Lab: Logistic Regression for Gene Expression Data

In this lab, we use logistic regression to predict biological characteristics ("phenotypes") from gene expression data. In addition to the concepts in breast_cancer.ipynb), you will learn to:

- · Handle missing data
- · Perform binary classification, and evaluating performance using various metrics
- Perform multi-class logistic classification, and evaluating performance using accuracy and confusion matrix
- Use L1-regularization to promote sparse weights for improved estimation (Grad students only)

Background

Genes are the basic unit in the DNA and encode blueprints for proteins. When proteins are synthesized from a gene, the gene is said to "express". Micro-arrays are devices that measure the expression levels of large numbers of genes in parallel. By finding correlations between expression levels and phenotypes, scientists can identify possible genetic markers for biological characteristics.

The data in this lab comes from:

https://archive.ics.uci.edu/ml/datasets/Mice+Protein+Expression (https://archive.ics.uci.edu/ml/datasets/Mice+Protein+Expression)

In this data, mice were characterized by three properties:

- Whether they had down's syndrome (trisomy) or not
- · Whether they were stimulated to learn or not
- Whether they had a drug memantine or a saline control solution.

With these three choices, there are 8 possible classes for each mouse. For each mouse, the expression levels were measured across 77 genes. We will see if the characteristics can be predicted from the gene expression levels. This classification could reveal which genes are potentially involved in Down's syndrome and if drugs and learning have any noticeable effects.

Load the Data

We begin by loading the standard modules.

```
import pandas as pd
import numpy as np
import matplotlib
import matplotlib.pyplot as plt
%matplotlib inline
from sklearn import linear_model, preprocessing
%config IPCompleter.greedy=True
```

Use the pd. read_excel command to read the data from

https://archive.ics.uci.edu/ml/machine-learning-databases/00342/Data_Cortex_Nuclear.xls (https://archive.ics.uci.edu/ml/machine-learning-databases/00342/Data_Cortex_Nuclear.xls)

into a dataframe df. Use the $index_col$ option to specify that column 0 is the index. Use the df. head() to print the first few rows.

```
In [2]:

# TODO
# df = ...
df = pd. read_excel("https://archive.ics.uci.edu/ml/machine-learning-databases/00342/Data_Cortex_Nu df. head(6)
```

Out[2]:

	DYRK1A_N	ITSN1_N	BDNF_N	NR1_N	NR2A_N	pAKT_N	pBRAF_N	pCAMKII_N
MouselD								
309_1	0.503644	0.747193	0.430175	2.816329	5.990152	0.218830	0.177565	2.373744
309_2	0.514617	0.689064	0.411770	2.789514	5.685038	0.211636	0.172817	2.292150
309_3	0.509183	0.730247	0.418309	2.687201	5.622059	0.209011	0.175722	2.283337
309_4	0.442107	0.617076	0.358626	2.466947	4.979503	0.222886	0.176463	2.152301
309_5	0.434940	0.617430	0.358802	2.365785	4.718679	0.213106	0.173627	2.134014
309_6	0.447506	0.628176	0.367388	2.385939	4.807635	0.218578	0.176233	2.141282

6 rows × 81 columns

This data has missing values. The site:

http://pandas.pydata.org/pandas-docs/stable/missing_data.html (http://pandas.pydata.org/pandas-docs/stable/missing_data.html)

has an excellent summary of methods to deal with missing values. Following the techniques there, create a new data frame df1 where the missing values in each column are filled with the mean values from the non-missing values.

```
In [3]:

# TODO
# df1 = ...
df1 = df. fillna(df. mean())
```

Binary Classification for Down's Syndrome

We will first predict the binary class label in df1['Genotype'] which indicates if the mouse has Down's syndrome or not. Get the string values in df1['Genotype']. values and convert this to a numeric vector y with 0 or 1. You may wish to use the np. unique command with the return inverse=True option.

```
In [4]:

# TODO
# y = ...
_, indices = np. unique( df1['Genotype'], return_inverse=True)
y = indices
print(y)
[0 0 0 ... 1 1 1]
```

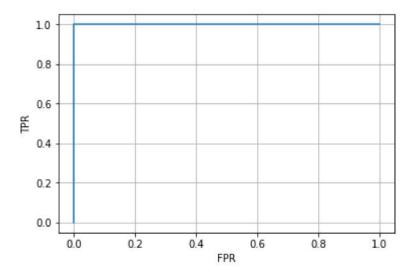
As predictors, get all but the last four columns of the dataframes. Standardize the data matrix and call the standardized matrix Xs. The predictors are the expression levels of the 77 genes.

Measure the accuracy of the classifer. That is, use the logreg.predict function to predict labels logreg.predict function logreg.predict function

multi_class='warn', n_jobs=None, penalty='12', random_state=None, solver='liblinear', tol=0.0001, verbose=0, warm start=False)

In [7]: # TODO yhat = logreg.predict(Xs) corrects = np. sum(yhat == y)print(f"Correct preditcions are {corrects}, accuracy is {corrects/y.shape[0]}") from sklearn import metrics yprob = logreg.predict_proba(Xs) fpr, tpr, thresholds = metrics.roc_curve(y, yprob[:, 1]) plt. plot (fpr, tpr) plt.grid() plt. xlabel('FPR') plt.ylabel('TPR') # plt.ylim([0.5, 1.1]) # p1t.x1im([0, 0.1]) plt.show() auc = metrics.roc_auc_score(y, yprob[:, 1]) print("AUC=%f" % auc)

Correct preditcions are 1080, accuracy is 1.0



AUC=1. 000000

Interpreting the weight vector

Create a stem plot of the coefficients, \mathbb{V} in the logistic regression model. You can get the coefficients from $logreg.\ coef_$, but you will need to reshape this to a 1D array.

```
[8]:
In
# TODO
W = logreg.coef_.flatten()
plt.stem(W)
plt.show()
 100
  75
  50
  25
   0
 -25
 -50
 -75
                     20
              10
                            30
                                   40
                                         50
                                                       70
                                                60
```

You should see that W[i] is very large for a few components i. These are the genes that are likely to be most involved in Down's Syndrome.

Find the names of the genes for two components i where the magnitude of W[i] is largest.

```
In [9]:
# TODO

name1, name2= df1.columns[np.argsort(-np.abs(W))[:2]]
print(f"Names are {name1}, {name2}")
Names are ITSN1_N, BRAF_N
```

Cross Validation

The above meaured the accuracy on the training data. It is more accurate to measure the accuracy on the test data. Perform 10-fold cross validation and measure the average precision, recall and f1-score, as well as the AUC. Note, that in performing the cross-validation, you will want to randomly permute the test and training sets using the <code>shuffle</code> option. In this data set, all the samples from each class are bunched together, so shuffling is essential. Print the mean precision, recall and f1-score and error rate across all the folds.

In [10]:

```
from sklearn. model selection import KFold
from sklearn.metrics import precision_recall_fscore_support
nfold = 10
kf = KFold(n splits=nfold)
prec = []
rec = []
f1 = \lceil \rceil
acc = []
for train, test in kf. split(Xs):
    # Get training and test data
    Xtr = Xs[train,:]
    ytr = y[train]
    Xts = Xs[test, :]
    yts = y[test]
    # Fit a model
    logreg. fit (Xtr, ytr)
    yhat = logreg.predict(Xts)
    # Measure performance
    preci, reci, fli, _= precision_recall_fscore_support(yts, yhat, average='binary')
    prec. append (preci)
    rec. append (reci)
    fl. append (fli)
    acci = np. mean(yhat == yts)
    acc. append (acci)
# Take average values of the metrics
precm = np. mean(prec)
recm = np. mean(rec)
f1m = np. mean(f1)
accm= np. mean (acc)
# Compute the standard errors
prec se = np. std(prec)/np. sqrt(nfold-1)
rec se = np. std(rec)/np. sqrt(nfold-1)
f1 \text{ se} = \text{np. std}(f1)/\text{np. sqrt}(\text{nfold-1})
acc_se = np. std(acc)/np. sqrt(nfold-1)
print ('Precision = {0:.4f}, SE={1:.4f}'.format (precm, prec se))
                  {0:.4f}, SE={1:.4f}'.format(recm, rec_se))
print('Recall =
print('f1 =
                     \{0:.4f\}, SE=\{1:.4f\}'.format(f1m, f1_se))
print ('Accuracy = \{0:.4f\}, SE=\{1:.4f\}'. format (accm, acc se))
```

E:\Anaconda3\lib\site-packages\sklearn\metrics\classification.py:1145: UndefinedMetricWarning: Recall and F-score are ill-defined and being set to 0.0 due to no true samples.

'recall', 'true', average, warn_for)

E:\Anaconda3\lib\site-packages\sklearn\metrics\classification.py:1145: UndefinedMetricWarning: Recall and F-score are ill-defined and being set to 0.0 due to no true samples.

'recall', 'true', average, warn_for)

E:\Anaconda3\lib\site-packages\sklearn\metrics\classification.py:1145: UndefinedMetricWarning: Recall and F-score are ill-defined and being set to 0.0 due to no true samples.

'recall', 'true', average, warn_for)

E:\Anaconda3\lib\site-packages\sklearn\metrics\classification.py:1145: UndefinedMetr

```
icWarning: Recall and F-score are ill-defined and being set to 0.0 due to no true sa
mples.
    'recall', 'true', average, warn_for)
E:\Anaconda3\lib\site-packages\sklearn\metrics\classification.py:1145: UndefinedMetr
icWarning: Recall and F-score are ill-defined and being set to 0.0 due to no true sa
mples.
    'recall', 'true', average, warn_for)

Precision = 0.4689, SE=0.1590
Recall = 0.3387, SE=0.1213
f1 = 0.3811, SE=0.1310
Accuracy = 0.6444, SE=0.0572
```

Multi-Class Classification

Now use the response variable in df1['class']. This has 8 possible classes. Use the <code>np.unique</code> funtion as before to convert this to a vector <code>y</code> with values 0 to 7.

```
In [11]:

# TODO
# y = ...
_, indices = np. unique( df1['class'], return_inverse=True)
y = indices
```

Fit a multi-class logistic model by creating a LogisticRegression object, logreg and then calling the logreg. fit method. In general, you could either use the 'one over rest (ovr)' option or the 'multinomial' option. In this exercise use the default 'ovr' and C=1. As an optional exercise, you could also compare the results obtained with these two options.

Measure the accuracy on the training data.

```
In [13]:

# TODO
yhat = logreg.predict(Xs)
corrects = np. sum(yhat == y)
print(f"Correct preditcions are {corrects}, accuracy is {corrects/y.shape[0]}")

Correct preditcions are 1079, accuracy is 0.9990740740740741
```

Now perform 10-fold cross validation, and measure the confusion matrix $\,^{\,}$ C on the test data in each fold. You can use the $\,^{\,}$ confustion_matrix method in the $\,^{\,}$ sklearn package. Add the confusion matrix counts across all folds and then normalize the rows of the confusion matrix so that they sum to one. Thus, each element $\,^{\,}$ C[i, j] will represent the fraction of samples where $\,^{\,}$ yhat==j given $\,^{\,}$ ytrue==i . Print the confusion matrix. You can use the command

```
print(np.array_str(C, precision=4, suppress_small=True))
```

to create a nicely formatted print. Also print the overall mean and SE of the test accuracy across the folds.

```
In [14]:
from sklearn.metrics import confusion matrix
from sklearn.model_selection import KFold
# TODO
nfold = 10
kf = KFold(n splits=nfold, shuffle=True)
C_S = \lceil \rceil
accs = []
for train, test in kf. split(Xs):
    # Get training and test data
    Xtr = Xs[train,:]
    ytr = y[train]
    Xts = Xs[test, :]
    yts = y[test]
    # Fit a model
    logreg. fit (Xtr, ytr)
    yhat = logreg.predict(Xts)
    # Measure performance
    C = confusion_matrix(yts, yhat)
    C = C/np. sum(C, axis=1)
    Cs. append (C)
    accs. append (np. mean (yhat == yts))
      print(yhat, yts)
#
      print(np. mean(yhat == yts))
    print(np.array str(C, precision=4, suppress small=True))
err mean = np. mean(accs)
err_se = np. std(accs)/np. sqrt(nfold-1)
print(f"Mean and SE of accuracy are {err_mean} and {err_se}")
[[1]
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 [0. 1. 0. 0. 0. 0. 0. 0.]
 [0, 0, 1, 0, 0, 0, 0, 0, ]
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              1. 0. 0. 0. ]
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                  1.
                     0. 0.]
```

[0. 0. 0. 0. 0. 0. 1. 0.] [0. 0. 0. 0. 0. 0. 0. 1.]

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[0. 1. 0.	0.	0.	0.	0.	0.]
[0. 0714 0. 0.	0. 9333	0.	0.	0.	0.]
[0. 0. 0.	0. 3333	1.	0.	0.	0.]
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[0. 0. 0.	0.	0.	0.	1.	0.]
[0. 0. 0.	0.	0.	0.	0.	1.]]
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[0. 0.9412 0.	0.	0.	0.1667	0.	0.]
[0. 0. 1.	0.	0.	0.	0.	0.]
[0. 0. 0.	1.	0.	0.	0.	0.]
[0. 0.1176 0.	0.	0.9048	0.	0.	0.]
[0. 0. 0.	0.	0.	1.	0.	0.]
[0. 0. 0.	0.	0.	0.	1.	0.]
[0. 0. 0.	0.	0.	0.	0.	1.]]
[[0. 9375 0. 0.	0.	0.0667	0.	0.	0.]
[0. 125 0. 8333 0.	0.	0.	0.	0.	0.]
[0. 0. 0. 9	0.	0.	0.	0.	0.0769	_
[0. 0. 0.	1.	0.	0.	0.	0.]
[0. 0. 0.	0.	1.	0.	0.	0.]
$\begin{bmatrix} 0. & 0. & 0. \\ 0. & 0. & 0. \end{bmatrix}$	0.	0.	1.	0.	0.]
[0. 0. 0.	0.	0.	0.	1.	0.]
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[0. 0.9167 0.	0.	0. 1	0.	0.	0.]
[0. 0. 1.	0.	0. 1	0.	0.	0.]
[0. 0. 0.	1.	0.	0.	0.	0.]
[0. 0. 0.	0.	1.	0.	0.	0.	j
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[0. 0. 0.	0.	0.	0.	1.	0.	j
[0. 0. 0.	0.	0.	0.	0.	1.]]
[[1. 0. 0.	0.	0.	0.	0.	0.]
[0.0667 0.9444 0.	0.	0.	0.	0.	0.]
[0. 0. 1.	0.	0.	0.	0.	0.]
[0. 0. 0.	1.	0.	0.	0.	0.	j
[0. 0. 0.	0.	1.	0.	0.	0.]
[0. 0. 0.	0.	0.	1.	0.	0.]
[0. 0. 0.	0.	0.	0.	1.	0.]
[0. 0. 0.	0.	0.	0.	0.	1.]]
Mean and SE of accura	rv are O	9879629	96296296	329 and	0.0039	16227635

Mean and SE of accuracy are 0.9879629629629 and 0.0039162276359412124

Re-run the logistic regression on the entire training data and get the weight coefficients. This should be a 8 x 77 matrix. Create a stem plot of the first row of this matrix to see the coefficients on each of the genes for the first

class.

```
[15]:
In
                                                                                                              M
# TODO
logreg = linear model.LogisticRegression(C=1, solver="liblinear", multi class='ovr')
logreg. fit (Xs, y)
W2 = 1ogreg. coef [0, :]
plt.stem(W2)
plt. show()
  2.0
  1.5
  10
  0.5
  0.0
 -0.5
 -1.0
 -1.5
 -2.0
                    20
                                                     70
```

L1-Regularization

Graduate students only complete this section.

In most genetic problems, only a limited number of the tested genes are likely influence any particular attribute. Hence, we would expect that the weight coefficients in the logistic regression model should be sparse. That is, they should be zero on any gene that plays no role in the particular attribute of interest. Genetic analysis commonly imposes sparsity by adding an I1-penalty term. Read the sklearn documentation (http://scikit-learn.org/stable/modules/generated/sklearn.linear_model.LogisticRegression.html) on the LogisticRegression class to see how to set the I1-penalty and the inverse regularization strength, C.

Using the model selection strategies from the <u>prostate cancer analysis demo</u> (.../unit03_model_sel/demo03_2_prostate.ipynb), use K-fold cross validation to select an appropriate inverse regularization strength.

- · Use 10-fold cross validation
- You should select around 20 values of C. It is up to you to find a good range.
- · For each C and each fold, you should compute the classification error rate
- For each C and each fold, you should also determine the nubmer of non-zero coefficients for the first class. For this purpse, you can assume coefficient with magnitude <0.01 as zero.

In [16]:

```
# TODO
npen = 20
C_{\text{test}} = \text{np. logspace}(-2, 2, \text{npen})
# Create the cross-validation object and error rate matrix
kf = KFold(n_splits=nfold, shuffle=True)
err_rate = np. zeros((npen, nfold))
num_nonzerocoef = np. zeros((npen, nfold))
# Create the logistic regression object
logreg = linear_model.LogisticRegression(penalty='ll', warm_start=True, solver="liblinear", multi_c
# Loop over the folds in the cross-validation
for ifold, Ind in enumerate(kf.split(Xs)):
    # Get training and test data
    Itr, Its = Ind
    Xtr = Xs[Itr, :]
    ytr = y[Itr]
    Xts = Xs[Its, :]
    yts = y[Its]
    # Loop over penalty levels
    for ipen, c in enumerate(C_test):
        # Set the penalty level
        logreg.C= c
        # Fit a model on the training data
        logreg. fit (Xtr, ytr)
        # Predict the labels on the test set.
        yhat = logreg.predict(Xts)
        # Measure the accuracy
        err rate[ipen, ifold] = np. mean(yhat != yts)
        num_nonzerocoef[ipen, ifold] = np. sum(abs(logreg.coef_)>0.01)
    print(f"Fold {ifold}")
```

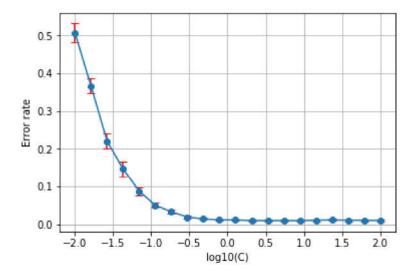
```
Fold 1
Fold 2
Fold 3
Fold 4
Fold 5
Fold 6
Fold 7
Fold 8
Fold 9
```

Fold 0

Now compute the mean and standard error on the error rate for each C and plot the results (Use errorbar() method). Also determine and print the minimum test error rate and corresponding C value.

In [17]: ▶

The minimum test error rate is 0.009259259259259259, SE is 0.001952023247017518 The C value corresponding to minimum error is 2.06913808111479



We see that the minimum error rate is significantly below the classifier that did not use the I1-penalty. Use the one-standard error rule to determine the optimal $\,^{\,\text{C}}\,$ and the corresponding test error rate. Note that because $\,^{\,\text{C}}\,$ is inversely proportional to the regularization strength, you want to select a $\,^{\,\text{C}}\,$ as *small* as possible while meeting the error target!

```
In [18]:

# TODO

# C_opt =
err_tgt = err_mean[imin] + err_se[imin]
iopt = np. argmax(err_mean < err_tgt)
C_opt = C_test[iopt]

print(f"Optimal C is {C_opt}")
print(f"The test error rate is {err_mean[iopt]:.4f}, SE is {err_se[iopt]:.4f}")

print(f'Accuracy = {1-err_mean[iopt]:.4f}, SE={err_se[iopt]:.4f}')

Optimal C is 0.7847599703514611
The test error rate is 0.0111, SE is 0.0012
Accuracy = 0.9889, SE=0.0012</pre>
```

Question: How does the test error rate compare with the classifier that did not use the I1-penalty? Explain why.

Type Answer Here:

The error rate with I1-penalty is much lower than before. As when using I1-penalty, coefficients tend to be close to zero. So only important coefficients remain, irrelevant coefficients are removed.

Now plot the nubmer of non-zero coefficients for the first class for different C values. Also determine and print the number of non-zero coefficients corresponding to C opt.

In [19]:

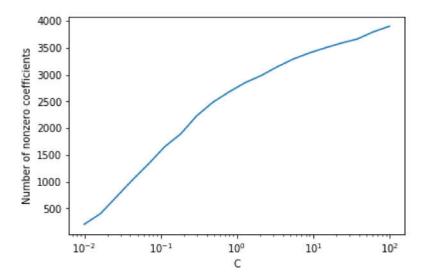
```
# TODO

num_nonzerocoef_mean = np. sum(num_nonzerocoef, axis=1)
plt. semilogx(C_test, num_nonzerocoef_mean)

plt. xlabel('C')
plt. ylabel('Number of nonzero coefficients')

print(f"The number of non-zero coefficients for the optimal C is {num_nonzerocoef_mean[iopt]}")
```

The number of non-zero coefficients for the optimal C is 2679.0



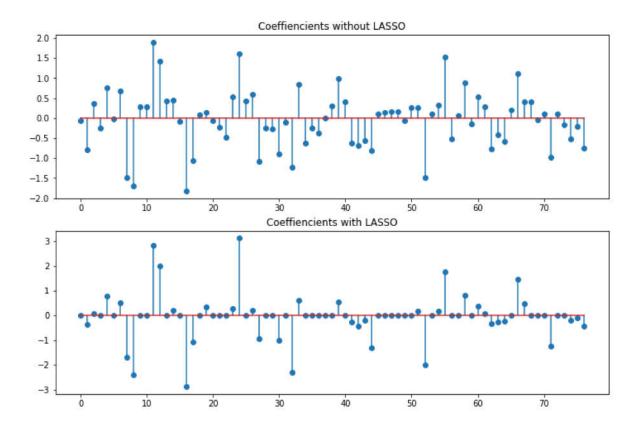
For the optimal $\,^{\circ}$ C, fit the model on the entire training data with I1 regularization. Find the resulting weight matrix, $\,^{\circ}$ W_11. Plot the first row of this weight matrix and compare it to the first row of the weight matrix without the regularization. You should see that, with I1-regularization, the weight matrix is much more sparse and hence the roles of particular genes are more clearly visible. Please also compare the accuracy for the training data using optimal $\,^{\circ}$ C with the previous results not using LASSO regularization. Do you expect the accuracy to improve?

In [20]:

```
# TODO
logreg = linear_model.LogisticRegression(C=C_opt, penalty='l1', solver="liblinear", multi_class='o
logreg.fit(Xs, y)
yhat = logreg.predict(Xs)
acc = np. mean(yhat == y)
print(f'Accuracy on the training data is {acc:f}')
W_l1 = logreg.coef_

plt.figure(figsize=(12, 8))
plt.subplot(2, 1, 1)
plt.stem(W2)
plt.title("Coeffiencients without LASSO")
plt.stem(W_l1[0])
plt.stem(W_l1[0])
plt.title("Coeffiencients with LASSO")
plt.show()
```

Accuracy on the training data is 0.998148



Yes, by choosing few coefficients, the model can detect the most importants coefficient. By doing so, disturbance can be reduced.