# 6.439 Problem Set 1

Xudong Sun

## 1.1 The Salk Vaccine Field Trial

(a)

The differences between the two experiments are as follows: compared to the randomized controlled double-blind experiment, 1) the experimenters in the NFIP study were not chosen randomly but according to their grade, therefore it was not randomized; 2) the NFIP study chose the grade 2 to be the experiment group and then asked for consent therefore the vaccine group and no vaccine group cannot be compared directly; 3) the control group in the NFIP study did not get the "placebo vaccine" such as salt injection, and everyone knows who actually got the treatment, therefore the study was not blind.

(b)

The polio rate data from the randomized controlled double-blind experiment. (28 compared to 71)

(c)

As polio is an infectious disease, people who thought they had a higher risk are more likely to accept the experiment. For example, they might live in an endemic area, have immune deficiency, or suffer from malnutrition[1]. If so, the no-consent group's polio rate is expected be lower than the population average. In the NFIP study, it's also possible that people of different age have different polio rate.

(d)

Yes. The study can be biased in both ways. It could exaggerate the effect of the vaccine because we cannot distinguish the true effect of the vaccine from the placebo effect. It could also understate the effect. If the experiment is not blind, the behavior of the vaccine group and no-vaccine group will be different regarding the prevention of the disease. The no-vaccine group knows they are not treated so they might try other ways to prevent the disease, or simply be more cautious, which can also decrease the polio rate.

(e)

They were more likely wrong. The polio rate difference between consent and the no-consent group was very low (highly possible to be statistically insignificant, if we can do a hypothesis test given enough samples), which means joining the experiment wasn't "more dangerous." More importantly, the polio rate difference between the vaccine group and control group was a strong proof that the vaccine was effective.

[1] From Wikipedia, https://en.wikipedia.org/wiki/Poliomyelitis#Prevention

# 6.439 Problem Set 1

Xudong Sun

## 1.2 NASA Compton Gamma Ray Observatory Data

(a)

The number of gamma-rays in a given time interval $X \sim Poisson(\lambda),\ \lambda$ is the emission rate. Gamma rays are received independently of one another at a given rate.

(b)

To determine whether X follows a Poisson distribution, the null and alternative hypothesis are as follows:

$$H_0: X\ follows\ a\ Poisson\ distribution\ with\ a\ constant\ \lambda$$

$$H_A: each\ interval\ has\ a\ different\ \lambda$$

Use likelihood ratio test.

(c)

Calculate the MLE $\hat{\lambda}$ for $X \sim Poisson(\lambda)$, The likelihood function is:

$$L(X_1, X_2, \dots, X_n; \lambda) = \prod_{i=1}^{n} e^{-\lambda} \cdot \frac{\lambda^{x_i}}{X_i!}$$

The log-likelihood:

$$\mathcal{L}(X_1, X_2, \dots, X_n; \lambda) = -n\lambda + \log(\lambda) \cdot \sum_{i=1}^{n} X_i - \sum_{i=1}^{n} log(X_i!)$$

The first derivative:

$$\frac{\partial \mathcal{L}}{\partial \lambda} = -n + \frac{1}{\lambda} \cdot \sum_{i=1}^{n} X_i = 0$$

$$\hat{\lambda} = \frac{1}{n} \cdot \sum_{i=1}^{n} X_i$$

The MLE is the average gamma-rays in a given time interval. In our data, the time intervals are not equal, therefore:

$$\hat{\lambda} = \frac{\sum counts}{\sum second} = 0.00388$$

(d)

The alternative hypothesis is that $\lambda$ is not constant, which means each interval $i$ has its own $\lambda_i$. Similar to (c), we can calculate the MLE for each interval:

$$\widehat{\lambda_i} = X_i$$

For the intervals in which $X_i = 0$, we think the interval has a Poisson(0) distribution. The likelihood for these intervals is 1.

The test statistic of the likelihood test:

$$\Lambda(\lambda) = -2\log\left(\frac{L(X_1, X_2, \dots, X_n; \lambda)}{L(X_1, X_2, \dots, X_n; \lambda_1, \lambda_2, \dots, \lambda_n)}\right)$$

$$= -2\log\left(\frac{\prod_{i=1}^{n} e^{-\lambda} \cdot \frac{\lambda^{x_i}}{X_i!}}{\prod_{i=1}^{n} e^{-\lambda_i} \cdot \frac{\lambda_i^{x_i}}{X_i!}}\right), \lambda_i > 0$$

(f)

(g)

### 1.3 P-values

I don't think it is a good idea just to ban the p-value from scientific papers, neither did the author of the article. In general, merely banning p-values does not solve any problem related to it, and what we need is just a bit more caution.

Firstly, the motivation of banning p-values is reasonable. As the article stated, the misunderstanding and misuse of p-values and null hypothesis significance testing has led to much confusion and even doubt about scientific conclusions. In scientific conclusions and business or policy decisions, reducing data analysis to achieving p-value thresholds can lead to wrong conclusions and bad decisions. By itself, a p-value does not provide a good measure of evidence regarding a model or hypothesis without context or other evidence, which researchers usually leave out.

However, it is still not wise to simply ban the p-value. The p-value is just an indicator summarizing the incompatibility between a particular set of data and a proposed model for the data. The problem is not that the p-value is "wrong" but it is misused and misunderstood without many contextual factors that is necessary for data analysis and scientific inference.

In sum, the p-value should be used with more caution. Researchers and audience should always use or interpret the p-value correctly.

### 1.4 Detecting Leukemia Types

For each gene, we use t-test on its expression level data of ALL and AML patients.

The number of genes that are associated with the different tumor types are as follows:

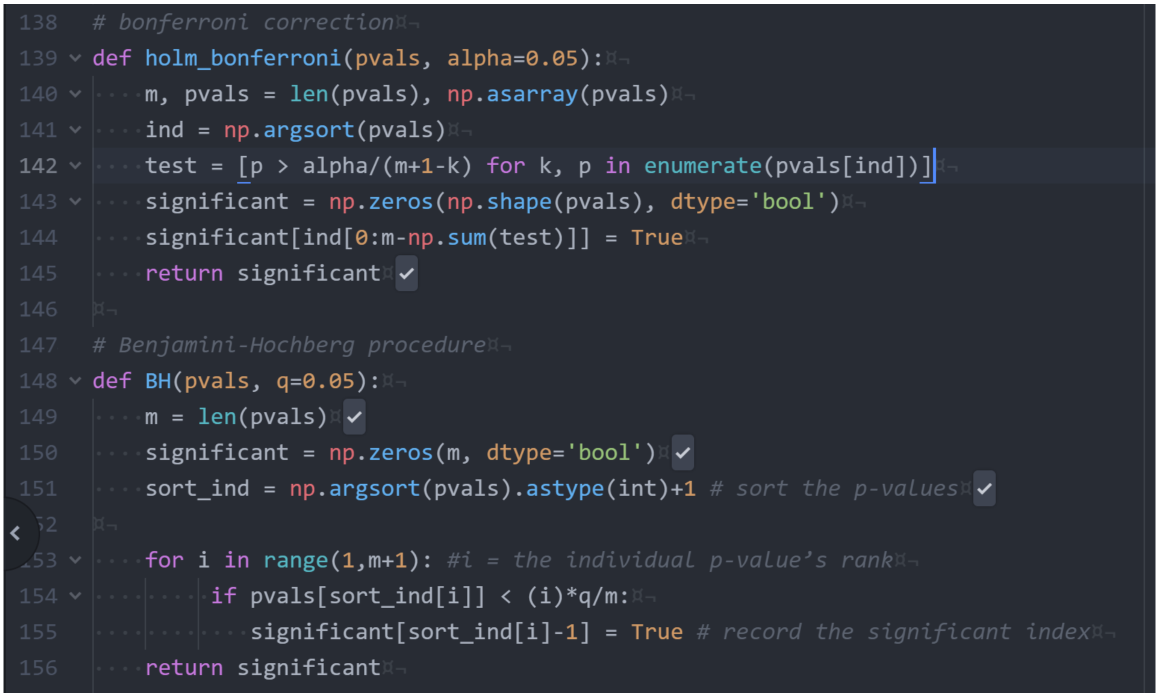
| | Number of genes |
|---|---|
| Uncorrected p-values | 1045 |

| | |
|---|---|
| Holm-Bonferroni correction | 98 |
| Benjamini-Hochberg correction | 681 |

As the expression level data of ALL and AML patients have different sample size, we try Welch’s t-test in case that the variance are unequal between two groups.

| | Number of genes |
|---|---|
| Uncorrected p-values | 1078 |
| Holm-Bonferroni correction | 103 |
| Benjamini-Hochberg correction | 695 |

The Python code are as follows:



```python
# bonferroni correction
def holm_bonferroni(pvals, alpha=0.05):
    m, pvals = len(pvals), np.asarray(pvals)
    ind = np.argsort(pvals)
    test = [p > alpha/(m+1-k) for k, p in enumerate(pvals[ind])]
    significant = np.zeros(np.shape(pvals), dtype='bool')
    significant[ind[0:m-np.sum(test)]] = True
    return significant

# Benjamini-Hochberg procedure
def BH(pvals, q=0.05):
    m = len(pvals)
    significant = np.zeros(m, dtype='bool')
    sort_ind = np.argsort(pvals).astype(int)+1 # sort the p-values

    for i in range(1,m+1): #i = the individual p-value’s rank
        if pvals[sort_ind[i]] < (i)*q/m:
            significant[sort_ind[i]-1] = True # record the significant index
    return significant
```

### 1.5 Why most published research findings are false

In this article, Ioannidis presented a mathematic model of the probability of false positive results in scientific research and concluded with a few principles of factors that affect the probability of a research finding being true.

In outlining the model framework, Ioannidis argues that the probability of a research finding being true depends on the power of the study, bias, some independent studies on the same question, and also the ratio of the number of ”true relationships” to ”no relationships” in the given research field. The first two factors represent the study itself, and the latter two factors represent the overall situation of the research field. Based on the model framework, Ioannidis puts forward a list of factors involved with a study itself or the given research field that could affect the probability of the study findings being true. First, studies with smaller sample sizes or smaller effect size would have smaller power, and the results are less likely to be true. Second, research fields with more tested relationships and less preselection on relationships would have a lower true-to-no relationship ratio pre-study, and would, therefore, have a lower probability of study results being true. Third, research fields with greater flexibility in designs, definitions, outcomes, and analytical modes, or greater interest conflicts and prejudice, or rapidly increasing research interest would increase bias of the studies in these fields and thus lead to the lower probability of research findings being correct. In the end, Ioannidis evaluates the current situation of various research fields by applying simulated data to the model. The results show that in most fields the research findings are more likely to be false than true, and they are often accurate measures of previous bias in their respective fields.

The most important lesson I learned from reading this paper is that most research findings are accurate measures of the prevailing bias in their fields. This argument challenges the way we see research results, as Ioannidis argues, we should be cautious about highly significant effects since they might indicate a significant bias in the research field. Furthermore, this argument expands to the topic of recognizing that some science fields could be ”null fields,” where there are no true relationships at all. This stimulates my thinking that maybe instead of looking at the statistical significance of effects in interpreting the study results, we can look at the deviation from previous understandings as a measure of significance. Since in most scientific fields, we can not know whether a relationship is true or not, more diverse findings on relationships should be encouraged to foster a better understanding of the fields.

Table 1 lists the PPV of finding or not finding true or no relationships. The first entry shows the probability of true relationships being observed in the research findings, which is the probability of finding a true relationship when there is a true relationship. The probability is represented by number of relationships $c$ multiplied by pre-study probability of true relationship $R/(R+1)$, and multiplied by power of study $1-\beta$. Similarly, the probability of finding true relationship when there is no relationship can be represented by number of relationships $c$ multiplied by pre-study probability of no relationship $1/(R + 1)$, and multiplied by Type I error $\alpha$. And the probabilities of not finding true or no relationships (second row in Table 1) are presented following the same logic.

In Table 2 bias was introduced as $u$, which represents the proportion of tested relationships that would not have been research findings but reported as such. The first entry of Table 2 adds the term $uc\beta R/(R+1)$, which represents the falsely counted research findings which are true relationships, to the previous one in Table 1. Similarly, the term $uc(1 - \alpha)/(R + 1)$ is added as falsely counted research findings which are not true relationships. These terms were subtracted from the values of second row in Table 1, to get the values in Table 2.

In Table 3, the effects of other studies on the same question was included. Given the number of independent studies with equal power $n$, the integrated power becomes $1 - \beta^n$, and the integrated Type I error becomes $1 - (1 - \alpha)^n$. Replacing these terms in Table 1 yields the values in Table 3.

Given the definition of PPV as the ratio of true predicted positives to the total number of predicted positives, it was calculated as follows:

$$PPV = \frac{P(research\ finding|true\ relationship)}{P(research\ finding)}$$

$$= \frac{\frac{c(1-\beta)R}{R+1}}{\frac{c(1-\beta)R}{R+1} + \frac{c\alpha}{R+1}}$$

$$= \frac{(1-\beta)R}{(1-\beta)R+\alpha}$$

Therefore, to have the $PPV > 0.5$, which means a research finding is more likely true than false, $(1-\beta)R$ needs to be larger than $\alpha$, i.e. $(1-\beta)R > \alpha$.

This means that in a research field where pre-study true relationships only take a small proportion of all investigated relationships, and when a study has lower power and higher Type I error, the research finding is most likely to be false.

# 6.439 Problem Set 1

Xudong Sun

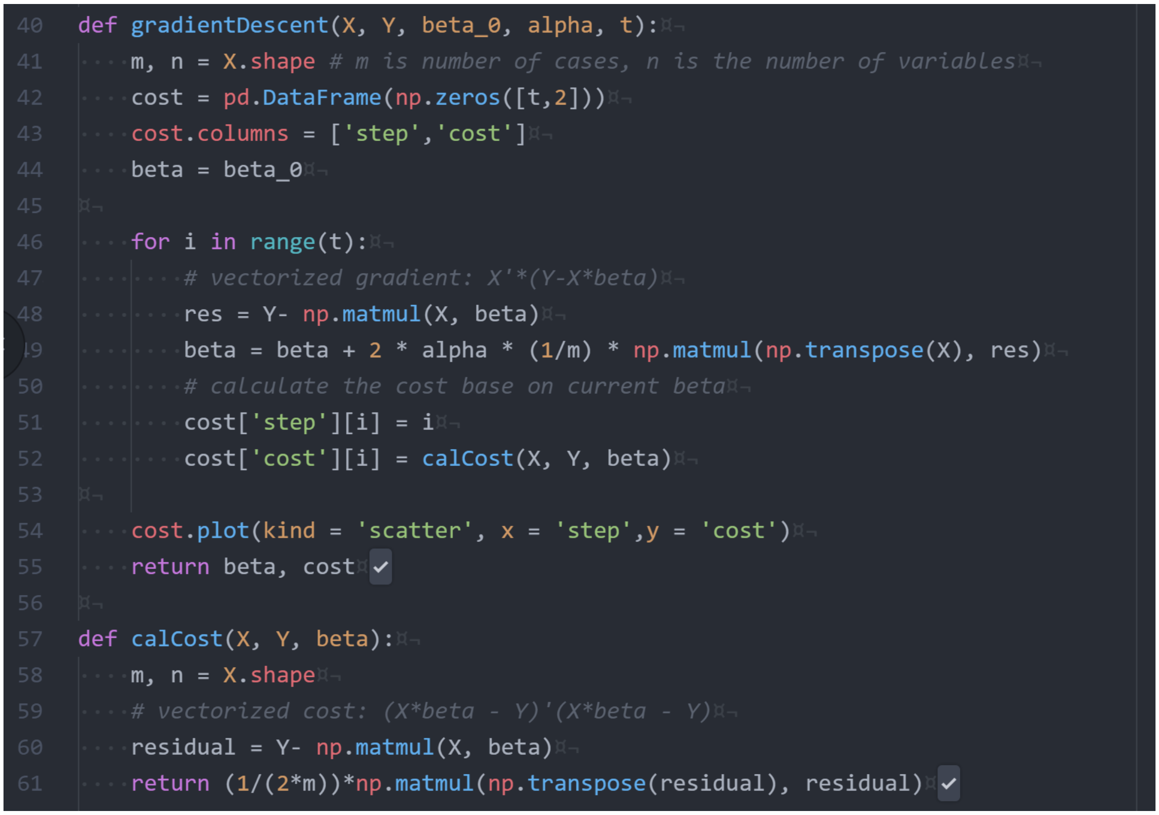
## 1.6 Regression and Gradient Descent

(a)

$$\hat{\beta} = (X^T X)^{-1} X^T Y = \begin{bmatrix} 1.9296 \\ 1.2640 \\ -4.5980 \end{bmatrix}$$

(b)

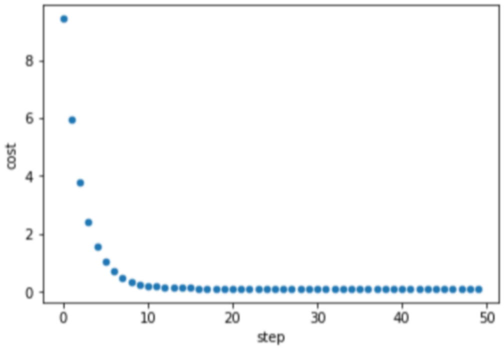
The Python code for gradient descent are as follows:



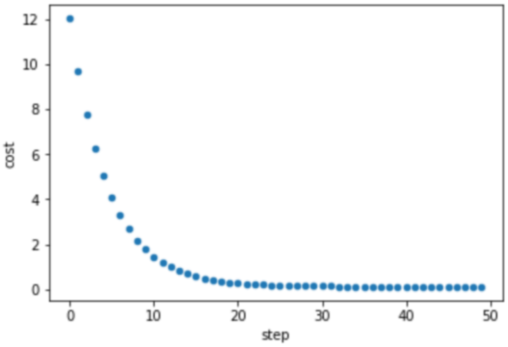
```
def gradientDescent(X, Y, beta_0, alpha, t):
    m, n = X.shape # m is number of cases, n is the number of variables
    cost = pd.DataFrame(np.zeros([t,2]))
    cost.columns = ['step','cost']
    beta = beta_0

    for i in range(t):
        # vectorized gradient: X'*(Y-X*beta)
        res = Y- np.matmul(X, beta)
        beta = beta + 2 * alpha * (1/m) * np.matmul(np.transpose(X), res)
        # calculate the cost base on current beta
        cost['step'][i] = i
        cost['cost'][i] = calCost(X, Y, beta)

    cost.plot(kind = 'scatter', x = 'step',y = 'cost')
    return beta, cost

def calCost(X, Y, beta):
    m, n = X.shape
    # vectorized cost: (X*beta - Y)'(X*beta - Y)
    residual = Y- np.matmul(X, beta)
    return (1/(2*m))*np.matmul(np.transpose(residual), residual)
```

Try different initial value and $\alpha$:

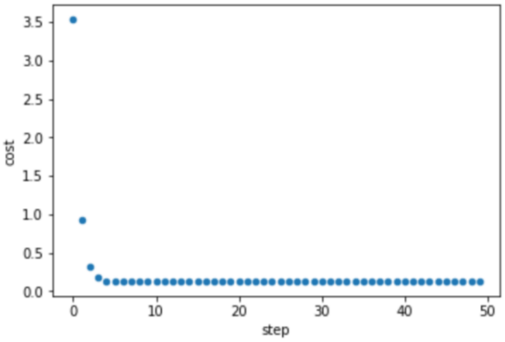
1. $\beta_0 = \begin{bmatrix} 0.5 \\ 0.5 \\ 0.5 \end{bmatrix}, \alpha = 0.1, t = 50$



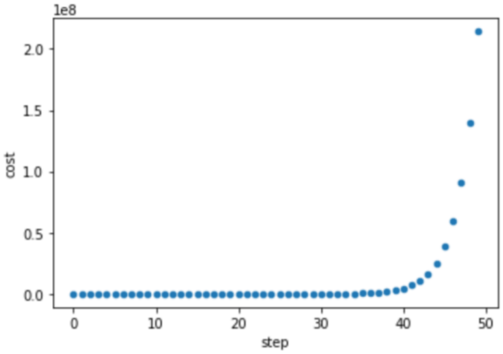
2. $\beta_0 = \begin{bmatrix} 0.5 \\ 0.5 \\ 0.5 \end{bmatrix}, \alpha = 0.05, t = 50$



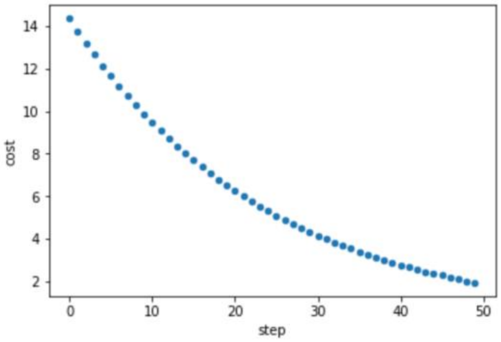
3. $\beta_0 = \begin{bmatrix} 0.5 \\ 0.5 \\ 0.5 \end{bmatrix}, \alpha = 0.25, t = 50$



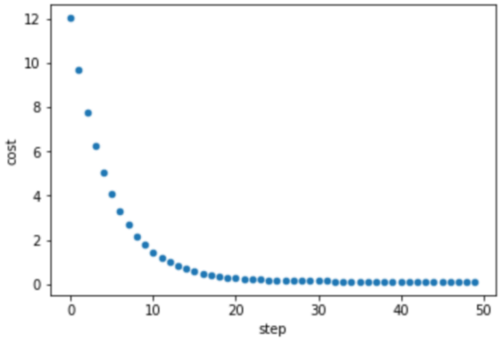
4. $\beta_0 = \begin{bmatrix} 0.5 \\ 0.5 \\ 0.5 \end{bmatrix}, \alpha = 0.8, t = 50$



5. $\beta_0 = \begin{bmatrix} 0.5 \\ 0.5 \\ 0.5 \end{bmatrix}, \alpha = 0.01, t = 50$



6. $\beta_0 = random\, number\, from\ (0,1), \alpha = 0.05, t = 50$



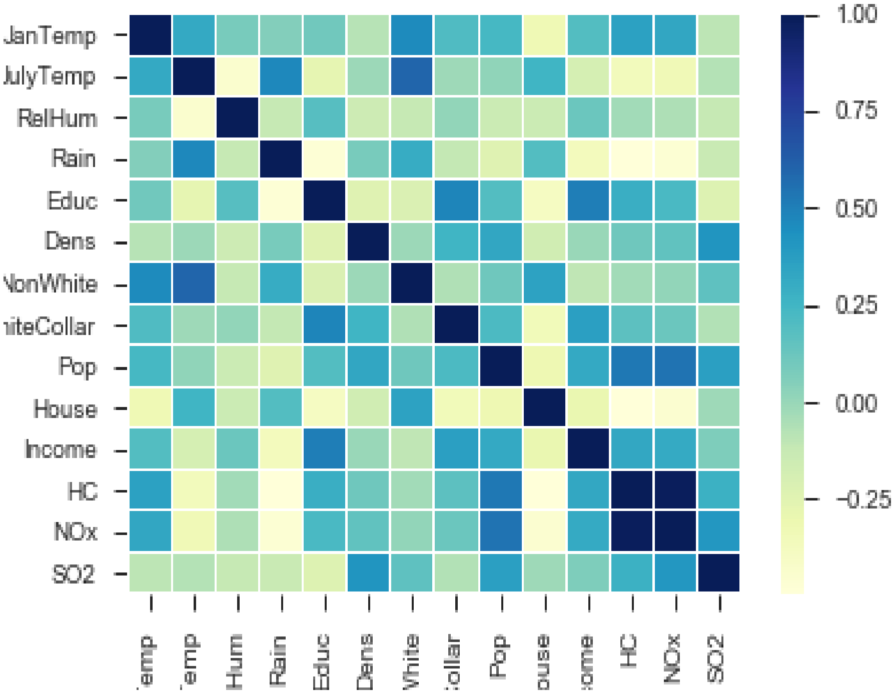
The optimal step size can be decided by setting a threshold $\varepsilon$. Theoretically, the optimal step size and threshold can be decided by finding bounds. Find constant L such that for all points $u$:

$$f(u) \le f(w) + \langle \nabla f(w), u - w \rangle + \frac{L}{2} \|u - w\|^2$$

The step size $\alpha_t = \frac{1}{L}$ gives convergence, $\varepsilon = \left(1 - \frac{m}{L}\right)^t (f\left(w^{(0)} - f(w^*)\right)$ need $O\left(\log\left(\frac{1}{\varepsilon}\right)\right)$ iterations for $f\left(w^{(t)}\right) - f(w^*) \le \varepsilon$.

(c)

We firstly check the correlation matrix of all explanatory variables:

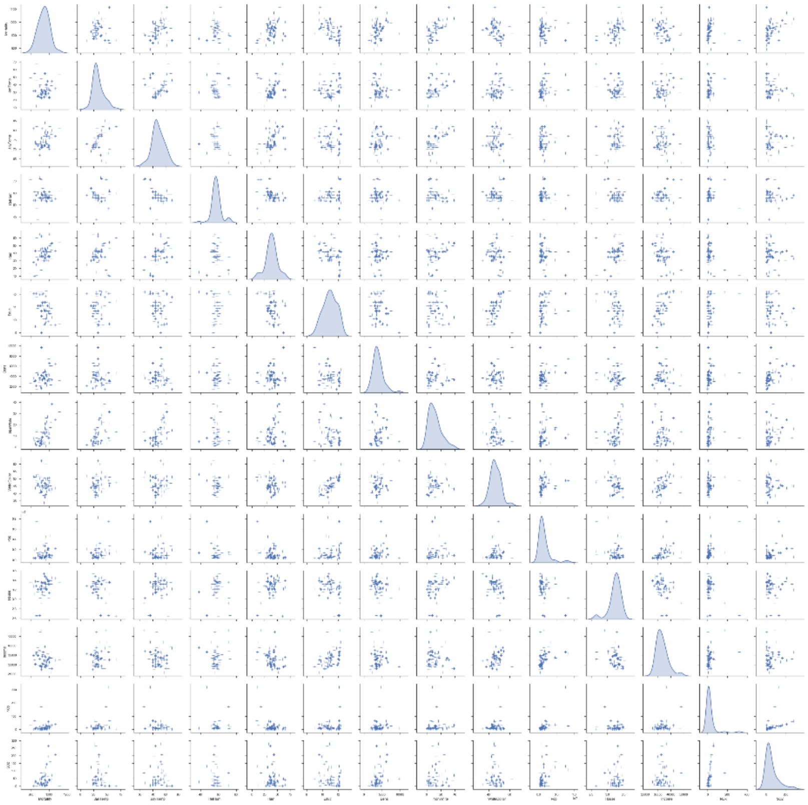


We found that the HC and NOx are highly correlated so one of them need to be removed from our model.

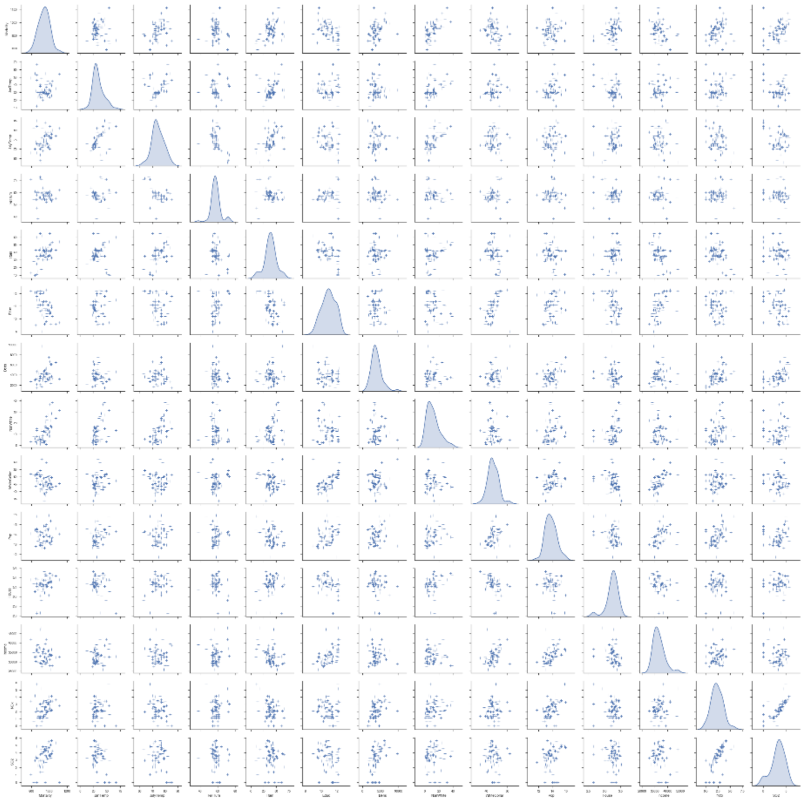
Then, we investigate the histograms and scatterplots of each variable/variable pairs. From the plot, we think SO2, NOx, and Pop need log-transformation.

# 6.439 Problem Set 1

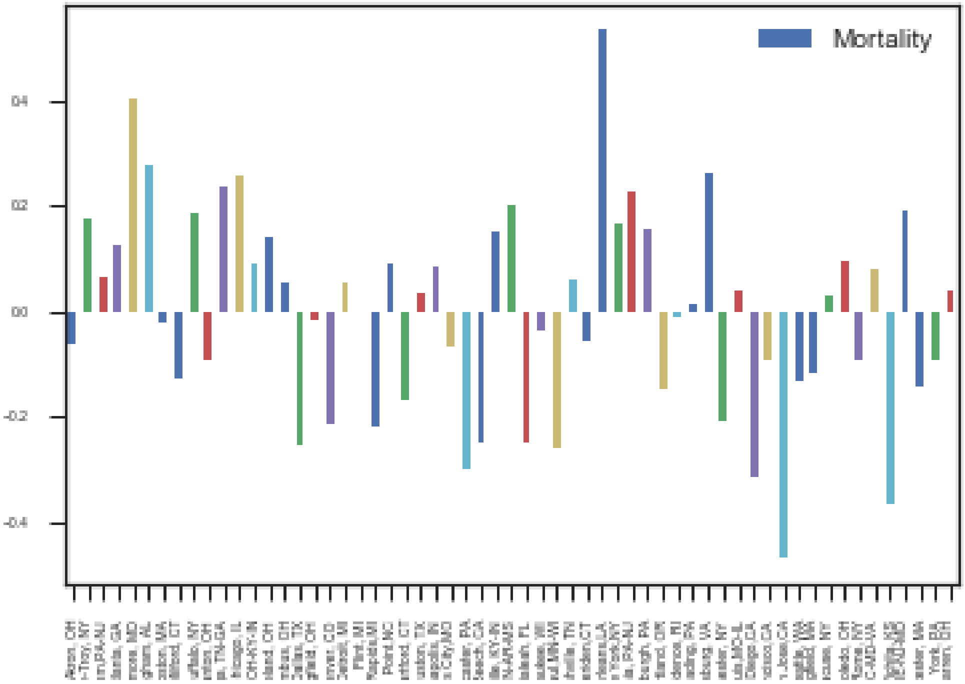
Xudong Sun



After log-transformation:



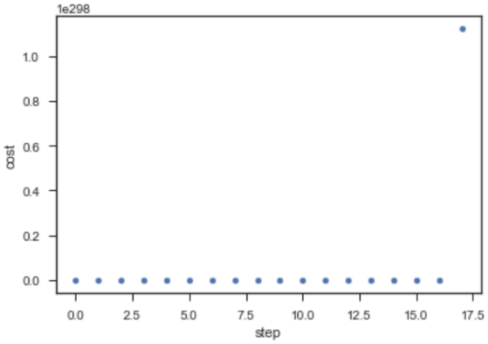
We then normalized all numeric variables. Plot the mortality rate of all cities:



New Orleans, LA, has the highest mortality while San Jose has the lowest.

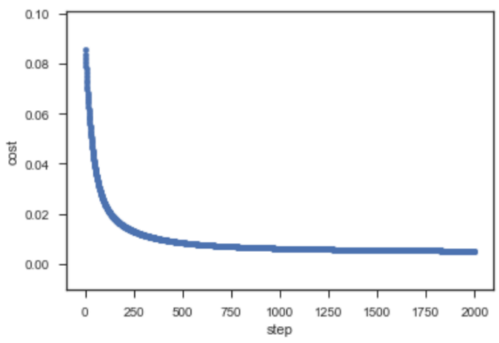
(d) (e)

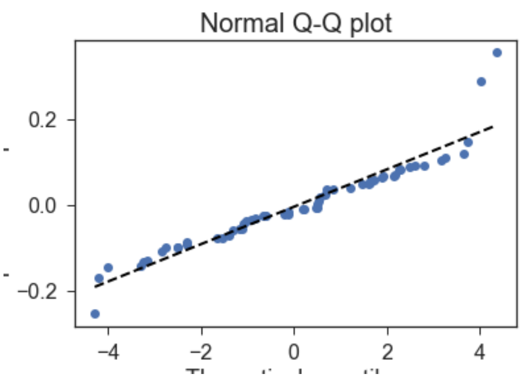
Run gradient descent on raw data:



The gradient descent does not converge.

Run gradient descent on transformed data:





The gradient descent successfully converged. We plot the q-q plot and the residuals are normally distributed.

(f) The function to minimize:

$$f(\beta) = \sum_i log(1 + exp(-y_i \beta^T x_i))$$

The derivative of $f(\beta)$ :

$$\nabla_\beta f(\beta) = \sum_i \nabla_\beta \log(1 + exp(-y_i \beta^T x_i))$$

$$= \sum_i \frac{1}{1 + \exp(-y_i \beta^T x_i)} \cdot \exp(-y_i \beta^T x_i) \cdot (-y_i x_i)$$

In each step of the gradient descent:

$$\beta := \beta - \alpha \cdot \nabla_\beta f(\beta)$$

### 1.7 Computational Aspects of Regression

(a)

To store the matrix X, we need $10^8 \times 200 \times 64/10^9 = 1280$gb of memory. It's (currently, in 2018) impossible to store or perform matrix calculations on common computers.

(b)

Use Stochastic Gradient Descent (SGD) or mini-batch gradient descent by doing 1 iteration of gradient descent on 1 data entry or a small batch of data. Thus, we can store the data on cloud and extract small amount of data each time.

(c)

The maximum rank of $X^T X$ is the number of rows, n, when the number of variables p is much larger than n, there will be many local optimums.