BIOS 7747: Machine Learning for Biomedical Applications

Feature exploration, pre-processing and normalization

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Outline

- Data cleaning and exploration
- Feature distributions
- Feature interactions
- Mitigating outlier effects and multicolinearity
- Feature scaling

Outline

- ❑ Data cleaning and exploration
- ❑ Feature distributions
- ❑ Feature interactions
- ❑ Mitigating outlier effects and multicolinearity
- ❑ Feature scaling

Feature exploration and data cleaning

❑ Types of features:

<u>Numerical</u>

- Continuous
- Discrete

<u>Categorial</u>

- Ordinal
- Nominal

Feature exploration and data cleaning

❑ Data cleaning: encoding categorical variables

- Label encoding (sklearn.preprocessing.LabelEncoder)

Cancer stage	Encoded value
Stage I	0
Stage II	1
Stage III	2

Often not recommended

- Distances cannot be assumed in most ordinal variables
- Order cannot be assumed in nominal variables

Feature exploration and data cleaning

❑ Data cleaning: encoding categorical variables

- One hot encoding (sklearn.preprocessing.OneHotEncoder)

Sample	Cancer stage
0	Stage III
1	Stage I
2	Stage II

Sample	Stage I	Stage II	Stage III
0	0	0	1
1	1	0	0
2	0	1	0

It can increase substantially the number of features:

$$M = M_{numerical} + \sum_{\forall i \in categorical} N_{classes}^{i}$$

Feature exploration and data cleaning

❑ Data cleaning: encoding categorical variables

- Binary encoding: every feature is coded as a binary number with a fixed number of digits. Each digit is a feature to consider in the model.

Sample	Cancer stage
0	Stage III
1	Stage I
2	Stage II

Sample	Feature 1	Feature 2
0	1	0
1	0	0
2	0	1

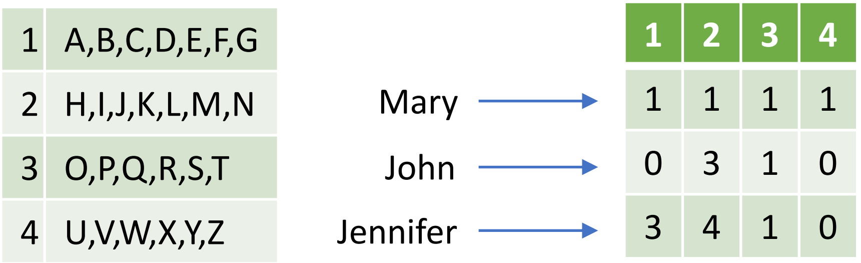
It requires less features than one-hot-encoding

$$M = M_{numerical} + \sum_{\forall i \in categorical} \log_2\left(N^{i}_{classes}\right)$$

Feature exploration and data cleaning

❑ Data cleaning: encoding categorical variables

- Feature hashing: Convert labels to “words” with predefined fixed size



1	A,B,C,D,E,F,G
2	H,I,J,K,L,M,N
3	O,P,Q,R,S,T
4	U,V,W,X,Y,Z

Hash function

	1	2	3	4
Mary	1	1	1	1
John	0	3	1	0
Jennifer	3	4	1	0

Great to standardize representations using low number of variables

Feature collision may happen

Feature exploration and data cleaning

❑ Data cleaning: Missing values

- Common reasons:
  - Incomplete data (e.g., prefer not to answer, data transfer errors)
  - Human error (e.g., forgot to annotate, incorrect annotations)
  - Study design (e.g., data does not apply

- Classification [D.B. Rubin, 1976]

  - Missing completely at random (MCAR): missing values are not related to the observations (the probability of having missing value is equation for all samples). Unusual in biomedicine.

  - Missing at random (MAR): the probability of missing value is a function of another variable (e.g., male are less likely to answer about mental health questions in a survey).

  - Missing not at random (MNAR): there is no insight about the probability of missing data.

Feature exploration and data cleaning

- Data cleaning: Missing values
  - **Sample dropping** (Pandas’ *dropna()* function):
    - MCAR: it may not affect predictions when “sufficient” data are available
      - But it may result in insufficient data
    - MAR: it can introduce biases that could potentially be identified
      - Example: male do not have mental illness problems
    - MNAR: it can introduce biases that are hard to identify

Feature exploration and data cleaning

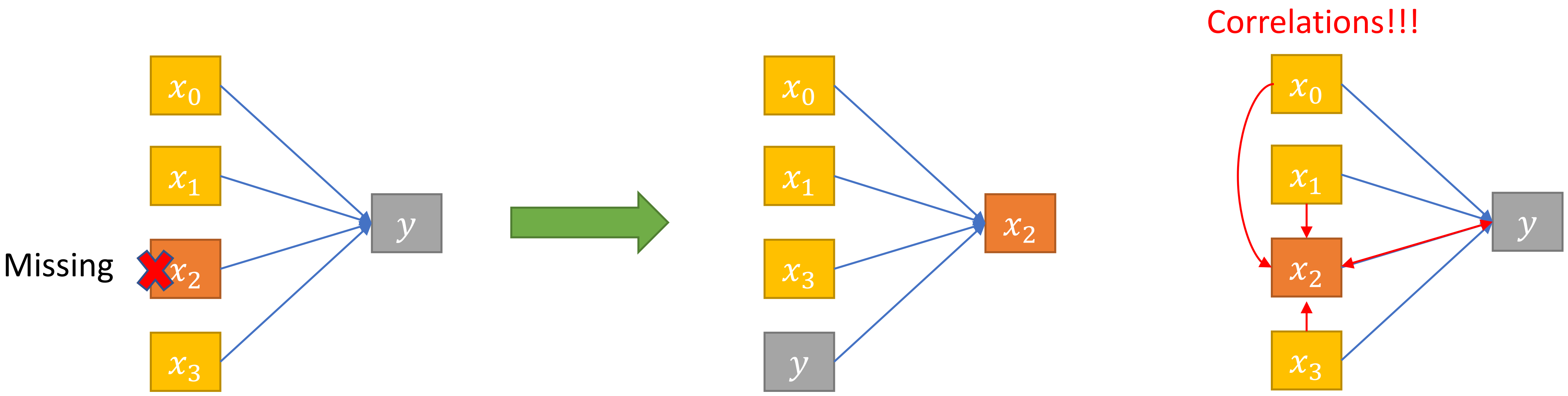
❑ Data cleaning: Missing values

- **Data imputation** (*sklearn.impute*)
  - Normal imputation: most likely value assuming a normal distribution
    - Numerical data: mean / median value
    - Categorial data: mode
  - Class label imputation: normal imputation using same-class samples
  - Model-based imputation: two-step approach
    1. Train a model to predict the missing value using samples with non-missing values
    2. Predict the missing values

Feature exploration and data cleaning

❑ Data cleaning: Missing values

- **Data imputation**
  - Model-based imputation (ext.): regression



Feature exploration and data cleaning

❑ Data cleaning: Missing values

- **Data imputation**
  - Model-based imputation (ext.):
    - Multiple imputation by chained equations (MICE)

      1. Perform a simple imputation (e.g., mean, median, mode)

      2. For each cycle *c*:
         - For each variable *v* with missing values (ascending order based on number of missing values):

           2.a. Use all variables except for *v* to predict the dependent values *y*

           2.b. Update previously missing values for *v* using a model trained with all other variables

      3. Evaluate convergence criterion (e.g., number of iterations, convergence of variable distributions…)

    - K-Nearest Neighbors and other clustering techniques

Feature exploration and data cleaning

❑ Data cleaning: Missing values

- **Incorporating missing values in model**
  - Adding a present/missing value feature k

Variable with missing values

$$y = \theta_0 + \theta_1 x_0 + \theta_2 x_1 + k\theta_2 x_2 + \theta_3 x_3$$

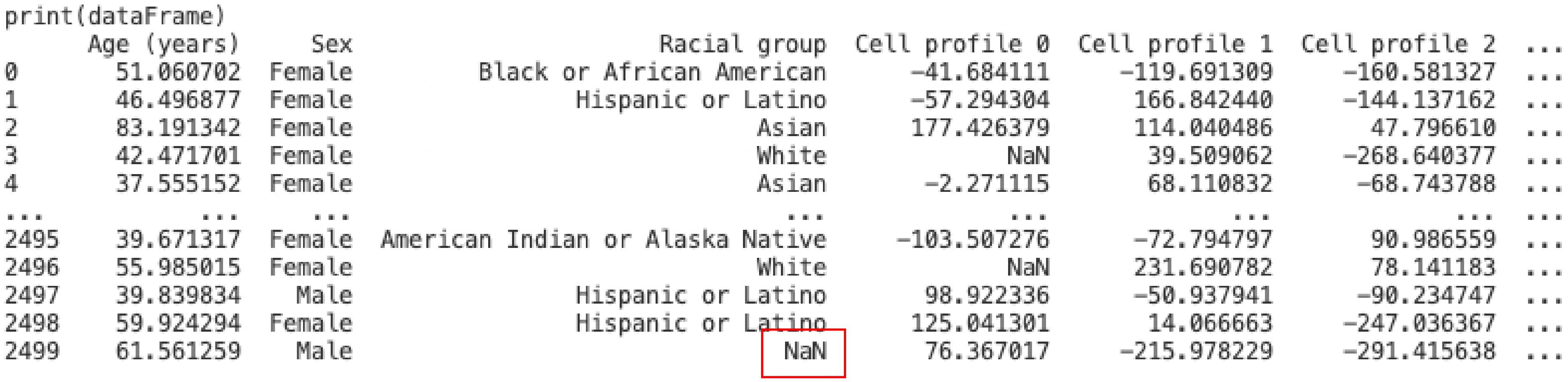
  - The zero contribution to the gradient from missing parameters in a group of samples may bias the optimization algorithm

<u>Note</u>: missing values may not seem like they are missing

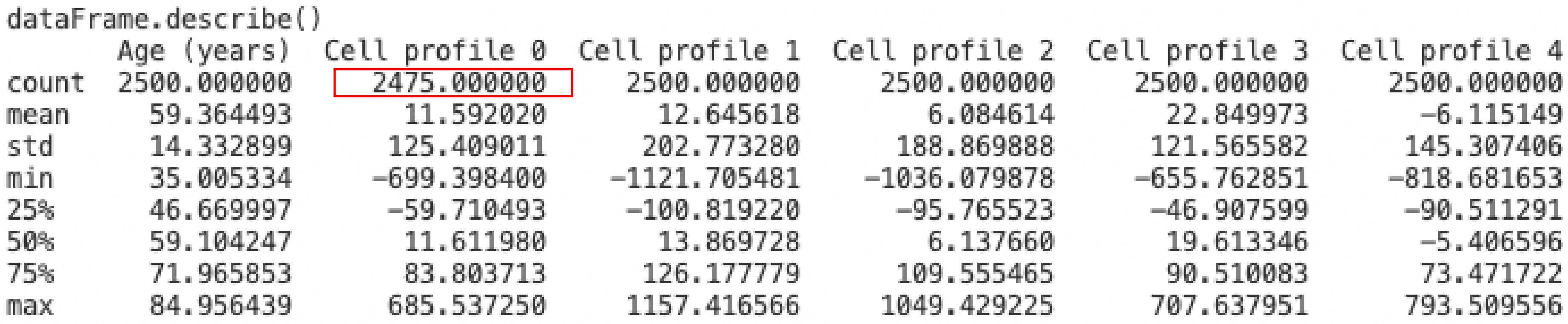
  - Datasets often present values of 0 or default value instead of n/a or empty.
  - Comprehensive visual data exploration is important before automated analysis.

Feature exploration and data cleaning

- Data exploration (with Pandas): data summary



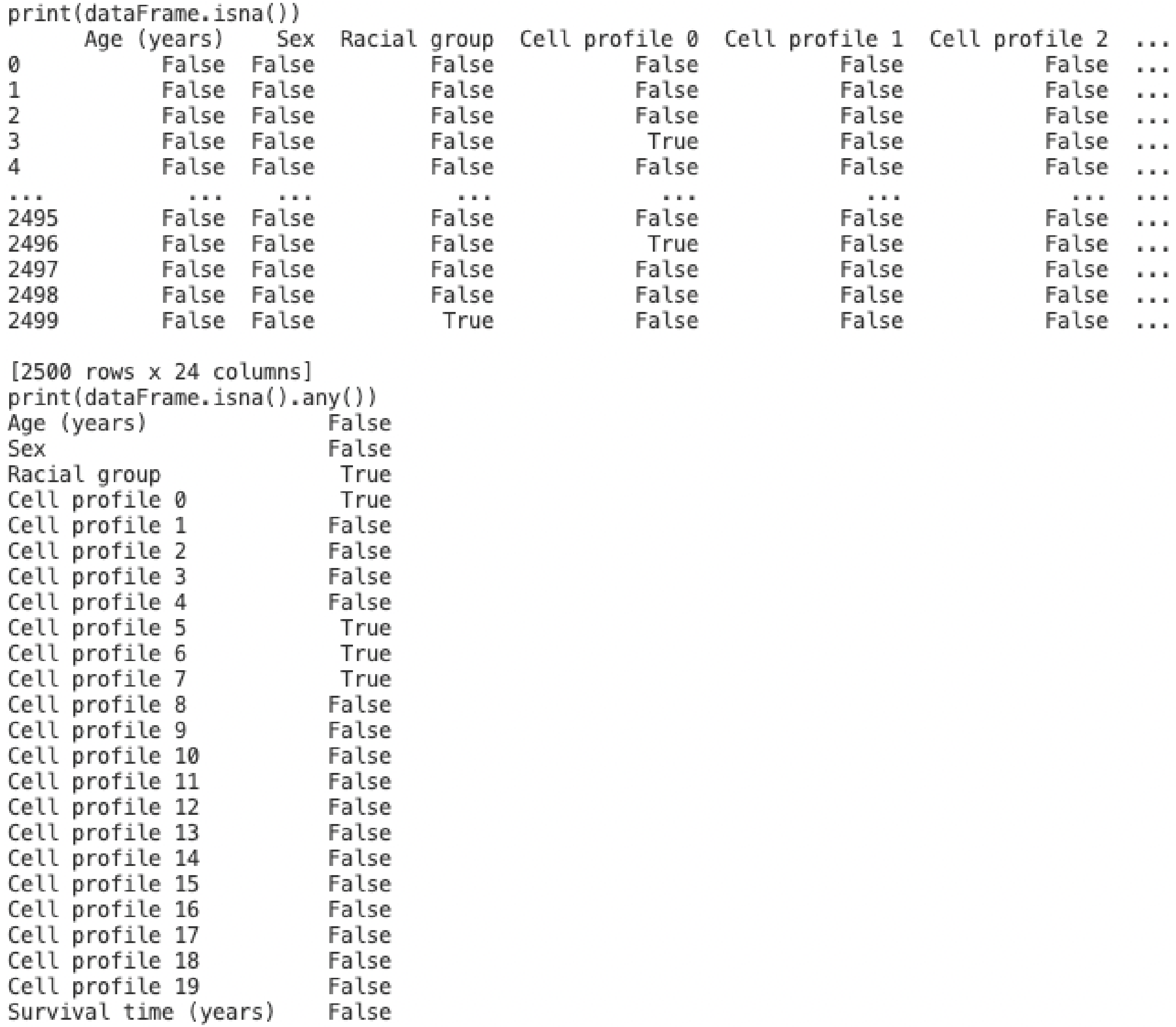
```
print(dataFrame)
      Age (years)     Sex                       Racial group  Cell profile 0  Cell profile 1  Cell profile 2  ...
0       51.060702  Female          Black or African American      -41.684111     -119.691309     -160.581327  ...
1       46.496877  Female                 Hispanic or Latino      -57.294304      166.842440     -144.137162  ...
2       83.191342  Female                              Asian      177.426379      114.040486       47.796610  ...
3       42.471701  Female                              White             NaN       39.509062     -268.640377  ...
4       37.555152  Female                              Asian       -2.271115       68.110832      -68.743788  ...
...           ...     ...                                ...             ...             ...             ...  ...
2495    39.671317  Female   American Indian or Alaska Native     -103.507276      -72.794797       90.986559  ...
2496    55.985015  Female                              White             NaN      231.690782       78.141183  ...
2497    39.839834    Male                 Hispanic or Latino       98.922336      -50.937941      -90.234747  ...
2498    59.924294  Female                 Hispanic or Latino      125.041301       14.066663     -247.036367  ...
2499    61.561259    Male                                NaN       76.367017     -215.978229     -291.415638  ...
```



```
dataFrame.describe()
       Age (years)  Cell profile 0  Cell profile 1  Cell profile 2  Cell profile 3  Cell profile 4
count  2500.000000     2475.000000     2500.000000     2500.000000     2500.000000     2500.000000
mean     59.364493       11.592020       12.645618        6.084614       22.849973       -6.115149
std      14.332899      125.409011      202.773280      188.869888      121.565582      145.307406
min      35.005334     -699.398400    -1121.705481    -1036.079878     -655.762851     -818.681653
25%      46.669997      -59.710493     -100.819220      -95.765523      -46.907599      -90.511291
50%      59.104247       11.611980       13.869728        6.137660       19.613346       -5.406596
75%      71.965853       83.803713      126.177779      109.555465       90.510083       73.471722
max      84.956439      685.537250     1157.416566     1049.429225      707.637951      793.509556
```

Feature exploration and data cleaning

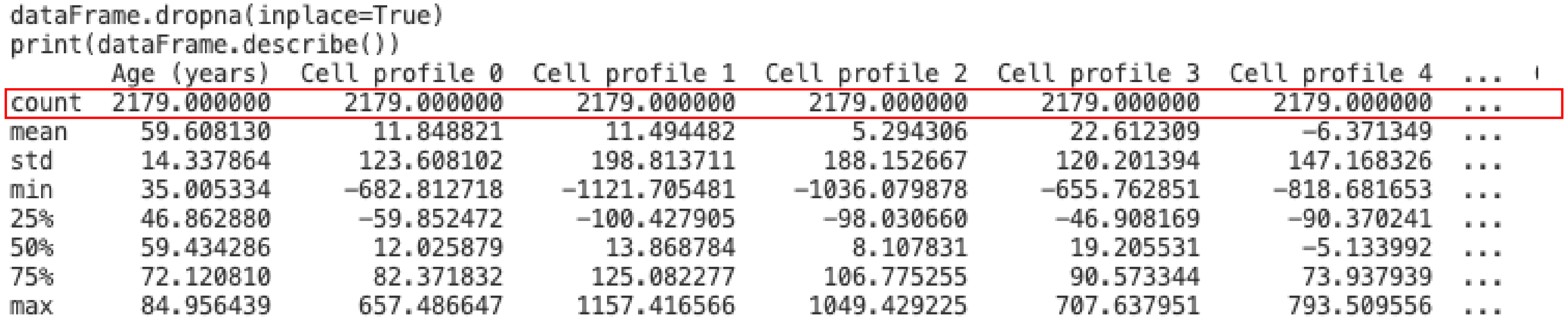
- Data exploration (with Pandas): missing values



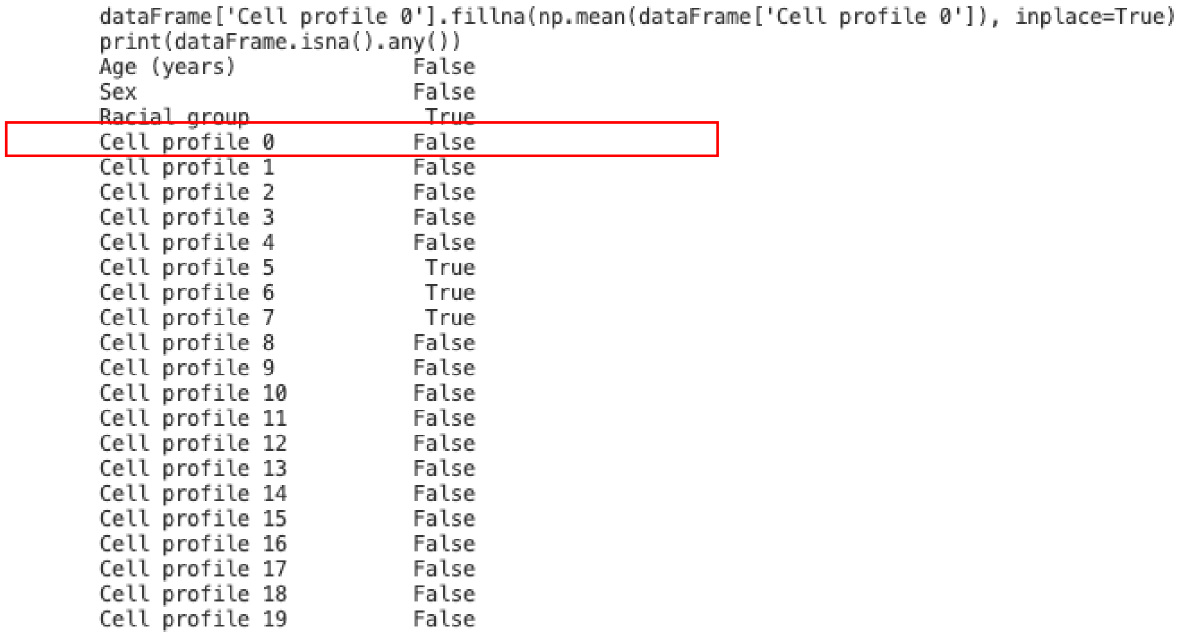
```
print(dataFrame.isna())
      Age (years)    Sex  Racial group  Cell profile 0  Cell profile 1  Cell profile 2  ...
0           False  False         False           False           False           False  ...
1           False  False         False           False           False           False  ...
2           False  False         False           False           False           False  ...
3           False  False         False            True           False           False  ...
4           False  False         False           False           False           False  ...
...           ...    ...           ...             ...             ...             ...  ...
2495        False  False         False           False           False           False  ...
2496        False  False         False            True           False           False  ...
2497        False  False         False           False           False           False  ...
2498        False  False         False           False           False           False  ...
2499        False  False          True           False           False           False  ...

[2500 rows x 24 columns]
print(dataFrame.isna().any())
Age (years)               False
Sex                       False
Racial group               True
Cell profile 0             True
Cell profile 1            False
Cell profile 2            False
Cell profile 3            False
Cell profile 4            False
Cell profile 5             True
Cell profile 6             True
Cell profile 7             True
Cell profile 8            False
Cell profile 9            False
Cell profile 10           False
Cell profile 11           False
Cell profile 12           False
Cell profile 13           False
Cell profile 14           False
Cell profile 15           False
Cell profile 16           False
Cell profile 17           False
Cell profile 18           False
Cell profile 19           False
Survival time (years)     False
```

Feature exploration and data cleaning

- Data exploration (with Pandas): missing values



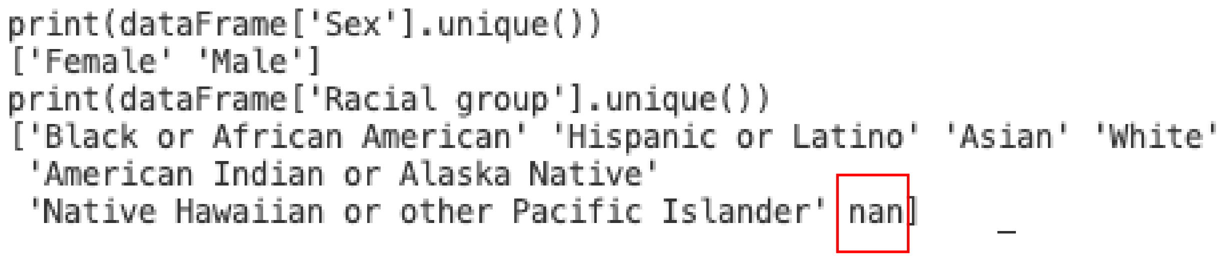
```
dataFrame.dropna(inplace=True)
print(dataFrame.describe())
        Age (years)  Cell profile 0  Cell profile 1  Cell profile 2  Cell profile 3  Cell profile 4  ...
count   2179.000000     2179.000000     2179.000000     2179.000000     2179.000000     2179.000000  ...
mean      59.608130       11.848821       11.494482        5.294306       22.612309       -6.371349  ...
std       14.337864      123.608102      198.813711      188.152667      120.201394      147.168326  ...
min       35.005334     -682.812718    -1121.705481    -1036.079878     -655.762851     -818.681653  ...
25%       46.862880      -59.852472     -100.427905      -98.030660      -46.908169      -90.370241  ...
50%       59.434286       12.025879       13.868784        8.107831       19.205531       -5.133992  ...
75%       72.120810       82.371832      125.082277      106.775255       90.573344       73.937939  ...
max       84.956439      657.486647     1157.416566     1049.429225      707.637951      793.509556  ...
```



```
dataFrame['Cell profile 0'].fillna(np.mean(dataFrame['Cell profile 0']), inplace=True)
print(dataFrame.isna().any())
Age (years)                False
Sex                        False
Racial group                True
Cell profile 0             False
Cell profile 1             False
Cell profile 2             False
Cell profile 3             False
Cell profile 4             False
Cell profile 5              True
Cell profile 6              True
Cell profile 7              True
Cell profile 8             False
Cell profile 9             False
Cell profile 10            False
Cell profile 11            False
Cell profile 12            False
Cell profile 13            False
Cell profile 14            False
Cell profile 15            False
Cell profile 16            False
Cell profile 17            False
Cell profile 18            False
Cell profile 19            False
```

Feature exploration and data cleaning

- Data exploration (with Pandas): categorial variables



```
print(dataFrame['Sex'].unique())
['Female' 'Male']
print(dataFrame['Racial group'].unique())
['Black or African American' 'Hispanic or Latino' 'Asian' 'White'
 'American Indian or Alaska Native'
 'Native Hawaiian or other Pacific Islander' nan]
```

Outline

- ❑ Data cleaning and exploration
- ❑ Feature distributions
- ❑ Feature interactions
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- ❑ Feature scaling

Feature distributions

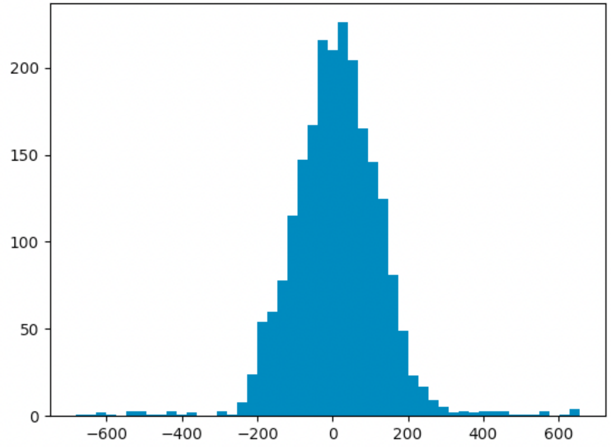
Information Visualization (BIOS 7719)

❑ Numerical features

- Quantitative values: mean, median, IQR, standard deviation, range… (numpy)

- Visualizations (matplotlib.pyplot as plt):

```
plt.hist(dataFrame['Cell profile 0'], bins=50)
plt.show()
```



- Testing normality:
  - Shapiro-Wilk test (scipy.stats) or other available tests

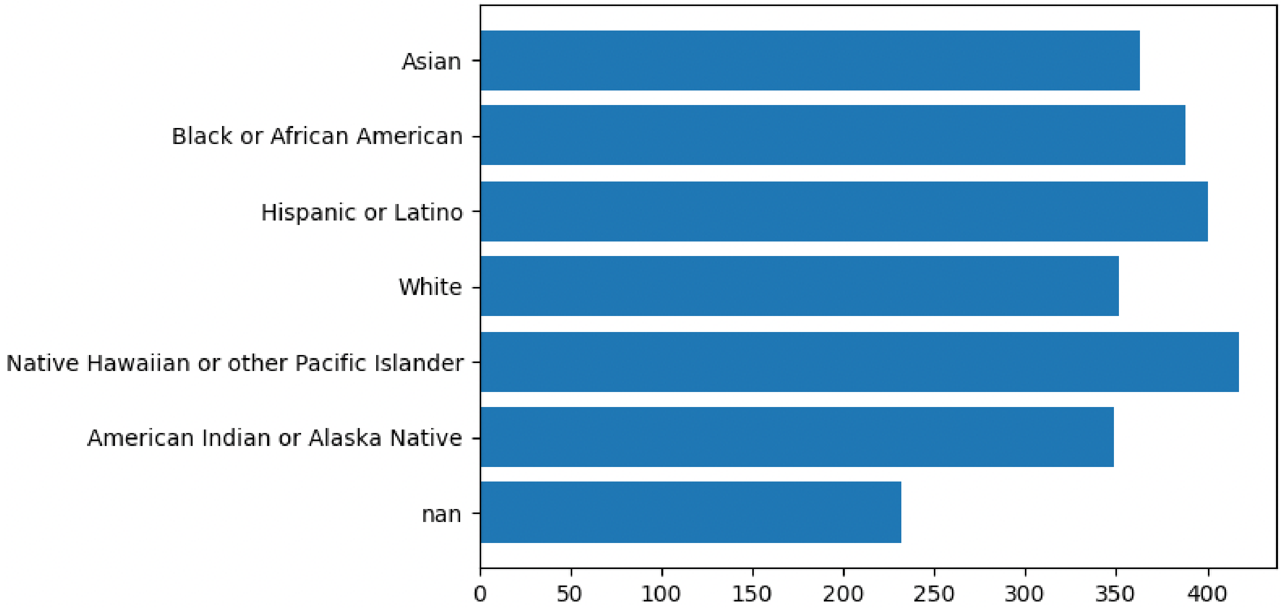
```
print(scipy.stats.shapiro(dataFrame['Cell profile 0']))
ShapiroResult(statistic=0.9458088278770447, pvalue=1.3563603337555129e-27)
```

  - Often data are only normally distributed for specific subgroups of samples

Feature distributions

- Categorical features

```
raceLabels = list(set(dataFrame['Racial group']))
raceCounts = [list(dataFrame['Racial group']).count(c) for c in raceLabels]
raceLabels[raceLabels==np.nan] = 'nan’ # Converting to string
plt.barh(raceLabels, raceCounts)
plt.show()
```



Feature distributions

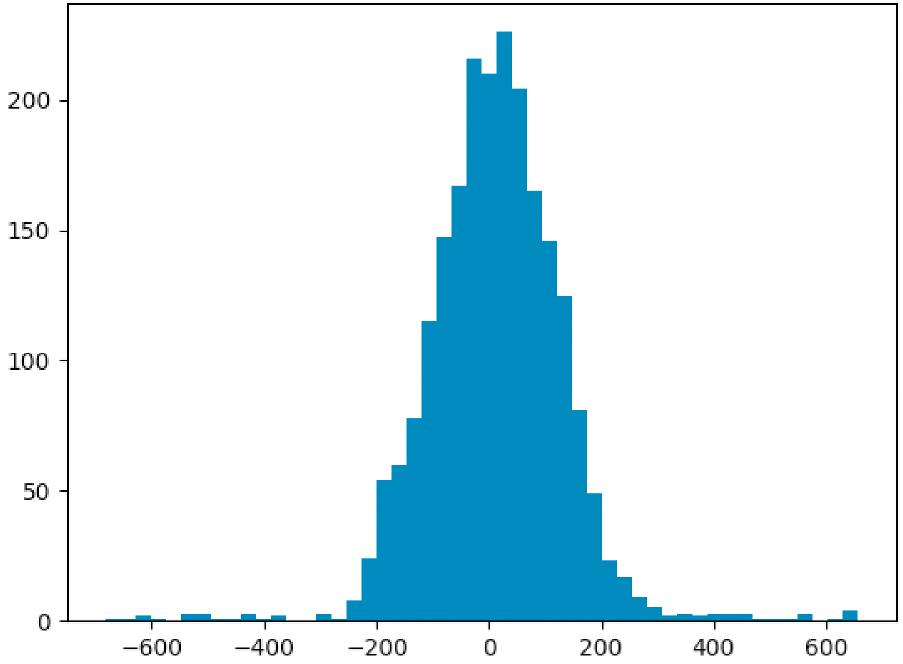
❑ Outliers

- Observations that do not follow the overall patterns in the population
- They can bias the training process and lead towards suboptimal models
- Types:
  - Natural: realistic/plausible observations that are uncommon
  - Error:
    - Data entry (human)
    - Measurement (instrument)
    - Experimental (extraction or execution)
    - Sampling (source of information)

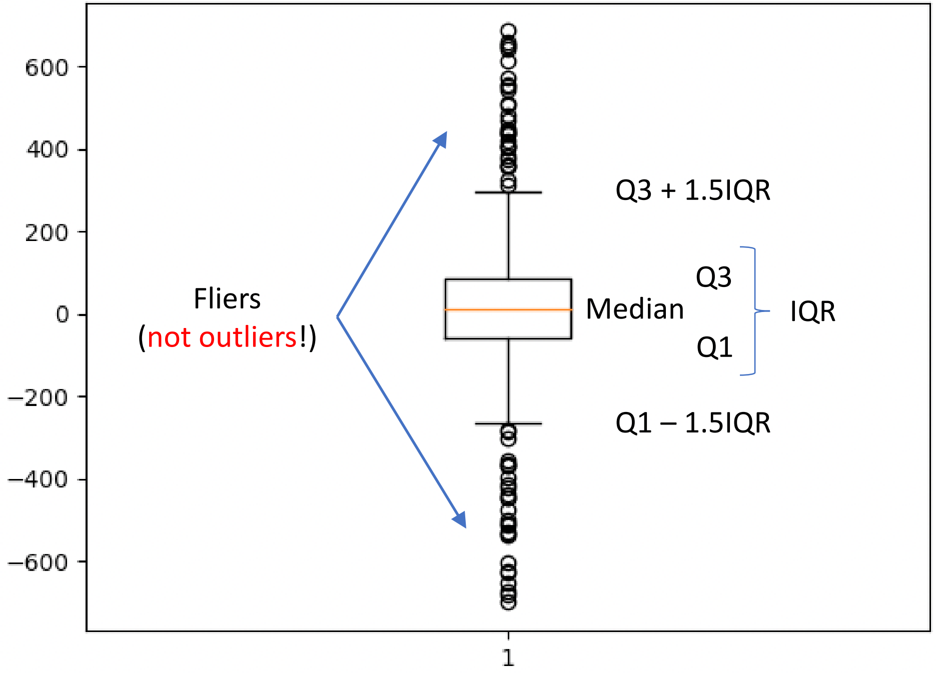
Feature distributions

❑ Outliers

- First step for outlier identification is visualization



```
plt.hist(dataFrame['Cell profile 0'], bins=50)
plt.show()
```



```
plt.boxplot(dataFrame['Cell profile 0’])
plt.show()
```

Feature distributions

❑ Identifying outliers

- *z*-score: assumes normal data distributions. A threshold must be established, usually ≥ 3.

$$z = \frac{x - \mu}{\sigma}$$

- Thomson's Tau test: Rejection interval: $z \leq \dfrac{t_{\alpha/2}(n-1)}{\sqrt{n}\sqrt{n-2+t^2_{\alpha/2}}}$

Critical value from Student's t distribution

- Tukey's "fences": $[Q_1 - k * (Q_3 - Q_1), Q_3 + k * (Q_3 - Q_1)]$
  - For $k = 1.5$: outliers. For 3: extreme values.

- Clustering methods: e.g., KNN, DBScan

[Martin et al, A density-based algorithm for discovering clusters in large spatial databases with noise. AAAI Press. pp. 226–231, 1996]

Feature distributions

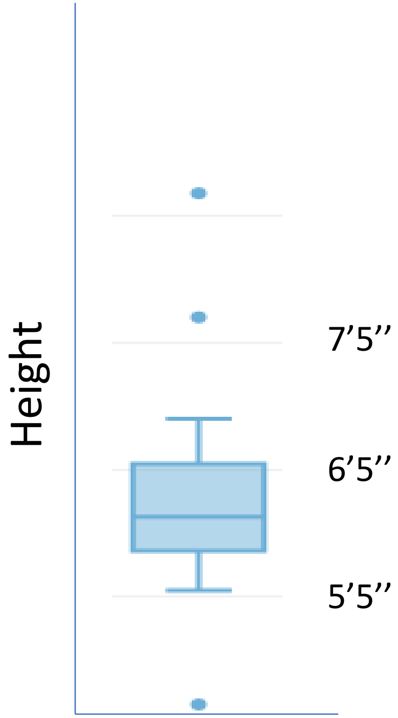
❑ Outliers

- Distinction between natural and error outliers in biomedicine is very important
- Underrepresented cases often appear as natural outliers of the normative population
  - There is a high risk of creating biased methods that discriminate specific populations
- Outlier treatment:
  - Natural outliers: highly encouraged to consider in model training. Consider creating separate models.
  - Error outliers:
    - Remove samples: when very extreme values are found or when multiple variables are affected.
    - Use data imputation techniques: when one or a very small percentage of features are affected in a small percentage of samples.

Feature distributions

❑ Outliers

- There are no robust methods to identify the outlier type and ensure a model free of biases
    - Understanding the dataset is essential



College students?

Basketball team?

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Feature interactions

❑ Feature interactions

- Multicollinearity: when an “independent” feature can be predicted to a degree from other independent features.

- Why is it a problem?

  - Linear regression: $\boldsymbol{X} = \begin{pmatrix} 1 & x_0^{(0)} & \dots & x_{M-1}^{(0)} \\ \vdots & & & \vdots \\ 1 & x_0^{(N-1)} & \dots & x_{M-1}^{(N-1)} \end{pmatrix}$ If columns are correlated, the rank of $\boldsymbol{X}$ is lower than $\boldsymbol{M} + \boldsymbol{1}$. Hence, $\boldsymbol{X}\boldsymbol{X}^T$ does not have an inverse.

  - Individual relationships between the dependent and independent variables cannot be recovered.

$f(x_0, x_1) = \alpha x_0 + \beta x_1$ and $x_0 = \gamma x_1$, then: $f(x_0, x_1) = \alpha x_0 + \beta x_1 = \frac{1}{N}\alpha x_0 + N\beta x_1$

Feature interactions

❑ Detection:

- Coefficients associated with correlated variables usually have high standard errors
- No significant contribution (or extreme contribution) of one variable to the regression model <u>may</u> indicate a collinearity (note that it may also mean lack of correlation or extreme correlation with predicted variable)
- Correlation matrix:
  - It can only evaluate pair-wise relationships and multicollinearity often involves several features.
- Variance inflation factor for predictor j : $\mathrm{VIF_j} = \frac{1}{1-R_j^2}$
  - A value over 5 <u>may</u> indicate collinearity
- High condition number

[O’Brien, R. M. (2007). "A Caution Regarding Rules of Thumb for Variance Inflation Factors". *Quality & Quantity*. **41** (5): 673–690]

Feature interactions

❑ What to do?

- Multicollinearity does not necessarily bias the predictions but their explanation (the contribution from the colinear variables).
- Feature dropping: may cause loss of information (lower predictive accuracy) in exchange for more significant coefficient values.
- Data transformations:
  - Transform the data to a new space where features are uncorrelated.
  - Example: principal component regression:
    - We will see PCA later in the course

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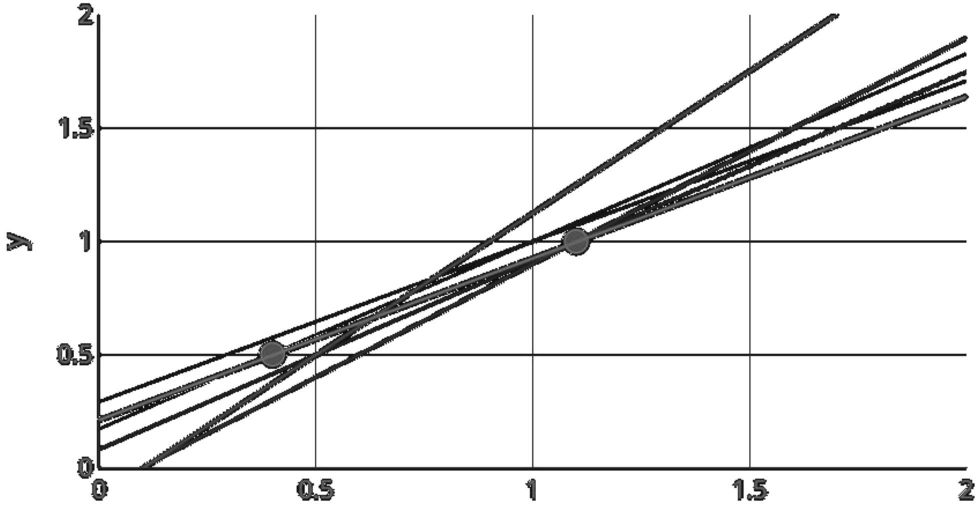
Mitigating multicollinearity and outlier values

- Regularization:
  - Can reduce the effect of both outliers and multicollinearity
  - L2-regularization (aka Ridge)

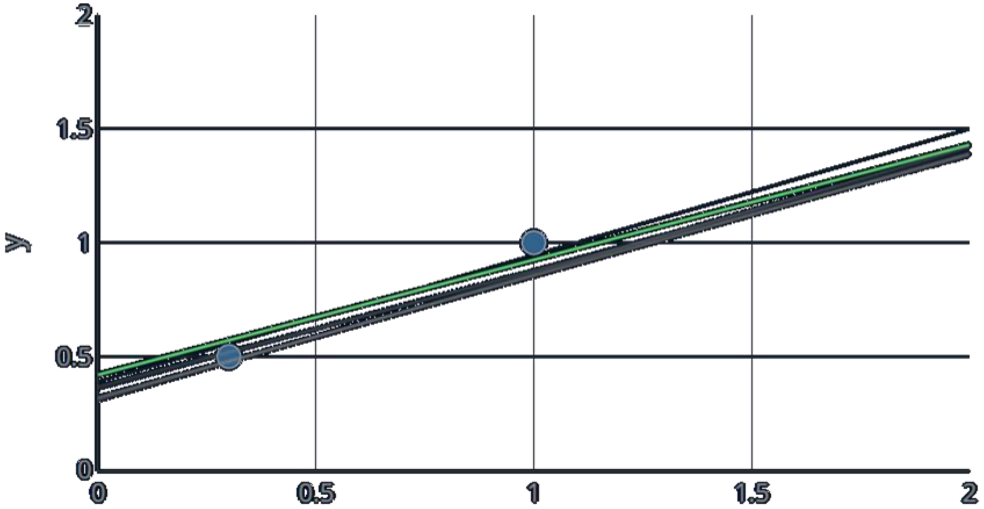
$$\frac{\partial}{\partial \boldsymbol{\theta}} J(\boldsymbol{\theta}) = \frac{\partial}{\partial \boldsymbol{\theta}} \frac{1}{2}\left((\boldsymbol{X\theta} - \boldsymbol{y})^T(\boldsymbol{X\theta} - \boldsymbol{y}) + \alpha\theta^T\theta\right)$$

$$\boldsymbol{\theta} = \left(\boldsymbol{X}^T\boldsymbol{X} + \alpha I_M\right)^{-1}\boldsymbol{X}^T\boldsymbol{y}$$

Promotes low parameter values, which tends to prevent extreme effects from independent variables



Without regularization



With L2-regularization

Mitigating multicollinearity and outlier values

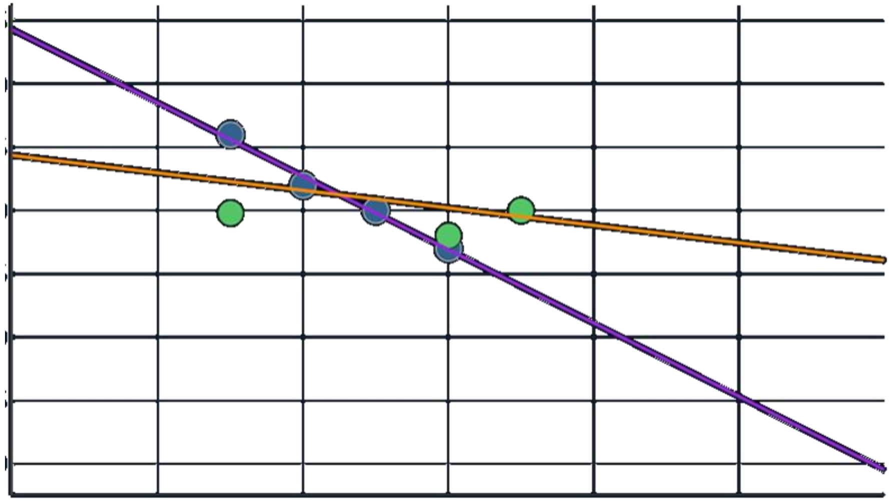
❑ Regularization:

- L1-regularization (aka Lasso)
  - Its origin comes from the introduction of a **soft** threshold to parameters estimates in linear regression

$$\boldsymbol{\theta} = \arg\min\left\{\frac{1}{2}(\boldsymbol{X\theta} - \boldsymbol{y})^T(\boldsymbol{X\theta} - \boldsymbol{y})\right\} \;\; \text{s.t.}\, \|\boldsymbol{\theta}\|_1 \leq t$$

$$\boldsymbol{\theta} = \arg\min\left\{\frac{1}{2}(\boldsymbol{X\theta} - \boldsymbol{y})^T(\boldsymbol{X\theta} - \boldsymbol{y}) + \alpha\|\boldsymbol{\theta}\|_1\right\}$$

Lagrangian form (we will see Lagrange multipliers later in the course)



Circles:

- Purple: training
- Green: test

Lines:

- Purple: MSE
- Orange: L1

Mitigating multicollinearity and outlier values

❑ Regularization

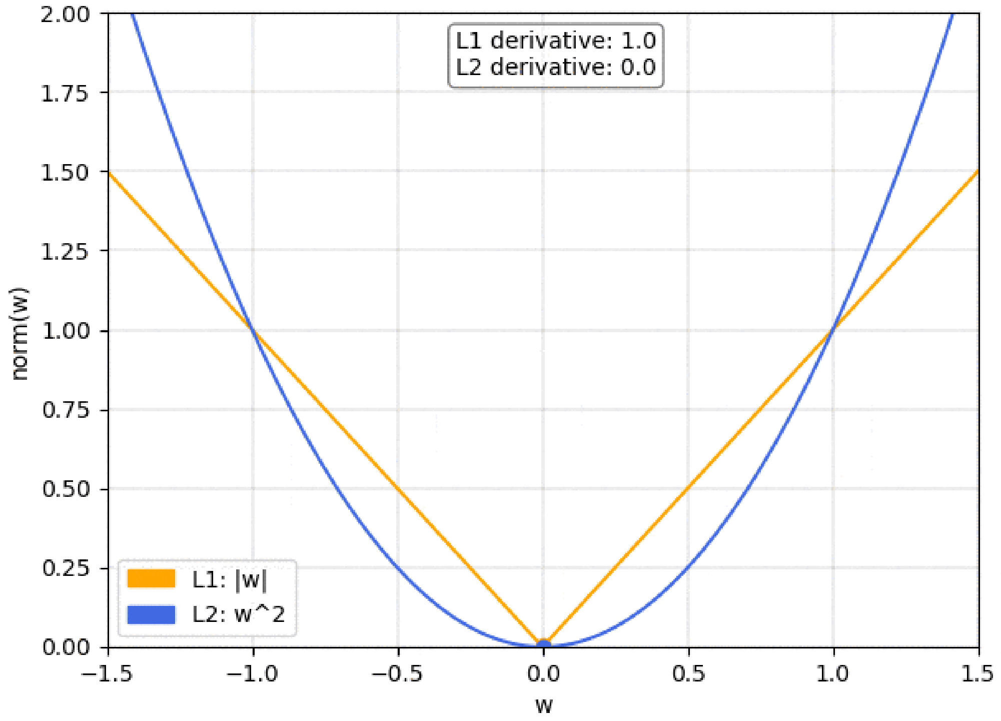
- L2: the gradient depends on the value of each coefficient
  - Coefficients with higher values will provide gradients with higher magnitude.
  - Gradient descent optimization will prioritize decreasing the value of coefficients with higher values
- L1: the gradient is constant and the same for all coefficients
  - Coefficients with lower values tend to be zeroed first
  - Zeroing coefficients is equivalent to feature selection… but coefficients with lower magnitude will tend to be eliminated first.

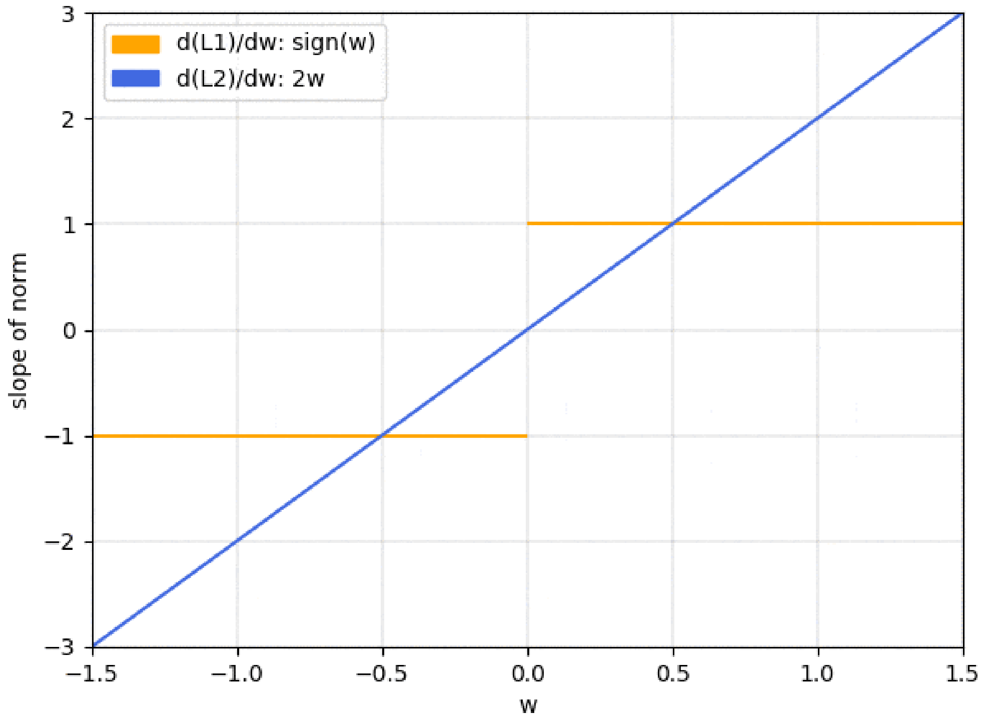
Mitigating multicollinearity and outlier values

- ❑ Regularization
  - Gradients: L2 vs. L1 regularization term

L2 $$\frac{1}{2}\alpha\,\frac{\partial\sum\theta_i^2}{\partial\theta_j}=\alpha\theta_j$$

L1 $$\alpha\,\frac{\partial\sum|\theta_i|}{\partial\theta_j}=\alpha\ \mathrm{sign}\left(\theta_j\right)$$



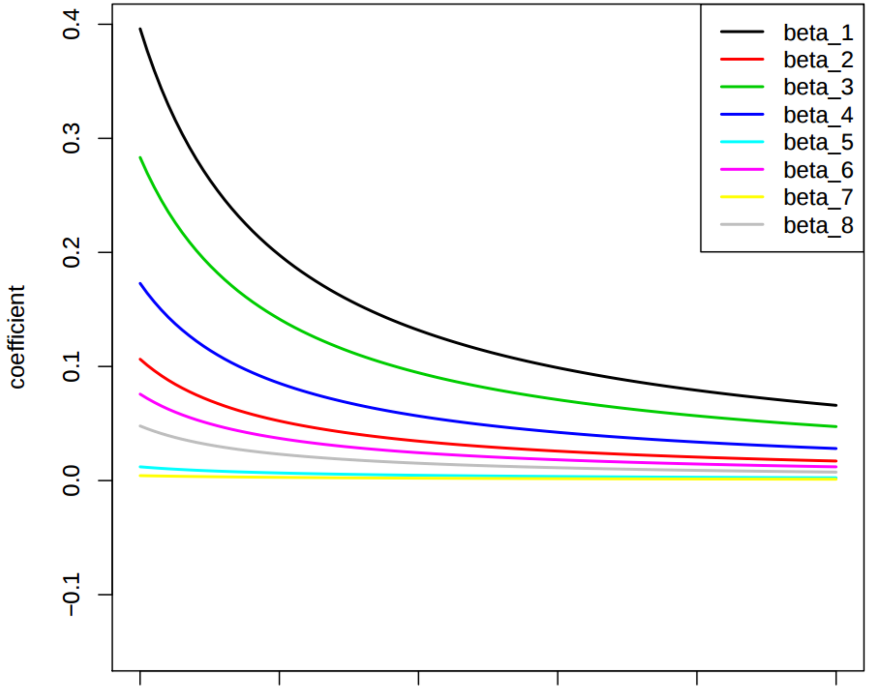


Mitigating multicollinearity and outlier values

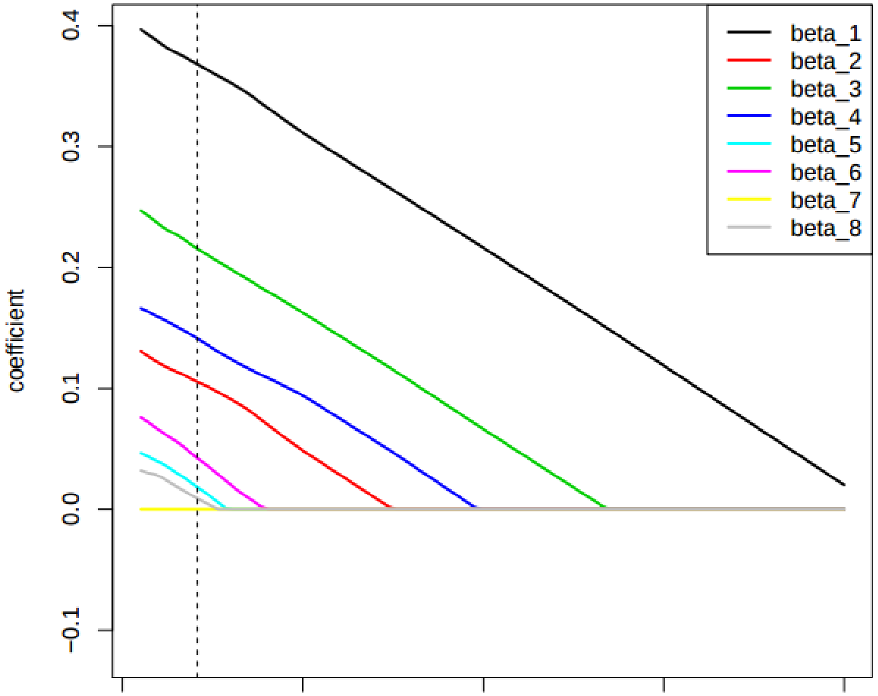
❑ Regularization

- Gradients: L2 vs. L1 regularization term

L2



L1



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Feature scaling

- Feature scaling: converting features values to present specific ranges or distributions

- Why?
  - Parameter updates: $\boldsymbol{\theta}_{t+1} = \boldsymbol{\theta}_t + \boldsymbol{\delta\theta}_{\mathbf{t}} = \boldsymbol{\theta}_t - \boldsymbol{\alpha} \boxed{\frac{\partial}{\partial \boldsymbol{\theta}_{\mathbf{t}}} \boldsymbol{J}(\boldsymbol{\theta}_{\mathbf{t}})}$
  - Linear regression: $\theta_0 \leftarrow \theta_0 - \alpha \sum_{i=0}^{N-1} \left(f\left(\boldsymbol{x}^{(i)}; \boldsymbol{\theta} \right) - y^{(i)} \right)$

$$\theta_1 \leftarrow \theta_1 - \alpha \sum_{i=0}^{N-1} \left(f\left(\boldsymbol{x}^{(i)}; \boldsymbol{\theta} \right) - y^{(i)} \right) \boxed{\boldsymbol{x}_0^{(i)}}$$

$$\theta_2 \leftarrow \theta_2 - \alpha \sum_{i=0}^{N-1} \left(f\left(\boldsymbol{x}^{(i)}; \boldsymbol{\theta} \right) - y^{(i)} \right) \boxed{\boldsymbol{x}_1^{(i)}}$$

Different magnitudes mean different rates of change

  - Features with higher magnitude tend to bias optimization algorithms (not only regression models) towards solutions that prioritize the adjustment of model parameters associated with them

Feature scaling

- Feature normalization (or scaling normalization): converts features to specific ranges

$$x_{scaled} = \frac{x - x_{min}}{x_{max} - x_{min}}$$

`sklearn.preprocessing.`**`MinMaxScaler`**

- Feature standardization (or z-score normalization): converts features to have zero-mean and unit standard deviation

$$x_{scaled} = \frac{x - \bar{x}}{\sigma_x}$$

`sklearn.preprocessing.`**`StandardScaler`**

Feature scaling

- Normalization vs. standardization:
  - Homogeneous ranges vs. homogeneous variance across features
  - Normalized scales vs. normalized distributions
  - Unknown distributions vs. assumed Gaussian distributions
  - Bounded vs. unbounded
  - Highly sensitive vs. robust to outliers
- In general, standardization is preferred on methods that assume normal distributions (e.g., Lasso regression), while normalization is preferred when features present uniform distributions and datasets don’t present extreme outliers (e.g., KNN)

Takeaway points

- First, explore your dataset visually and try to understand it as much as possible
- Proper data encoding and management of missing values and outliers has a significant impact in any machine learning models
- Exploring automated data summaries (e.g., using Pandas) and plotting feature distributions is the first step to identify if certain assumptions can be made
- Try to remove feature dependencies when possible. Slightly lower accuracy may be preferred to improve confidence and reproducibility
- If the dataset may be underpowered or there is evidence of partial multicollinearity and/or possible outliers, consider model regularization
- Normalize or standardize your data

Next class

- Assignment #2

Study summary

The National Institutes of Health funded a study to analyze what factors may predict the survival time after diagnosis of a terminal type of liver cancer. 2,500 patients were enrolled in ten different U.S. hospital and each patient underwent a biopsy that provided a measurement of twenty quantitative cell measurements. The overall goal of this study is to identify which cell measurements may be predictors of the survival time (if any) in addition to basic patient demographic information.

Goal

1. Build and evaluate a regression model that can predict the survival time using the available data. Provide:
   a. A description and justification of the pre-processing steps to use categorical features, solve errors in the dataset, explore feature correlations and tackle potential problem related to colinear features.
   b. A mathematical equation that predicts the survival time.
   c. A performance evaluation of the predictive model in the training dataset.