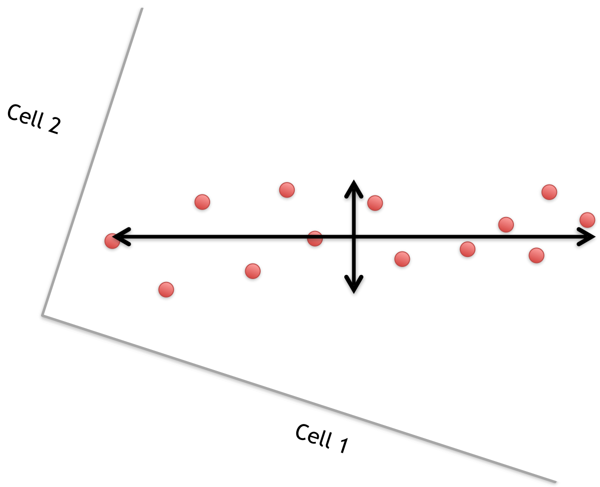
Generally speaking, the dots are also spread out a little above and below the first line.



Generally speaking, the dots are also spread out a little above and below the first line.

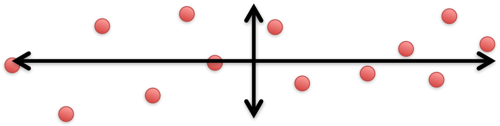
Another way to think about this is that the 2nd largest amount of variation is at the endpoints of the new line.

If we rotate the whole graph, the two lines that we drew make new X and Y axes.



If we rotate the whole graph, the two lines that we drew make new X and Y axes.

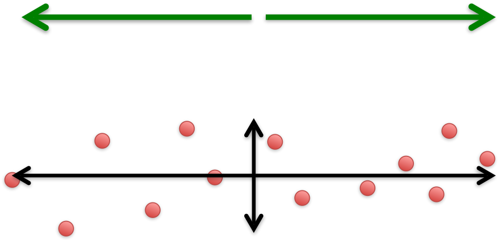
This makes the left/right, above/below variation easier to see.



If we rotate the whole graph, the two lines that we drew make new X and Y axes.

This makes the left/right, above/below variation easier to see.

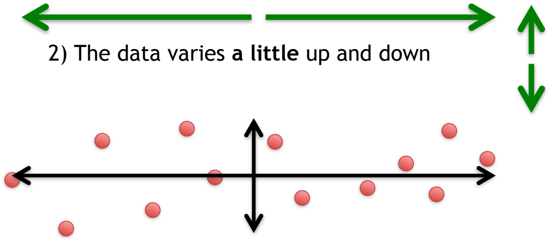
1) The data varies **a lot** left and right



If we rotate the whole graph, the two lines that we drew make new X and Y axes.

This makes the left/right, above/below variation easier to see.

1) The data varies **a lot** left and right



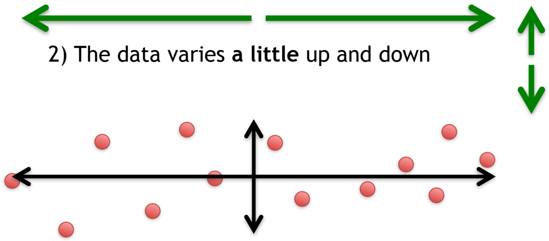
2) The data varies **a little** up and down

If we rotate the whole graph, the two lines that we drew make new X and Y axes.

This makes the left/right, above/below variation easier to see.

1) The data varies **a lot** left and right

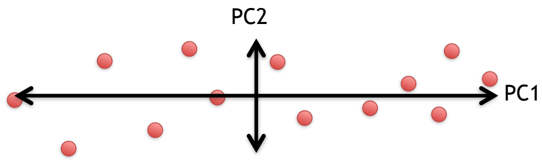
2) The data varies **a little** up and down



Note: All of the points can be drawn in terms of left/right + up/down, just like any other 2-D graph.

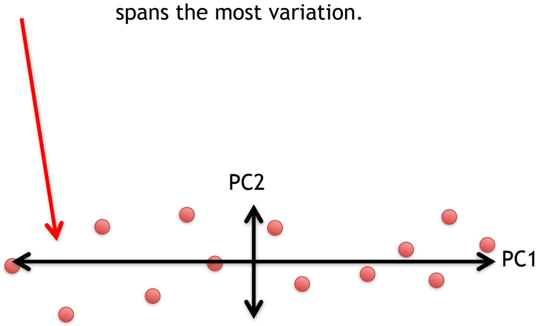
That is to say, we do not need another line to describe “diagonal” variation – we’ve already captured the two directions that can have variation.

These two “new” (or “rotated”) axes that describe the variation in the data are “Principal Components” (PCs)



These two “new” axes that describe the variation in the data are “Principal Components” (PCs)

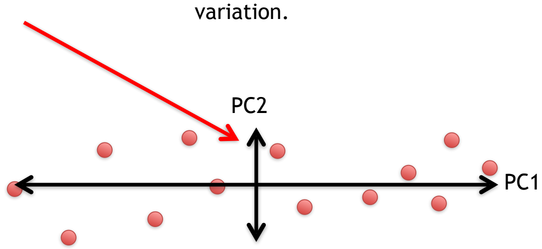
PC1 (the first principal component) is the axis that spans the most variation.



These two “new” axes that describe the variation in the data are “Principal Components” (PCs)

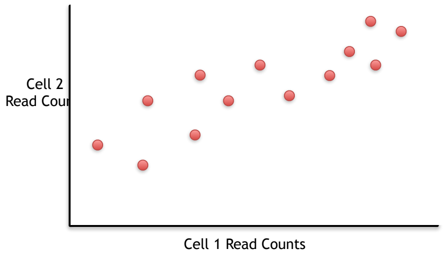
PC1 (the first principal component) is the axis that spans the most variation.

PC2 is the axis that spans the second most variation.



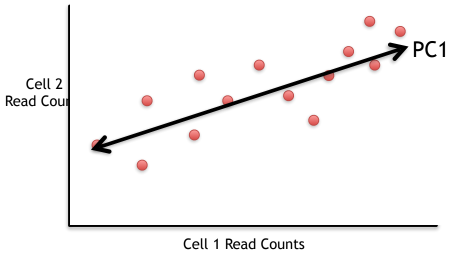
General ideas so far…

- For each gene, we plotted a point based on how many reads were from each cell.



General ideas so far…

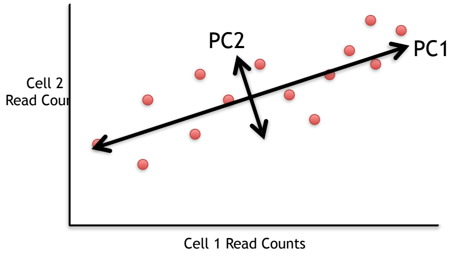
- For each gene, we plotted a point based on how many reads were from each cell.



- PC1 captures the direction where most of the variation is.

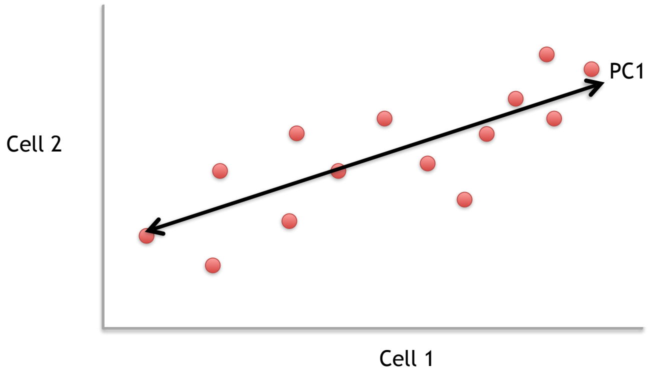
General ideas so far…

- For each gene, we plotted a point based on how many reads were from each cell.

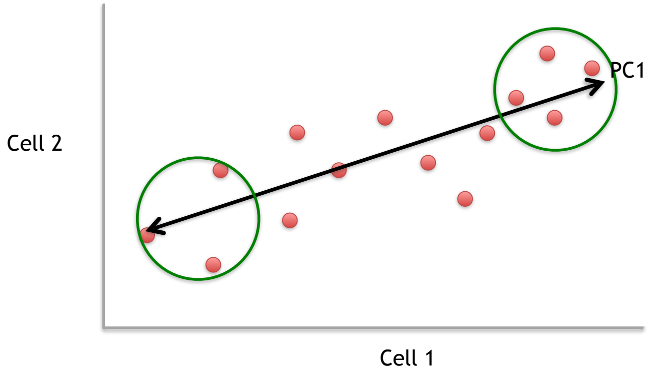


- PC1 captures the direction where most of the variation is.
- PC2 captures the direction with the 2nd most variation.

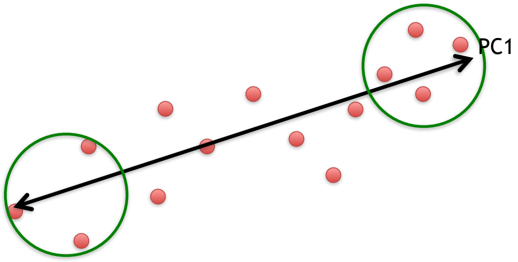
For now, let's focus on PC1



The length and direction of PC1 is mostly determined by the circled genes.

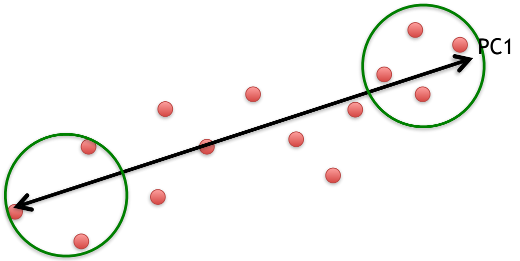


The length and direction of PC1 is mostly determined by the circled genes.

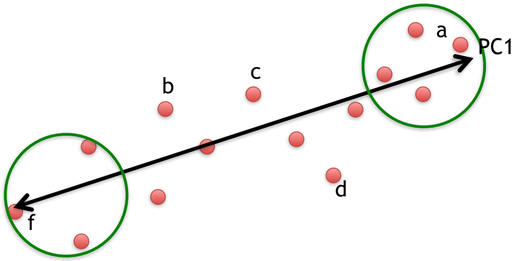


The length and direction of PC1 is mostly determined by the circled genes.

We can score genes based on how much they influence PC1.



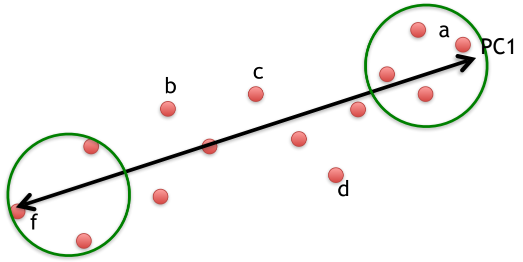
The length and direction of PC1 is mostly determined by the circled genes.



We can score genes based on how much they influence PC1.

Gene	Influence on PC1
a	high
b	low
c	low
d	low
e	high
f	high
…	…

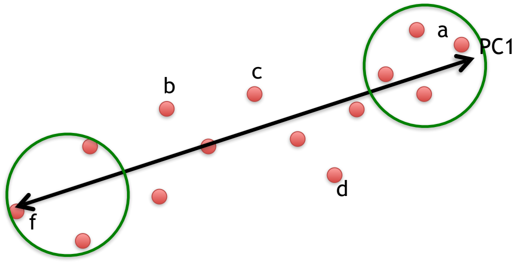
The length and direction of PC1 is mostly determined by the circled genes.



Some genes have more influence on PC1 than others.

Gene	Influence on PC1
a	high
b	low
c	low
d	low
e	high
f	high
…	…

The length and direction of PC1 is mostly determined by the circled genes.

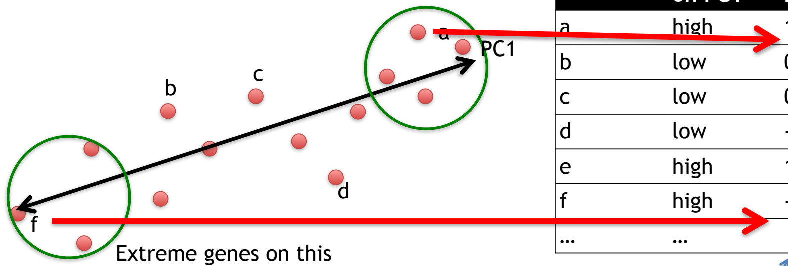


Some genes have more influence on PC1 than others.

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
…	…	

Genes with little influence on PC1 get values close to zero, and genes with more influence get numbers further from zero.

Extreme genes on this end get large positive numbers…



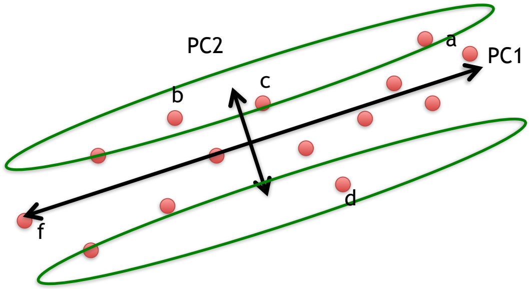
Extreme genes on this end get large negative numbers…

Some genes have more influence on PC1 than others.

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
…	…	

Genes with little influence on PC1 get values close to zero, and genes with more influence get numbers further from zero.

Genes that influence PC2



Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
…	…	

Our two PCs

PC1

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
...	...	

PC2

Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
...	...	

Using the two Principal Components to plot cells

Combining the read counts for all genes in a cell to get a single value.

PC1

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
...	...	

PC2

Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
...	...	

Using the two Principal Components to plot cells

Combining the read counts for all genes in a cell to get a single value.

The original read counts

Gene	Cell1	Cell2
a	10	8
b	0	2
c	14	10
d	33	45
e	50	42
f	80	72
g	95	90
h	44	50
i	60	50
etc	etc	etc

PC1

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
...	...	

PC2

Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
...	...	

Using the two Principal Components to plot cells

Combining the read counts for all genes in a cell to get a single value.

The original read counts

Gene	Cell1	Cell2
a	10	8
b	0	2
c	14	10
d	33	45
e	50	42
f	80	72
g	95	90
h	44	50
i	60	50
etc	etc	etc

PC1

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
...	...	

PC2

Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
...	...	

Cell1 PC1 score = (read count * influence) + … for all genes

Using the two Principal Components to plot cells

Combining the read counts for all genes in a cell to get a single value.

The original read counts

Gene	Cell1	Cell2
a	10	8
b	0	2
c	14	10
d	33	45
e	50	42
f	80	72
g	95	90
h	44	50
i	60	50
etc	etc	etc

PC1

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
...	...	

PC2

Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
...	...	

Cell1 PC1 score = (10 * 10) + ...

Using the two Principal Components to plot cells

Combining the read counts for all genes in a cell to get a single value.

The original read counts

Gene	Cell1	Cell2
a	10	8
b	0	2
c	14	10
d	33	45
e	50	42
f	80	72
g	95	90
h	44	50
i	60	50
etc	etc	etc

PC1

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
...	...	

PC2

Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
...	...	

Cell1 PC1 score = (10 * 10) + (0 * 0.5) + ...

Using the two Principal Components to plot cells

Combining the read counts for all genes in a cell to get a single value.

The original read counts

Gene	Cell1	Cell2
a	10	8
b	0	2
c	14	10
d	33	45
e	50	42
f	80	72
g	95	90
h	44	50
i	60	50
etc	etc	etc

PC1

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
...	...	

PC2

Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
...	...	

Cell1 PC1 score = (10 * 10) + (0 * 0.5) + ... etc... = 12

Using the two Principal Components to plot cells

Combining the read counts for all genes in a cell to get a single value.

The original read counts

Gene	Cell1	Cell2
a	10	8
b	0	2
c	14	10
d	33	45
e	50	42
f	80	72
g	95	90
h	44	50
i	60	50
etc	etc	etc

PC1

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
...	...	

PC2

Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
...	...	

Cell1 PC1 score = (10 * 10) + (0 * 0.5) + ... etc... = 12

Cell1 PC2 score = (10 * 3) + ...

Using the two Principal Components to plot cells

Combining the read counts for all genes in a cell to get a single value.

The original read counts

Gene	Cell1	Cell2
a	10	8
b	0	2
c	14	10
d	33	45
e	50	42
f	80	72
g	95	90
h	44	50
i	60	50
etc	etc	etc

PC1

Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
…	…	

PC2

Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
…	…	

Cell1 PC1 score = (10 * 10) + (0 * 0.5) + … etc… = 12

Cell1 PC2 score = (10 * 3) + (0 * 10) + …

Using the two Principal Components to plot cells

Combining the read counts for all genes in a cell to get a single value.

The original read counts

Gene	Cell1	Cell2
a	10	8
b	0	2
c	14	10
d	33	45
e	50	42
f	80	72
g	95	90
h	44	50
i	60	50
etc	etc	etc

PC1

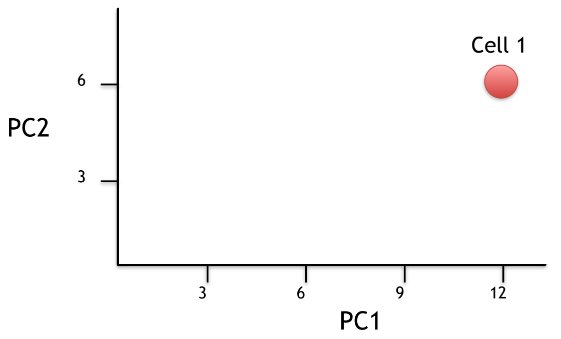
Gene	Influence on PC1	In numbers
a	high	10
b	low	0.5
c	low	0.2
d	low	-0.2
e	high	13
f	high	-14
…	…	

PC2

Gene	Influence on PC2	In numbers
a	medium	3
b	high	10
c	high	8
d	high	-12
e	low	0.2
f	low	-0.1
…	…	

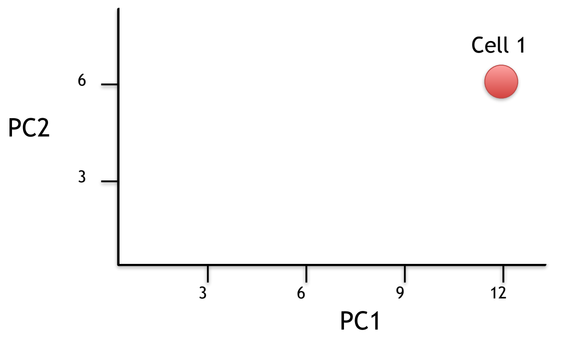
Cell1 PC1 score = (10 * 10) + (0 * 0.5) + … etc… = 12

Cell1 PC2 score = (10 * 3) + (0 * 10) + … etc… = 6

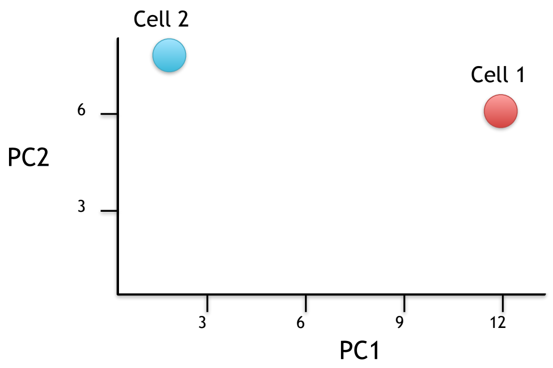


Cell1 PC1 score = (10 * 10) + (0 * 0.5) + … etc… = 12

Cell1 PC2 score = (10 * 3) + (0 * 10) + … etc… = 6



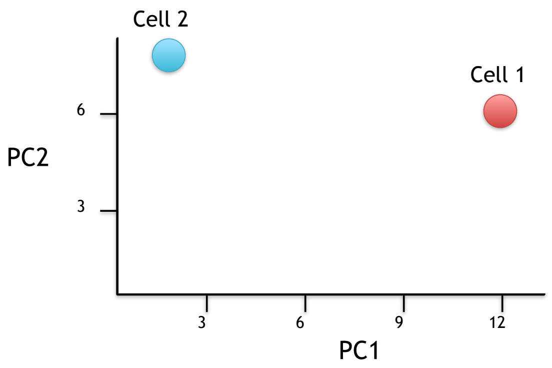
Now calculate scores for Cell2



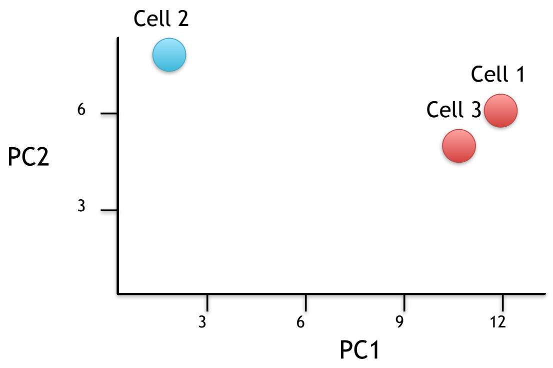
Now calculate scores for Cell2

Cell2 PC1 score = (8 * 10) + (2 * 0.5) + … etc… = 2

Cell2 PC2 score = (8 * 3) + (2 * 10) + … etc… = 8

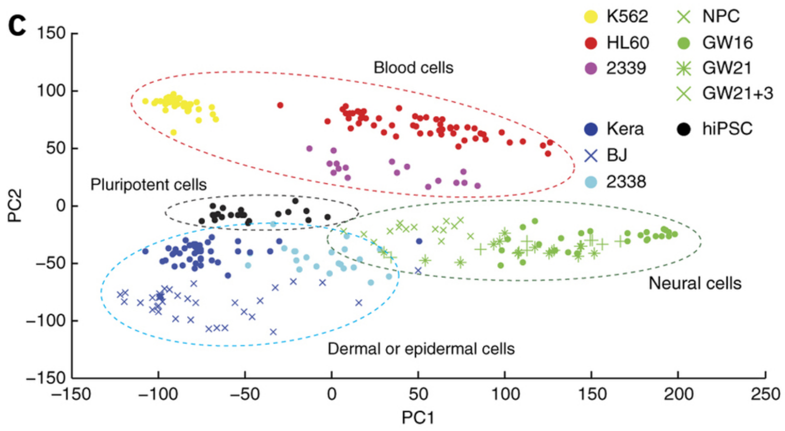


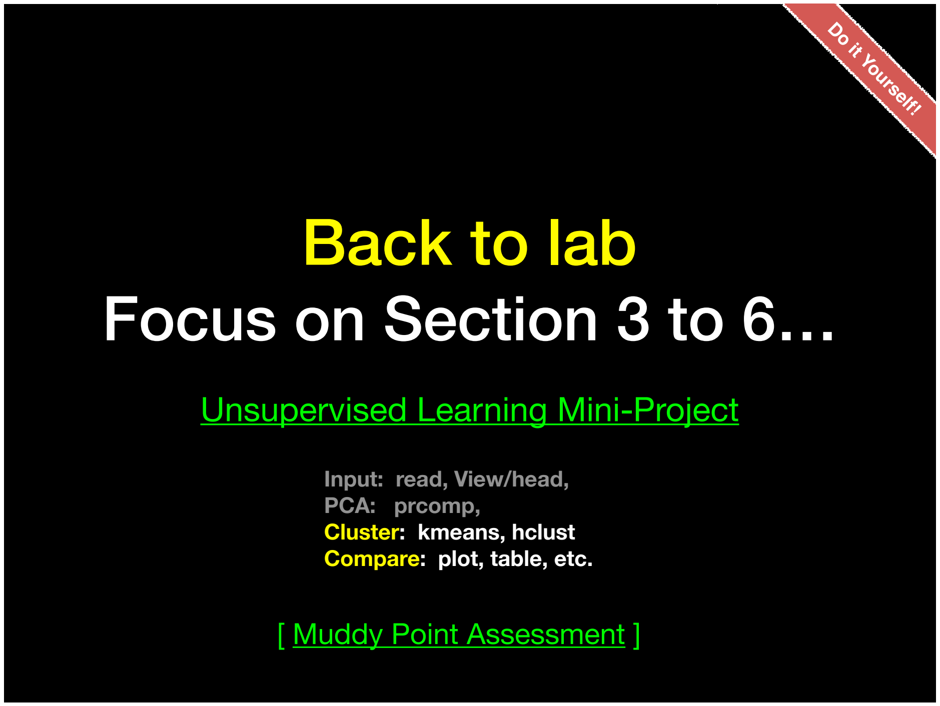
If we sequenced a third cell, and its transcription was similar to cell 1, it would get scores similar to cell 1's.



If we sequenced a third cell, and its transcription was similar to cell 1, it would get scores similar to cell 1's.

Hooray! We know how they plotted all of the cells!!!





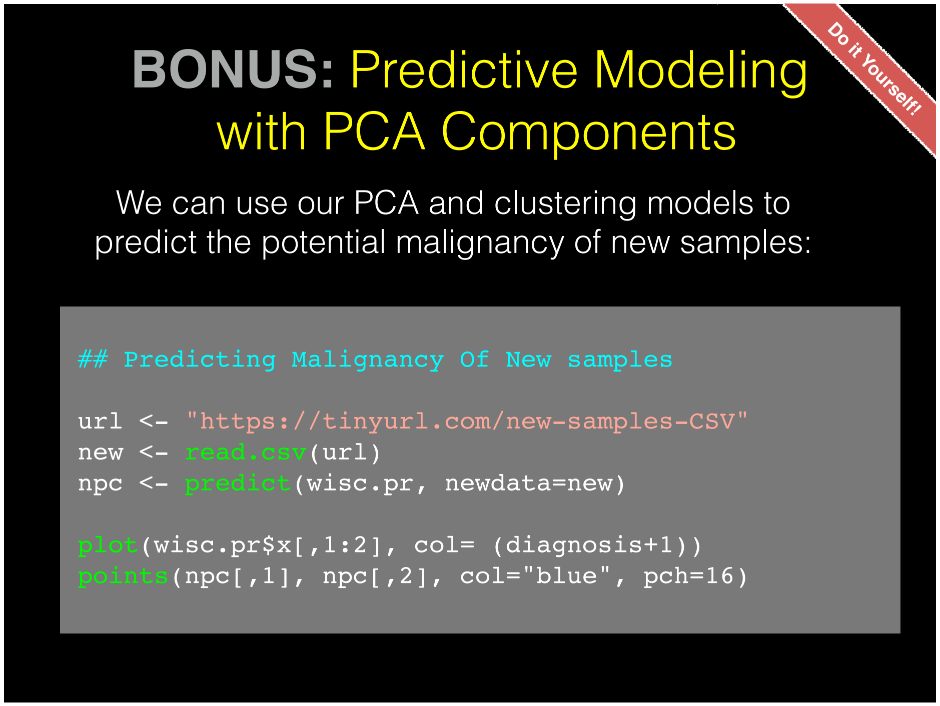
Do it Yourself!

Back to lab
Focus on Section 3 to 6…

Unsupervised Learning Mini-Project

Input: read, View/head,
PCA: prcomp,
Cluster: kmeans, hclust
Compare: plot, table, etc.

[Muddy Point Assessment]



Do it Yourself!

BONUS: Predictive Modeling with PCA Components

We can use our PCA and clustering models to predict the potential malignancy of new samples:

```
## Predicting Malignancy Of New samples

url <- "https://tinyurl.com/new-samples-CSV"
new <- read.csv(url)
npc <- predict(wisc.pr, newdata=new)

plot(wisc.pr$x[,1:2], col= (diagnosis+1))
points(npc[,1], npc[,2], col="blue", pch=16)
```

Do it Yourself!

[Muddy Point Assessment]