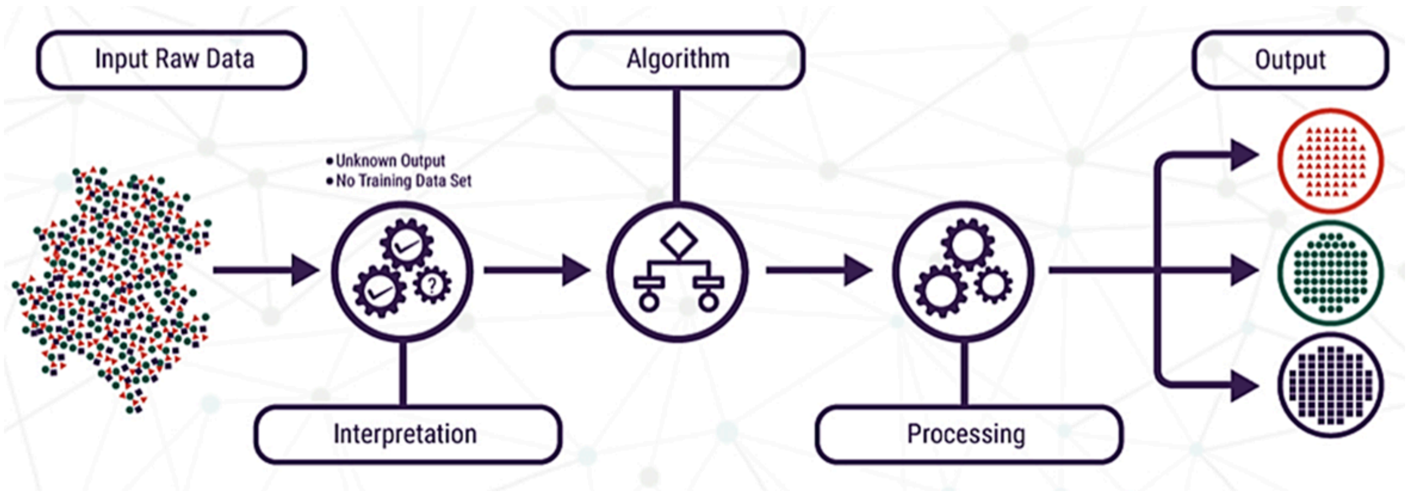
Introduction to Unsupervised Learning

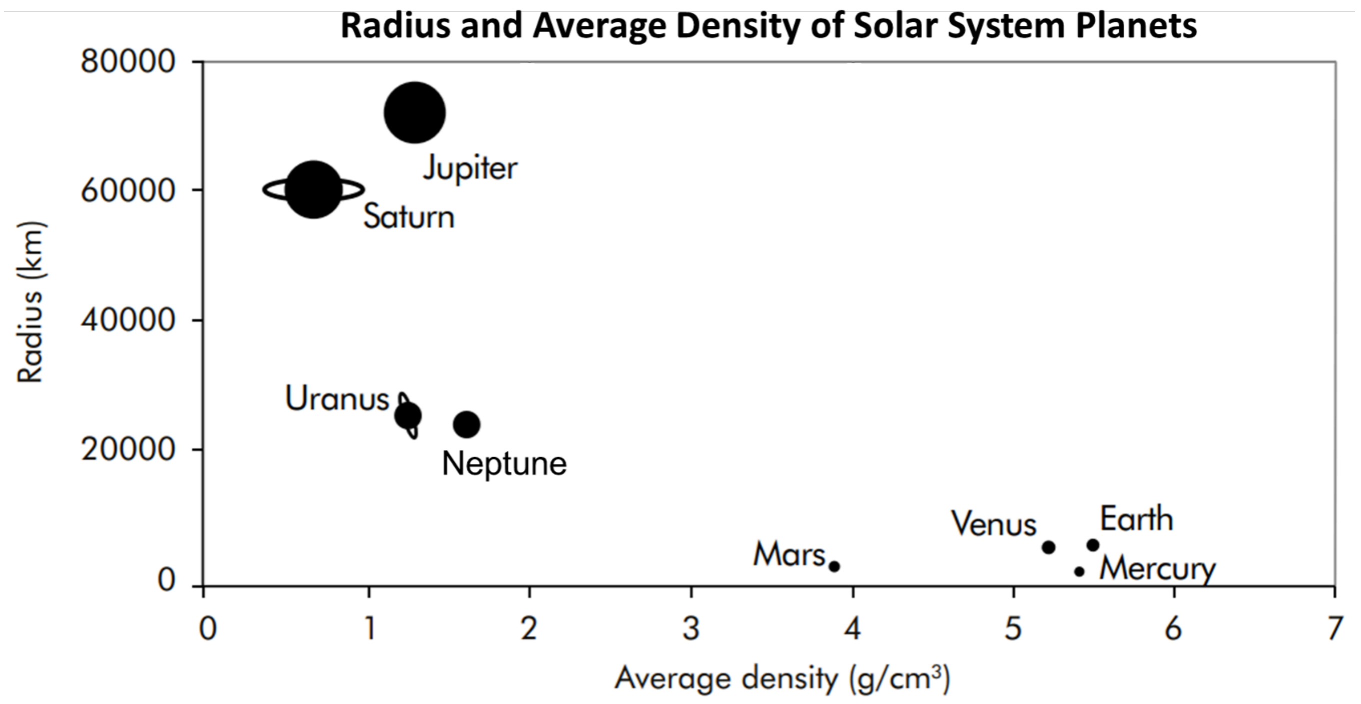
Unsupervised learning refers to a machine learning algorithm that infers information from a given dataset without any guidance. The algorithm relies on underlying similarities and patterns within the data to learn how the variables are related to one another. So in a way, we're "letting the data speak for itself."



This is a great tool to use for initial exploration of a dataset without any defined hypothesis. Unsupervised learning is especially valuable in assessing a large dataset with multiple variables. For today's lecture, we'll be going over two broad applications of unsupervised learning: (1) **clustering** and (2) **dimensionality reduction**.

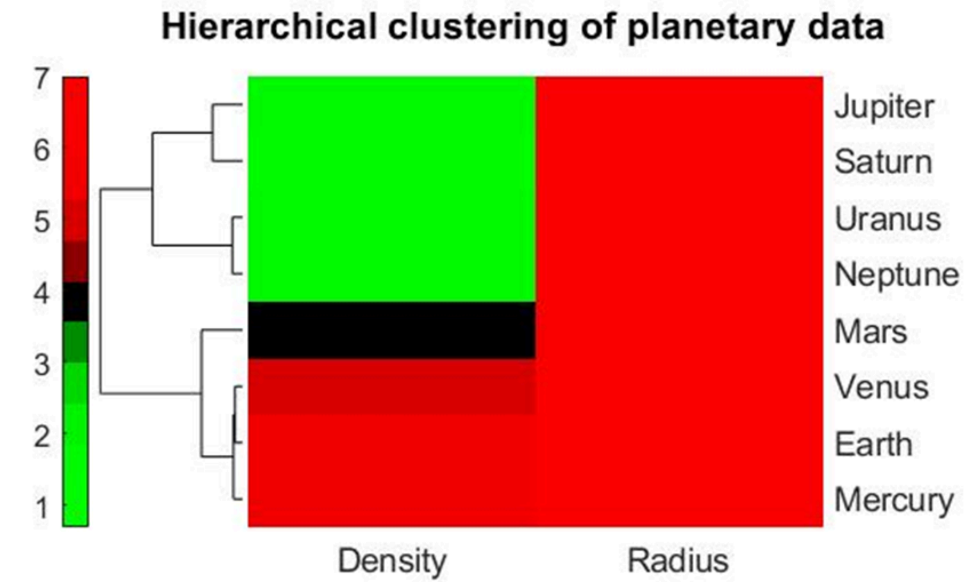
Clustering - Identifying distinct groups based on similarity

We'll be covering two types of clustering techniques: **hierarchical** and **k-means** clustering. To introduce these methods, we'll consider the following planetary data:

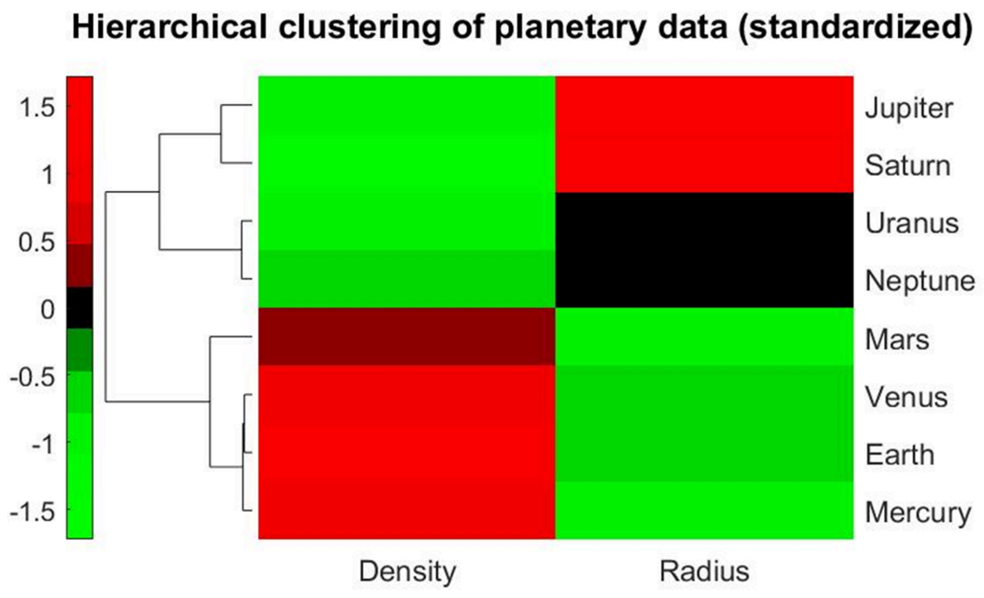


Hierarchical Clustering

In **hierarchical clustering**, each observation starts in its own cluster at the base of the hierarchy. As we move up the hierarchy, observations that are most similar group together first until all observations are linked. This hierarchy of observations is often depicted as a **dendrogram**. In MATLAB, we can also plot a **clustergram** to visualize how similar the observations (e.g. planets) are based on different measurements (e.g. density, radius). The plot below shows an example of hierarchical clustering of planets in the solar system based on their average density and radius:

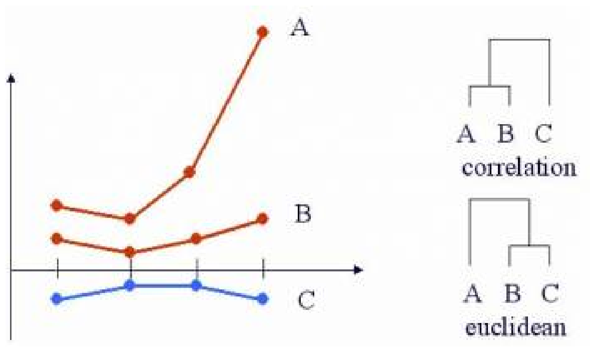


You may have noticed that the radius column doesn't show any differences between planets. This is because the range of values represented by the color gradient is limited to 1 through 7 (recall that planet radius was in the 10,000 range). To have a better visual sense in how a metric (e.g. radius) differs between observations (e.g. planets), we can **standardize** the values within a metric. Below is what the same clustergram of planetary data would look like with standardized density and radius:



Defining Similarity

One of the most common ways to apply unsupervised learning is to assess the similarity within a dataset. Similarity can be quantitatively described using a **distance metric** between two variables. There are various types of distance metrics that can be used, but we'll just go over two of the most common ones: **Euclidean** and **correlation** distance. The plot below shows how these distance metrics differ:

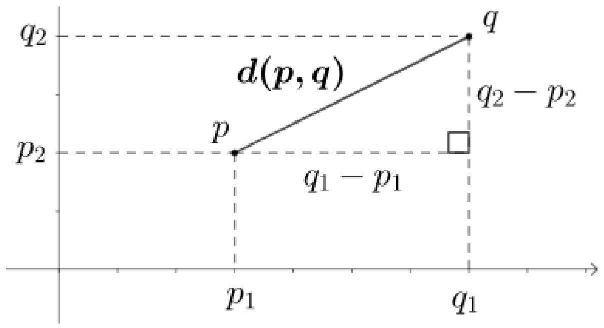


Euclidean Distance

The **Euclidean distance** is broadly defined by the following formula:

$$d(p,q) = \sqrt{\sum_{i=1}^{n} (p_i - q_i)^2}$$

This is what the distance between p and q would look like when n = 2:



When analyzing biological data in MATLAB, we'll mostly be dealing with large vectors. In these cases, we let n be equal to the length of the vectors we're comparing (note: the vectors must have the same length).

For instance, let's say we're comparing vectors a and b as defined below:

```
load('distance_data.mat')
a
```

```
a = 1×4
    2.0000    1.5000    3.0000    7.0000
```

```
b
```

```
b = 1×4
    1.0000    0.5000    1.0000    1.5000
```

For this example, n = 4. We can calculate the Euclidean distance manually:

```
d_euclid_man = sqrt(sum((a-b).^2))
```

```
d_euclid_man = 6.0208
```

We can also use the built-in function *pdist*:

```
d_euclid_fun = pdist([a;b],'euclidean')
```

```
d_euclid_fun = 6.0208
```

Note that when using *pdist*, we combined vectors a and b into a matrix. This is because the *pdist* function is used to calculate the distance between all vectors in a matrix. If we had a matrix with three vectors, we would be calculating the distance for three pairwise combinations (C(3,2) = 3):

```
c = [-1 -0.5 -0.5 -1];
d_euclid_3 = pdist([a;b;c])
```

```
d_euclid_3 = 1×3
    6.0208    9.4472    3.6742
```

Note: Euclidean distance is the default metric for the *pdist* function.

Correlation Distance

Another commonly used distance metric is **correlation**, and this is broadly defined as follows:

$$d(p,q) = 1 - r$$

where r is the correlation coefficient between two vectors.

Going back to our example vectors a and b, the correlation distance can be calculated manually:

```
d_corr_man = 1-corr(a',b')
```

```
d_corr_man = 0.1004
```

Or using the *pdist* function:

```
d_corr_fun = pdist([a;b],'correlation')
```

```
d_corr_fun = 0.1004
```

Let's calculate the distances between vectors a, b, and c based on correlation:

```
d_corr_3 = pdist([a;b;c],'correlation')
```

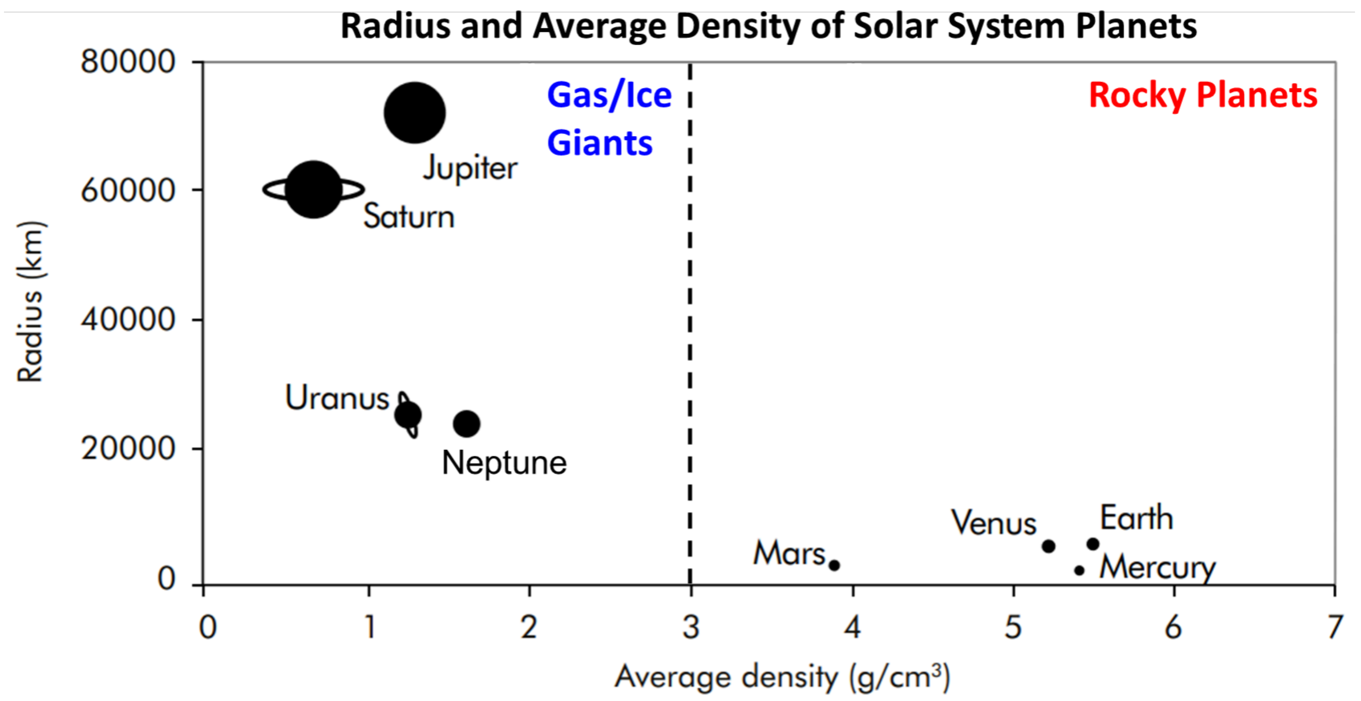
```
d_corr_3 = 1×3
    0.1004    1.5205    1.7071
```

Note that the correlation distance can only range from 0 (similar) to 2 (dissimilar).

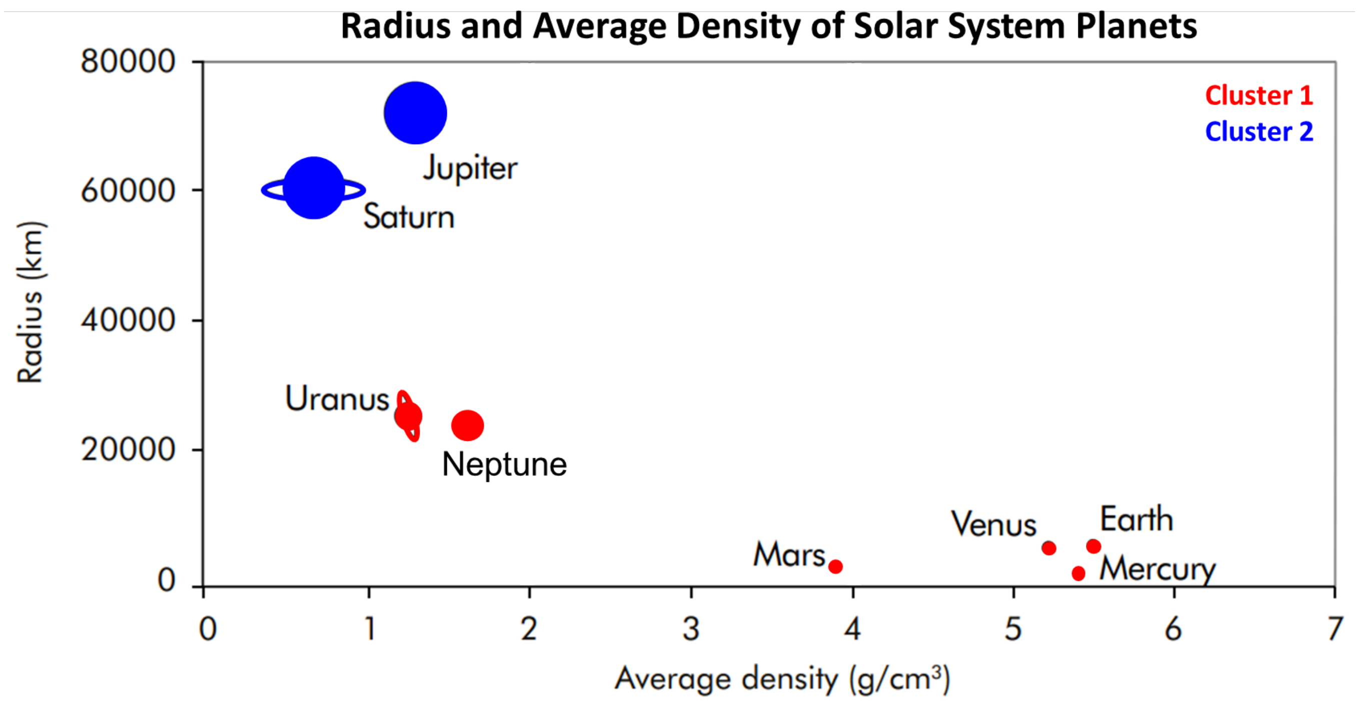
Additional information: refer to the *pdist* documentation for all available distance metrics.

K-means Clustering

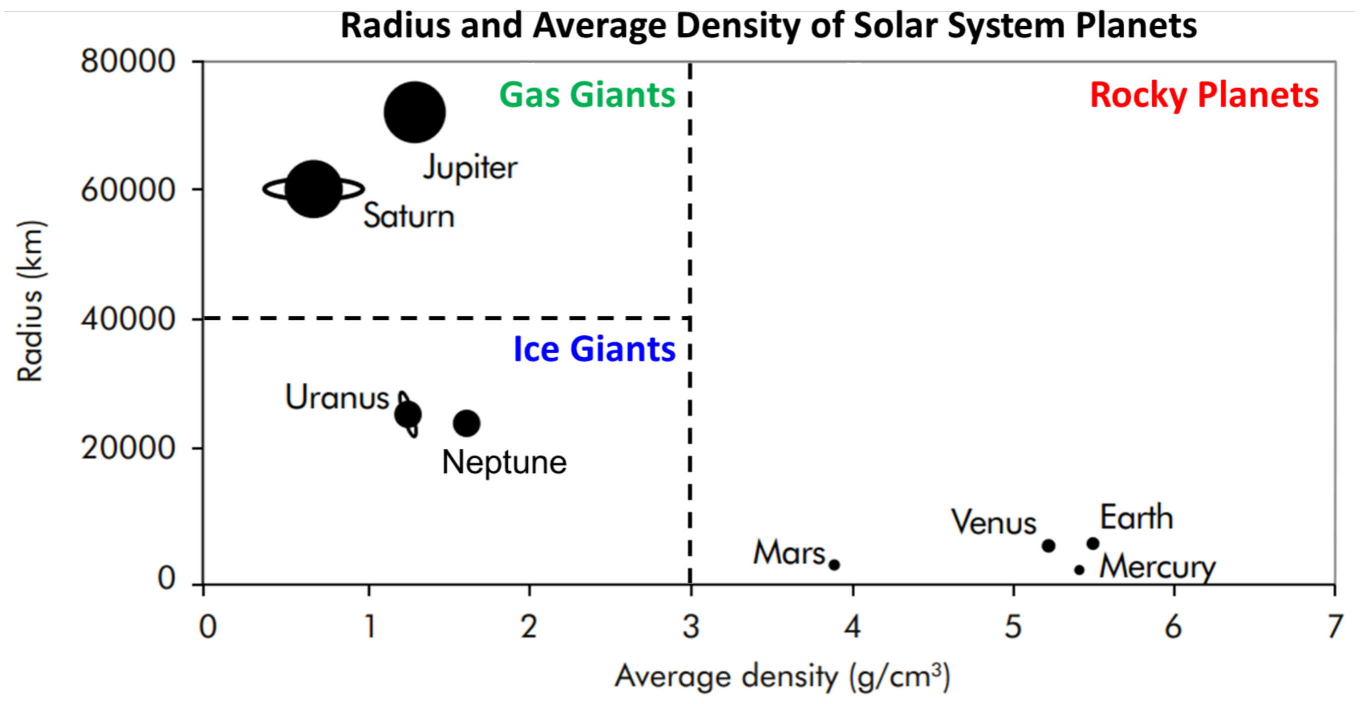
For **k-means clustering**, we specify how many distinct groups we think that the data will cluster into. K-means clustering then allocates data points to a cluster by minimizing the in-cluster sum of squares (more on this later). The value for k is typically chosen based on *a priori* information we may have on the data. Referring back to our planetary data:



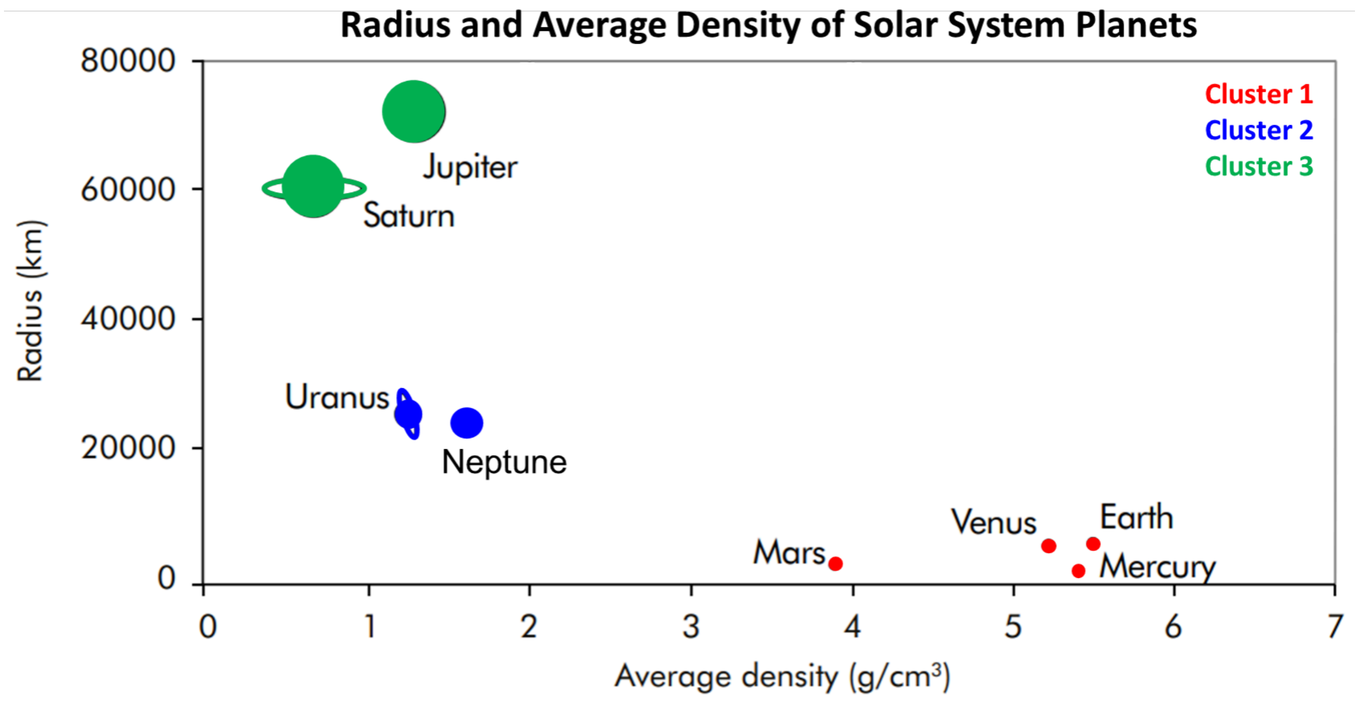
Based on this additional information, we could apply k-means clustering with k = 2 to group our planets:



This is probably not how we expected the planets to cluster based on our reason to use k = 2. However, if we delve deeper into the information we were given before:



Let's see how the planets cluster based on k-means clustering with k = 3:



Now our results match what we expected based on our reason to use k = 3.

Silhouette Analysis

You must be wondering: what if we don't have any prior knowledge of the data? What value do we use for k, and how do we know if this was a good choice? To consider these questions, we can conduct a **silhouette**

analysis to determine which k value best minimizes the in-cluster sum of squares**.** For this analysis, we calculate the silhouette value for each observation and assess how they compare within a cluster by generating a **silhouette plot**. The silhouette value measures how similar an observation is to its own cluster compared to others based on a distance metric. This value ranges from -1 to 1, where a higher positive value implies that an observation is well-matched to its cluster and vice-versa.

One way to assess whether we chose a good value for k is to evaluate the mean of all silhouette values. For the purposes of this lesson, we'll refer to the mean of all silhouette values as the **silhouette score**. In general, a silhouette score above 0.5 indicates that the data is well separated. The following code calculates the silhouette score for our planetary data based on k-means clustering with different k values and visualizes the clustered data:

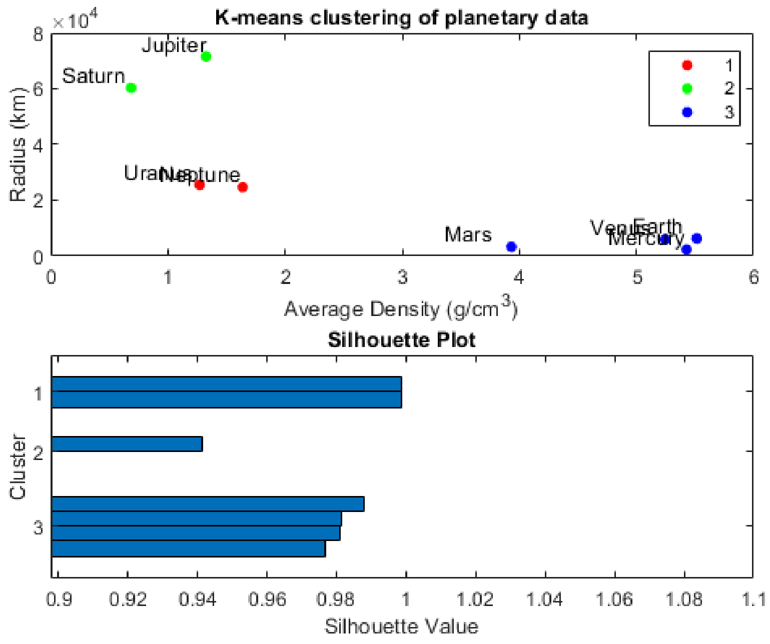
```
% Load and view planetary data
load('planetary_data.mat')                          % load planetary data
disp(planet_table)                                  % display data table
```

```
     Planet      Density     Radius
    _______    _______    ______

    Mercury     5.427      2439.5
    Venus       5.243        6052
    Earth       5.514        6378
    Mars        3.933        3396
    Jupiter     1.326       71492
    Saturn      0.687       60268
    Uranus      1.271       25559
    Neptune     1.638       24764
```

```
% Do k-means clustering and calculate silhouette score
X = [density radius];                               % array of planetary data
idx = kmeans(X,3);      % k-means clustering
s = silhouette(X,idx);                              % silhouette values
s_score = mean(s)                                   % silhouette score
```

```
s_score = 0.9705
```

```
% Plot of clustered data
subplot(2,1,1)
gscatter(density, radius, idx)
labelpoints(density, radius, planet)
xlabel('Average Density (g/cm^3)')
ylabel('Radius (km)')
title('K-means clustering of planetary data')

% Silhouette plot
subplot(2,1,2)
silhouette(X,idx)
title('Silhouette Plot')
```



Note: As the placement of cluster centroid is random for every iteration, clustering results may fluctuate for different iterations. The *kmeans* function contains additional properties that can be used to address this problem. For the purposes of this lesson, we'll use the *kmeans* function as is, but we'll keep in mind that our clustering results may differ between iterations.

Hierarchical vs. K-means Clustering

Both hierarchical clustering and k-means clustering are unsupervised learning methods for grouping data based on similarity. The difference between these two clustering methods is that hierarchical clustering takes a "bottom-up" approach, whereas k-means clustering takes a "top-down" approach.

In MATLAB, we can perform hierarchical clustering using the *clustergram* function, and k-means clustering using the *kmeans* function. The *silhouette* function is used to calculate the silhouette value for each observation based on its cluster assignment from k-means clustering. This function also generates a silhouette plot.

In-class practice: clustering of the Framingham data

Applying hierarchical clustering for cardiovascular health measurements

Let's say we're interested in what the subset of cardiovascular-related measurements for a small set of patients can tell us about a their diabetes status using hierarchical clustering. The first step is to load the data and define the subset we're interested in:

```
fram = readtable('frmgham2.xls');            % load the Framingham data
disp(fram.Properties.VariableNames)          % see what variables the dataset contains
```

```
Columns 1 through 7
  'RANDID'    'SEX'    'TOTCHOL'    'AGE'    'SYSBP'    'DIABP'    'CURSMOKE'
Columns 8 through 13
  'CIGPDAY'    'BMI'    'DIABETES'    'BPMEDS'    'HEARTRTE'    'GLUCOSE'
Columns 14 through 19
```

```
    'educ'     'PREVCHD'     'PREVAP'     'PREVMI'     'PREVSTRK'     'PREVHYP'
  Columns 20 through 26
    'TIME'     'PERIOD'     'HDLC'     'LDLC'     'DEATH'     'ANGINA'     'HOSPMI'
  Columns 27 through 32
    'MI_FCHD'     'ANYCHD'     'STROKE'     'CVD'     'HYPERTEN'     'TIMEAP'
  Columns 33 through 38
    'TIMEMI'     'TIMEMIFC'     'TIMECHD'     'TIMESTRK'     'TIMECVD'     'TIMEDTH'
  Column 39
    'TIMEHYP'
```

```
cardio_vars = {'DIABETES','TOTCHOL','SYSBP','DIABP','BMI',...
    'HEARTRTE','GLUCOSE','HDLC','LDLC'}     % define cardiovascular-related variables (+ diabet
```

```
cardio_vars = 1×9 cell array
'DIABETES'    'TOTCHOL'    'SYSBP'     'DIABP'     'BMI'       'HEARTRTE'    ...
```

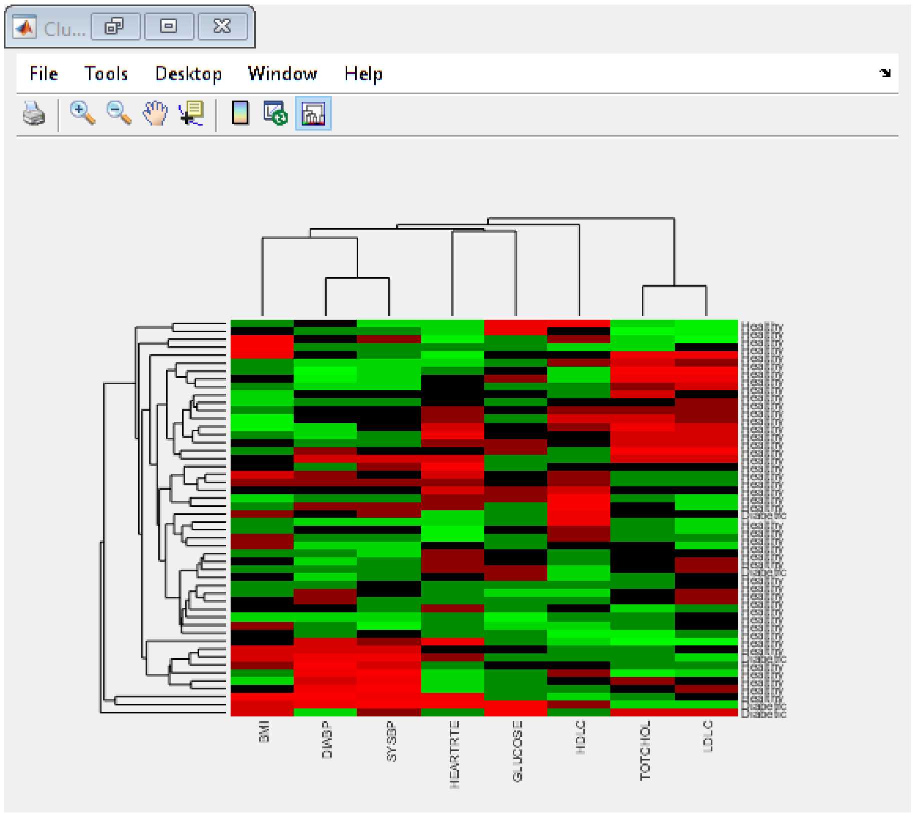
```
fram_cardio = fram(:,cardio_vars);          % create variable for data of interest
```

We'll remove rows containing NaN values and get the subset for the first 50 entries. We'll also create a variable for the patient diabetes status and a numerical array for the cardiovascular-related measurements:

```
fram_cardio = rmmissing(fram_cardio);                          % remove rows containing NaN values
fram_cardio = fram_cardio(1:50,:);                             % subset of 50 entries
diabetes_status = repmat({'Healthy'},50,1);                    % patient diabetes status (0 = heal
diabetes_status(fram_cardio.DIABETES == 1) = {'Diabetic'};     % patient diabetes status (1 = diab
fram_cardio_data = table2array(fram_cardio(:,2:end));          % numerical data array (- diabetes
```

Now we can perform hierarchical clustering for this data subset. For this example, we'll use Euclidean distance (default) as our distance metric for assessing similarity. We'll also cluster along both rows and columns (default) and provide labels (rows = patient diabetes status, columns = measurements). Finally, we'll standardize each column to better compare measurements between patients:

```
col_names = fram_cardio.Properties.VariableNames(2:end); % variable for column names (- diabete
fram_cardio_cg = clustergram(fram_cardio_data,...        % clustergram with...
    'RowLabels',diabetes_status,...                      % labeled rows (patient diabetes statu
    'ColumnLabels',col_names,...                         % labeled columns (measurements)
    'Standardize','column')                              % standardized columns
```



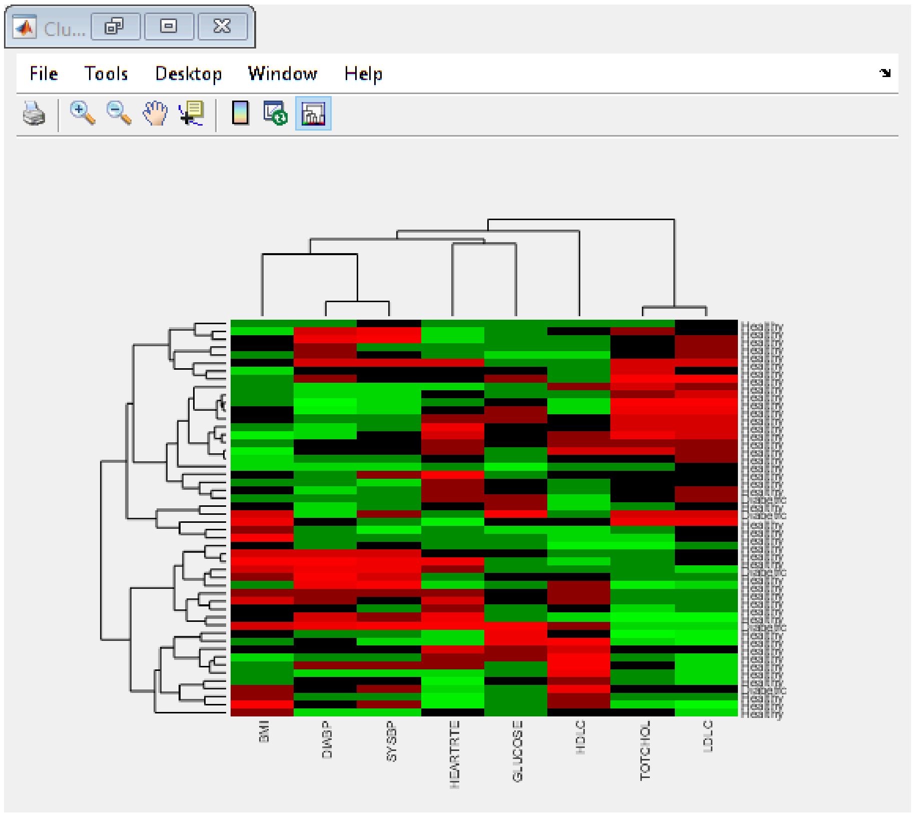
```
Clustergram object with 50 rows of nodes and 8 columns of nodes.
```

This clustergram shows how specific measurements compare between patient clusters, and which patients are most similar based on Euclidean distance.

<u>Question:</u> Are diabetic patients similar based on these measurements?

Let's see how the clustergram changes if we use Pearson's correlation as our distance metric:

```
fram_cardio_cg_corr = clustergram(fram_cardio_data,...   % clustergram with...
    'RowLabels',diabetes_status,...                      % labeled rows (patient diabetes status
    'ColumnLabels',col_names,...                         % labeled columns (measurements)
    'Standardize','column',...                           % standardized columns
    'RowPDist','correlation',...                         % correlation as distance metric (rows)
    'ColumnPDist','correlation')                         % correlation as distance metric (colum
```



```
Clustergram object with 50 rows of nodes and 8 columns of nodes.
```

<u>Question</u>: How did the clustering change when using correlation as our distance metric? Are diabetic patients similar?

Applying k-means clustering for the Framingham data

To more easily visualize k-means clustering, we'll consider how the previous set of patients cluster solely based on BMI and blood glucose level:

```
fram_kmeans = fram_cardio(:,{'DIABETES','BMI','GLUCOSE'}); % define dataset to use
```

Let's see if we're able to pick out diabetic patients from our data using k = 2:

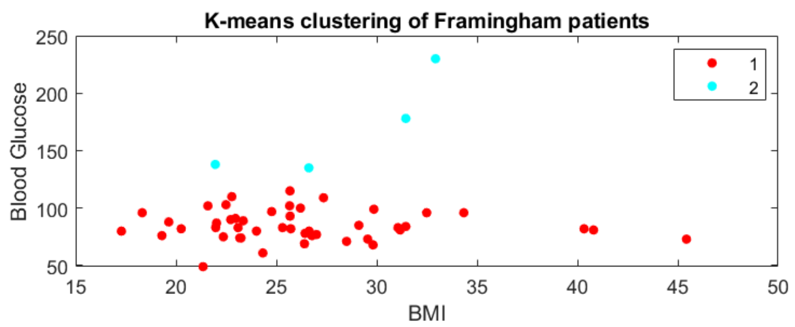
```
X = table2array(fram_kmeans);                       % numerical array of dataset
idx = kmeans(X,2);        % k-means clustering (idx = cluster identity)
s = silhouette(X,idx);                              % vector for silhouette values
s_score = mean(s)                                   % silhouette score
```

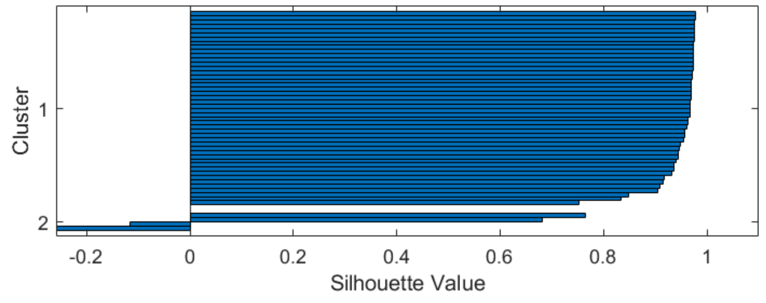
```
s_score = 0.8949
```

Let's visualize a scatter plot of our data clustered into 2 groups. We'll also look at the corresponding silhouette plot:

```
subplot(2,1,1)
gscatter(fram_kmeans.BMI,fram_kmeans.GLUCOSE,idx);  % scatter plot with cluster annotation
xlabel('BMI'); ylabel('Blood Glucose')              % add axis labels
title('K-means clustering of Framingham patients')  % add title
subplot(2,1,2)
```

```
silhouette(X,idx)                                          % silhouette plot
```





Question: Does one of our clusters correspond to diabetic patients?

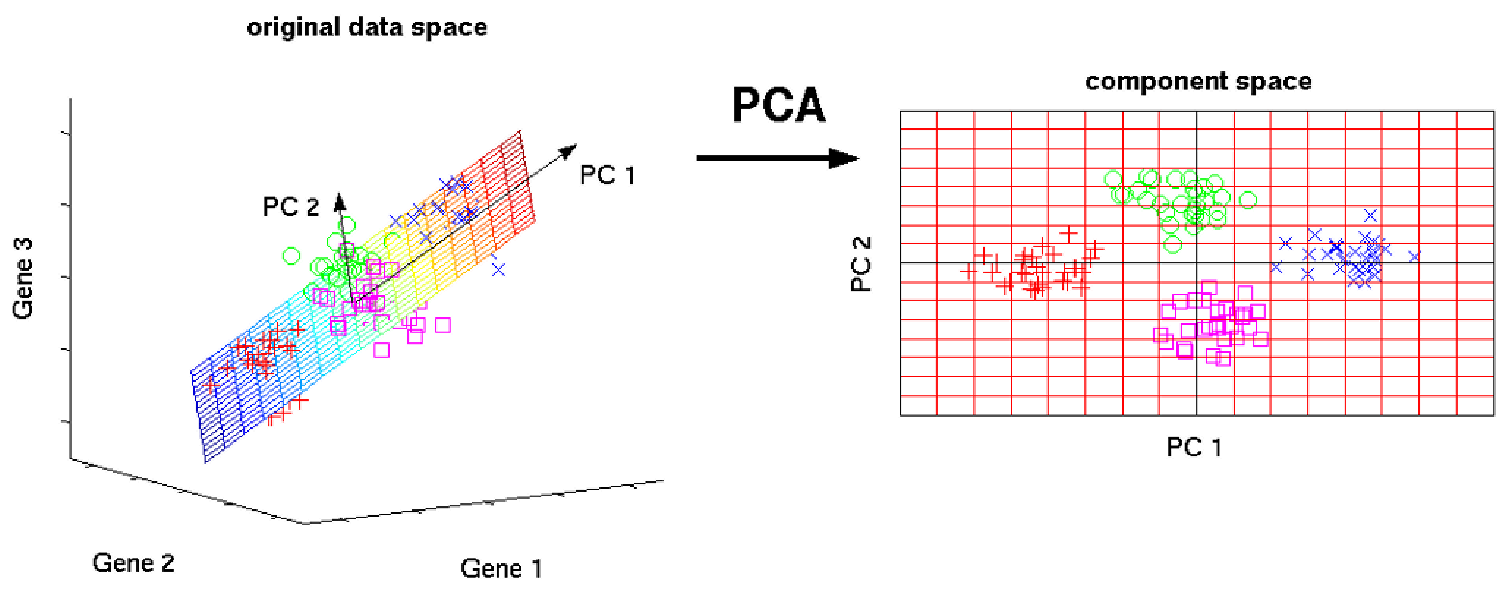
Activity: How can we modify the code above to apply k-means clustering for k = 3? How does the s_score value compare between k = 3 and k = 2?

Dimensionality Reduction - Representing the variability in the dataset in lower dimensions

Biomedical data is often tremendously large and highly complex. Thus, it's hard to interpret this data when considering all the information available. By applying **dimensionality reduction**, we can transform the data into a lower-dimension representation that is much easier to interpret. In this lesson, we'll go over one type of dimensionality reduction method known as **principal component analysis**, or **PCA**.

Principal Component Analysis

In PCA, an orthogonal linear transformation is applied to the data, projecting it onto a new coordinate system defined by principal components.



A **principal component (PC)** is a linear combination of the **features**, or descriptive variables, in the dataset. Note that the number of features dictates the number of PCs that are determined. In the image below, **P** represents the matrix of principal components that is used to linearly transform the original data (**X**) into a new representative data (**Y**) that can be visualized in a component space:

$$\underset{(m\times m)}{\mathrm{P}}\;\underset{(m\times n)}{\mathrm{X}} = \underset{(m\times n)}{\mathrm{Y}}$$

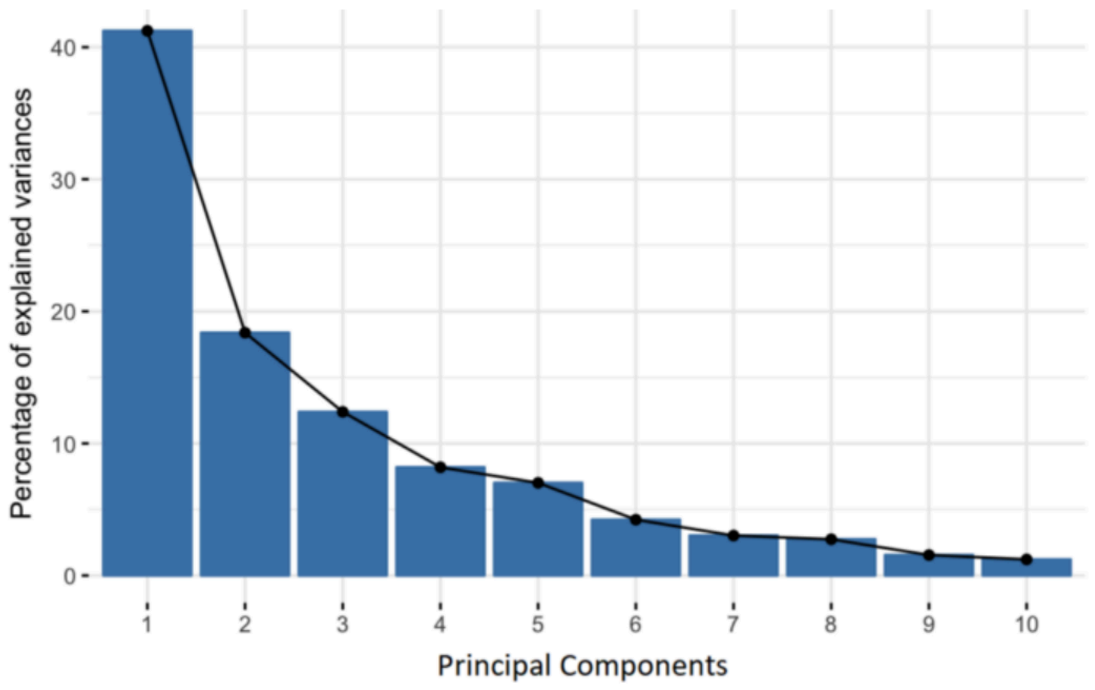
$$\mathrm{PX} = \begin{bmatrix} \mathbf{p}_1 \\ \vdots \\ \mathbf{p}_m \end{bmatrix} \begin{bmatrix} \mathbf{x}_1 & \cdots & \mathbf{x}_n \end{bmatrix} = \begin{bmatrix} \mathbf{p}_1 \cdot \mathbf{x}_1 & \cdots & \mathbf{p}_1 \cdot \mathbf{x}_n \\ \vdots & \ddots & \vdots \\ \mathbf{p}_m \cdot \mathbf{x}_1 & \cdots & \mathbf{p}_m \cdot \mathbf{x}_n \end{bmatrix}$$

in PCA, **P** (matrix of PCs) is typically determined by (1) **eigenvalue decomposition (EVD)** of the data covariance matrix, or (2) **singular vector decomposition (SVD)** of the data. For this lesson, we'll not delve into the specifics of how EVD or SVD is applied (for more information, refer to this link for EVD and this link for SVD).

Note: refer to the *pca* MATLAB documention for additional information on algorithms used for PCA.

Why do PCA?

The main goal when conducting PCA is to determine a reduced representation of the original data that can be visualized. This is done by determining a ranked list of linearly independent principal components that altogether describe the variance within the data. This list of PCs is ranked by decreasing percentage of variance explained, where the first PC explains the most variance, or is best representative, of the data. The figure below shows an example of how much variance each PC explains for a dataset with 10 features:



For the example shown above, we are able to represent ~60% of the variance using the first two PCs. In other words, if we were to plot the data based on PC1 and PC2, we would be visualizing a two-dimensional representation of the data that explains ~60% of the variance.

Note 1: Each PC is a linear combination of the features; thus, PCs differ in the **weights** (or coefficients) associated with the features. If a PC (e.g. PC1) can describe most of the variance in the data (> 50%), then we can evaluate the coefficients in this PC to see which feature(s) are most important (have the greatest absolute weight). In other words, the coefficient values for a PC can tell us which features are most responsible for the patterns seen in our data.

Note 2: As the new representations of the observations in the principal component space are linear combinations of the original variables (features), it's important to **normalize the data** before conducting PCA. This ensures a unit variance for all variables, thus allowing comparable contributions from all variables when the data is transformed. In other words, normalizing the data reduces any bias there might be for a particular feature.

In MATLAB, the *pca* function is used to perform PCA based on SVD. The *zscore* function can be used to normalize the data before doing PCA.

Example: applying PCA for the Framingham data

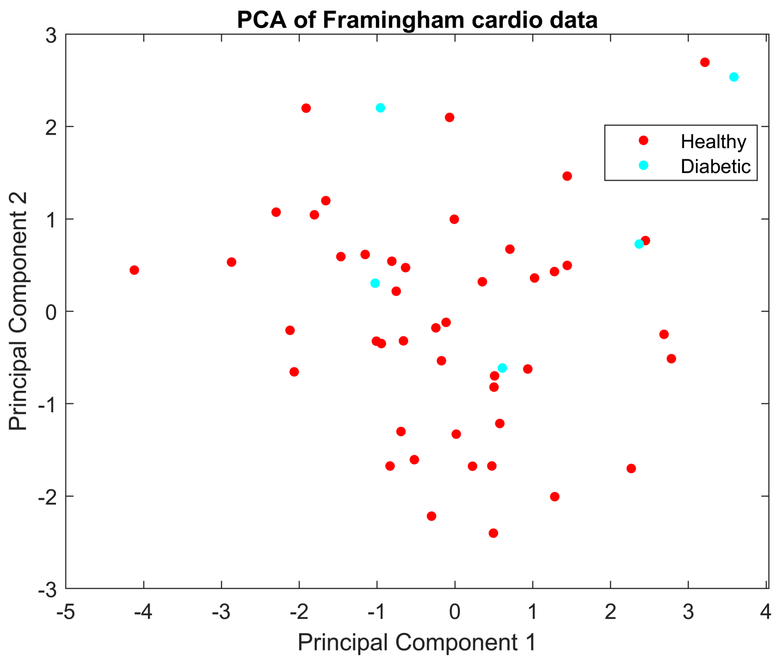
For this analysis, we'll consider the same dataset of cardiovascular measurements we used for hierarchical clustering. Recall that this dataset contains 8 measurements, or features. This means that we'll be determining 8 linearly independent PCs by peforming PCA. Let's first normalize this data, then determine the matrix of principal components (*coeff*), the matrix of the transformed data (*score*), and a vector for the variance explained by each PC:

```
% Normalize cardio data
norm_cardio_data = zscore(fram_cardio_data);
```

```
% Do PCA (coeff = PC matrix, score = transformed data, explained = variance explained)
[coeff, score, ~, ~, explained] = pca(norm_cardio_data);
```

Now we'll visualize our transformed data in the component space by plotting PC1 vs. PC2. We'll also use diabetes status to label our data:

```
% Visualize transformed data on PC1 vs. PC2 plot
figure
gscatter(score(:,1), score(:,2), diabetes_status)
xlabel('Principal Component 1')
ylabel('Principal Component 2')
title('PCA of Framingham cardio data')
```



For this dataset, we don't see clear separation of diabetic patients from healthy individuals. However, if we were to see any clustering patterns along a PC (e.g. PC1), then the coefficient values (weights) for this PC might tell us which features are responsible for the patterns we see. For the purposes of this lesson, let's check the coefficient matrix (*coeff*) to see which features contribute the most for PC1 and PC2:

```
% Assess coefficient values for PC1 and PC2
feature = col_names';                   % feature names (measurements)
pc1_coeff = coeff(:,1);                 % coefficient values for PC1
pc2_coeff = coeff(:,2);                 % coefficient values for PC2
table(feature, pc1_coeff, pc2_coeff)    % table of features matched to coefficient values
```

```
ans = 8×3 table
```

	feature	pc1_coeff	pc2_coeff
1	'DIABP'	0.4975	0.3172
2	'SYSBP'	0.4259	0.4640
3	'BMI'	0.3080	0.1195

	feature	pc1_coeff	pc2_coeff
4	'HEARTRTE'	0.0865	0.4261
5	'HDLC'	0.0825	-0.2129
6	'GLUCOSE'	0.0080	0.2654
7	'LDLC'	-0.4784	0.4603
8	'TOTCHOL'	-0.4827	0.4007

Lastly, we can inspect our *explained* vector to see how much variance is explained by each PC:

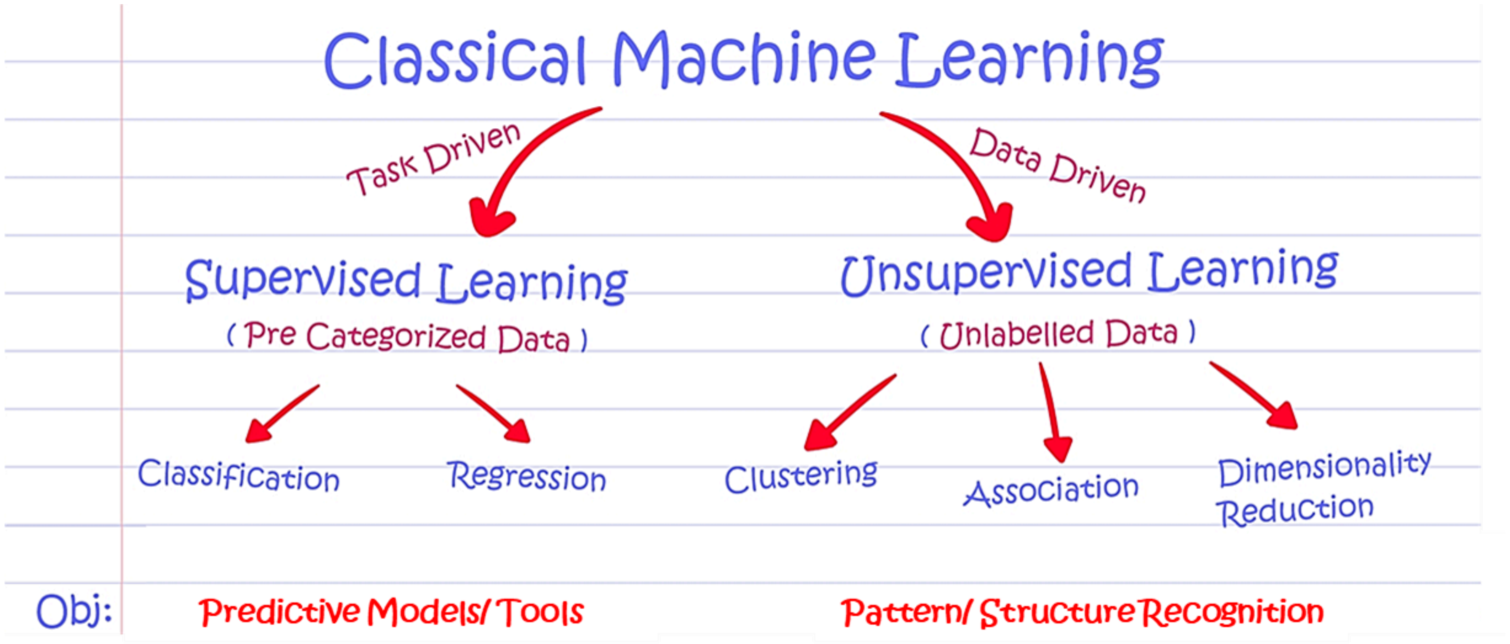
```
disp(explained)
```

```
   32.3024
   19.2774
   15.7793
   12.9420
   10.7258
    6.7674
    1.6609
    0.5448
```

Question: How much variance is exlained by PC1 and PC2?

Unsupervised vs. Supervised Learning

All of the methods discussed in this lesson serve as applications for unsupervised learning. In machine learning, we can also process data using **supervised learning**, where information on the output data (e.g. labels) is considered during the learning process. While unsupervised learing is used for data exploration, supervised learning is typically used to train and develop predictive or classification tools based on labeled data.



Summary

- Unsupervised learning allows us to infer information about a dataset without any user guidance based on underlying similarities and patterns
- Common applications of unsupervised learning to analyze biomedical data include clustering (hierarchical, k-means) and dimensionality reduction (principal component analysis)
- Hierarchical clustering involves a "bottom-up" approach, whereas k-means clustering applies a "top-down" approach, to assign data into groups
- Principal component analysis (PCA) allows us to transform highly complex data into lower-dimension representations that are easier to interpret
- In contrast to unsupervised learning, supervised learning includes information on the output variables (e.g. labels) that can be used to train and develop predictive or classification tools

Built-in MATLAB functions covered in this lesson:

• *pdist:*	quantifies similarity using a distance metric (e.g. Euclidean, correlation)
• *clustergram:*	performs hierarchical clustering
• *kmeans:*	performs k-means clustering
• *silhouette:*	calculates silhouette values and generates a silhouette plot for k-means clustering
• *pca:*	performs principal component analysis (PCA)
• *zscore:*	normalizes each column in a matrix to have mean 0 and standard deviation of 1

References for additional information:

- Eigenvalue Decomposition (EVD)
- Singular Vector Decomposition (SVD)