3.1-section-result

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1 Section 3 - Identifying features that may drive outcomes

- Building models that can predict outcomes from a set of features is one of the most common applications of statistics in the sciences
- This statistical method is broadly referred to as **regression**
- Typically, a scientist selects a set of features that they think influence their outcome and builds a (linear, logistic, *etc.*) model based on these features
- Least Absolute Shrinkage and Selection Operator (**LASSO**, also termed **L1 regularization**) is one regression method that helps identify features that drive outcomes
  - In simple terms, LASSO builds a model using all features as independent variables
  - Some coefficients for features are allowed to pass to zero if they do not strongly influence the results
  - LASSO thus provides **feature selection** by determining which features are most important to predicting the outcome
- As we will see, the features that do not drop out of the analysis may be helpful in generating hypotheses

1.1 Example 3.1

Application 3.1: Determining which features predict whether or not a segment of amino acids will be involved in an entanglement

- For this application we will use a dataset of 810 features computed for proteins in yeast
- Each protein was broken up into 9 amino acid segments using a sliding window (*e.g.*, residues [1-9] form segment 1, residues [2-10] form segment 2, *etc.*)
- This is a binary classification problem - we want to predict which segments will be entangled (outcome = 1) and which will not be entangled (outcome = 0)
- As we are trying to predict a binary outcome, we will apply LASSO to **logistic regression**
- Let's get started on our analysis in Python

1.1.1 Step 0 - Load libraries

[1]:
```
import pandas as pd
from sklearn.linear_model import LogisticRegression
from sklearn.model_selection import StratifiedKFold, train_test_split,␣
↪cross_validate
from sklearn.metrics import roc_auc_score, balanced_accuracy_score
import numpy as np
from datetime import datetime
```

```python
import matplotlib.pyplot as plt
```

1.1.2 Step 1 - Load the data & explore

[2]:
```python
# load data set as a pandas DataFrame object
data_path = "/home/jovyan/data-store/data/iplant/home/shared/NCEMS/
↪BPS-training-2025/"
data6     = pd.read_csv(data_path+"yeast-processed_v2.csv")

print ("Create a quick summary of the DataFrame:\n")
data6.info()

print ("\nVisualize the first ten rows of the DataFrame:\n")
display(data6.head())
```

```
Create a quick summary of the DataFrame:

<class 'pandas.core.frame.DataFrame'>
RangeIndex: 15000 entries, 0 to 14999
Columns: 811 entries, A_-4_pssm to target_value
dtypes: float64(810), int64(1)
memory usage: 92.8 MB

Visualize the first ten rows of the DataFrame:


   A_-4_pssm  R_-4_pssm  N_-4_pssm  D_-4_pssm  C_-4_pssm  Q_-4_pssm  \
0  -1.166467   3.063321  -0.464957  -0.637332  -1.258442   0.177605
1  -0.315714  -0.407209   0.251464   2.509363   0.807513   0.177605
2  -1.166467  -1.448368  -1.539589  -1.581340  -0.432060  -1.375564
3   0.960415   0.633950   1.326096   0.306677  -0.018869   0.954189
4  -0.741091  -0.407209  -0.464957  -0.637332  -0.432060  -0.598979

   E_-4_pssm  G_-4_pssm  H_-4_pssm  I_-4_pssm  …  KARS160118_aaindex  \
0  -0.130065  -0.530745  -0.375076  -0.947012  …           -0.183969
1   1.967388   0.106022  -0.375076   0.003443  …           -0.346913
2  -1.528368  -1.485896  -1.501882   1.904353  …            0.328332
3   0.569086   2.016322   0.000526  -0.630194  …            0.681985
4  -0.479641  -0.530745   1.127332  -0.313376  …            0.371299

   KARS160119_aaindex  KARS160120_aaindex  KARS160121_aaindex  \
0           -0.513191            0.575881           -0.238002
1            0.314936            0.479027            0.802531
2            1.503480            0.441555            1.767465
3            0.552420            0.716875            0.090801
4           -1.482826            0.962661           -1.057253
```

```
   KARS160122_aaindex  str__AlphaHelix  str__Coil  str__Strand  str__Turn  \
0           -1.247483        -1.808274  -0.035613     2.162757  -0.245399
1           -0.506544         0.553014  -0.035613    -0.462373  -0.245399
2            0.037106         0.553014  -0.035613    -0.462373  -0.245399
3            0.035261         0.553014  -0.035613    -0.462373  -0.245399
4           -1.117966         0.553014  -0.035613    -0.462373  -0.245399

   target_value
0             1
1             1
2             0
3             0
4             0

[5 rows x 811 columns]
```

- We have 811 columns corresponding to the 810 feature columns and the single outcome column
- In this instance, the outcome we are trying to predict is named `target_value`
- We will now check to see if the feature space has been scaled correctly

[3]:
```
print ("\nInformation about mean and standard deviation of parameters:")
data6.describe()
```

```
Information about mean and standard deviation of parameters:
```

[3]:
```
           A_-4_pssm     R_-4_pssm     N_-4_pssm     D_-4_pssm     C_-4_pssm  \
count   1.500000e+04  1.500000e+04  1.500000e+04  1.500000e+04  1.500000e+04
mean    9.947598e-18  3.457975e-17  1.444770e-17 -4.263256e-17  1.728987e-17
std     1.000033e+00  1.000033e+00  1.000033e+00  1.000033e+00  1.000033e+00
min    -3.718725e+00 -2.836580e+00 -3.330643e+00 -2.840018e+00 -2.911205e+00
25%    -7.410907e-01 -7.542619e-01 -8.231681e-01 -6.373316e-01 -4.320599e-01
50%    -3.157144e-01 -4.072089e-01 -1.067468e-01 -3.226621e-01 -1.886905e-02
75%     5.350384e-01  2.868972e-01  6.096745e-01  6.213463e-01  3.943218e-01
max     3.512673e+00  3.757428e+00  3.833570e+00  3.453372e+00  6.178994e+00

           Q_-4_pssm     E_-4_pssm     G_-4_pssm     H_-4_pssm     I_-4_pssm  \
count   1.500000e+04  1.500000e+04  1.500000e+04  1.500000e+04  1.500000e+04
mean   -1.894781e-18 -4.547474e-17 -1.705303e-17 -3.505344e-17 -1.326346e-17
std     1.000033e+00  1.000033e+00  1.000033e+00  1.000033e+00  1.000033e+00
min    -2.928732e+00 -2.926670e+00 -2.441046e+00 -2.628689e+00 -2.531105e+00
25%    -5.989794e-01 -8.292166e-01 -5.307452e-01 -7.506783e-01 -6.301941e-01
50%    -2.106873e-01 -1.300654e-01 -2.123618e-01  5.258429e-04 -3.133757e-01
75%     5.658969e-01  5.690857e-01  4.244051e-01  3.761279e-01  6.370796e-01
max     4.060526e+00  3.365690e+00  3.289856e+00  4.883353e+00  3.171627e+00

       …  KARS160118_aaindex  KARS160119_aaindex  KARS160120_aaindex  \
count  …        1.500000e+04        1.500000e+04        1.500000e+04
```

```
mean   …      -1.894781e-18       -2.664535e-17       2.178998e-17
std    …       1.000033e+00        1.000033e+00       1.000033e+00
min    …      -4.262544e+00       -4.514611e+00      -5.694541e+00
25%    …      -6.377679e-01       -6.089267e-01      -5.958938e-01
50%    …       4.078276e-02        9.482615e-02       1.684588e-01
75%    …       6.489334e-01        7.449061e-01       7.464071e-01
max    …       4.139189e+00        2.378900e+00       1.468525e+00

       KARS160121_aaindex  KARS160122_aaindex  str__AlphaHelix     str__Coil  \
count        1.500000e+04        1.500000e+04     1.500000e+04  1.500000e+04
mean         1.657933e-18       -2.036889e-17    -1.117921e-16  3.907985e-17
std          1.000033e+00        1.000033e+00     1.000033e+00  1.000033e+00
min         -4.451064e+00       -2.835015e+00    -1.808274e+00 -3.561282e-02
25%         -6.142900e-01       -7.175470e-01     5.530135e-01 -3.561282e-02
50%          9.080126e-02       -8.773702e-02     5.530135e-01 -3.561282e-02
75%          7.231234e-01        6.367197e-01     5.530135e-01 -3.561282e-02
max          3.428023e+00        5.120849e+00     5.530135e-01  2.807977e+01

        str__Strand     str__Turn  target_value
count  1.500000e+04  1.500000e+04  15000.000000
mean   1.148711e-16  1.411612e-16      0.500000
std    1.000033e+00  1.000033e+00      0.500017
min   -4.623728e-01 -2.453987e-01      0.000000
25%   -4.623728e-01 -2.453987e-01      0.000000
50%   -4.623728e-01 -2.453987e-01      0.500000
75%   -4.623728e-01 -2.453987e-01      1.000000
max    2.162757e+00  4.075001e+00      1.000000

[8 rows x 811 columns]
```

- Critically, we can see that the feature space has already been scaled such that each feature has a **mean of zero** and a **standard deviation of one**
- We need to check one final thing about our data set - whether or not the outcome classes are balanced

[4]:
```python
# calculate counts per outcome class
class_counts = data6["target_value"].value_counts()
print (class_counts)
```

```
target_value
1    7500
0    7500
Name: count, dtype: int64
```

- The outcome classes are perfectly balanced with 7,500 occurrances of both `0` and `1` - we are ready to proceed

1.1.3 Step 2 - Prepare data for model building

- We need to split our complete dataset of 15,000 entries into three portions:
  - 1 - a dataset used to **train** the model *during* parameter tuning
  - 2 - a dataset used to **test** the model *during* parameter tuning
  - 3 - a **holdout** dataset used to **test** performance *after* parameter tuning
- We will first reserve a holdout dataset for final testing and use the rest for model training and parameter tuning
- In this example, we will use **k-fold cross validation** paired with a grid search to select the value of , the **hyperparameter** that determines the strength of regularization (how aggressively coefficients are collapsed to zero) in LASSO, while training and testing the model simultaneously
- In `sklearn`, regularization strength is controlled by the hyperparameter C = 1/

1.1.4 K-Fold Cross Validation

- In **k-fold cross validation**, the set of non-holdout data is split into various different train-test subsets (**Figure 3.1.1**)

Figure 3.1.1. *In k-fold cross validation, every data point will be used to both train & test the model. Modified from https://en.wikipedia.org/wiki/Cross-validation_(statistics)*

- The cell below sets up the data splitting - we will reserve 20% of the data for final testing and use the other 80% for model training

[5]:
```
# set a random seed to get deterministic behavior
random_seed = 1

# number of folds for cross-validation
Nfolds      = 5

# define feature and outcome datasets
X           = data6.drop(columns=["target_value"])
y           = data6["target_value"]

# reserve 20% of data for final testing after hyperparameter tuning
```

```
X_train, X_holdout, y_train, y_holdout = train_test_split(X, y, test_size=0.2,␣
↪random_state=random_seed, stratify=y)

# set up k-fold cross-validation with outcome stratification
kf = StratifiedKFold(n_splits=Nfolds, shuffle=True, random_state=random_seed)

# set up set of lambda values for hyperparameter tuning
lambda_vals = np.logspace(-1, 4, 6)
```

1.1.5 Step 3 - Optimize

- We are ready to run cross-validation and select the value of

[6]:
```
# save the start time of the cell
startTime     = datetime.now()

# maximum number of iterations to be run
max_iter      = 10000

# setup dictionary to store results for each value of lambda
results_dict = {}

# loop over lambda values
for lambda_val in lambda_vals:

    # setup logistic regression model
    model                       = LogisticRegression(penalty="l1", solver="saga",
                                                      max_iter=max_iter, C=1/
↪lambda_val)

    # run cross-validation for current lambda_val
    cv_results                  = cross_validate(model, X_train, y_train, cv=kf,␣
↪return_estimator=True,
                                                  scoring=['balanced_accuracy',␣
↪'roc_auc'], n_jobs=-1)

    # store results for later
    results_dict[lambda_val] = cv_results

    # calculation elapsed time and print it to the screen
    elapsed_sec                 = (datetime.now() - startTime).total_seconds()
    print(f"{lambda_val:10.4f} {elapsed_sec:10.2f} s")
```

```
  0.1000      67.10 s
  1.0000     124.93 s
 10.0000     175.24 s
100.0000     204.51 s
```

```
 1000.0000      225.21 s
10000.0000      226.17 s
```

- Now that we have run cross-validation for each value of , let's assess the results
- We will use two performance metrics:
  - **Balanced accuracy**
    - Balanced accuracy = 1 indicates perfect predictions
    - Balanced accuracy = 0.5 indicates random classification
    - Balanced accuracy < 0.5 indicates *worse* than random classification
  - Area Under the Receiver Operating Characteristic Curve (**AUROC**)
    - AUROC = 1 indicates perfect classification
    - AUROC = 0.5 indicates random classification
    - AUROC < 0.5 indicates worse than random classification

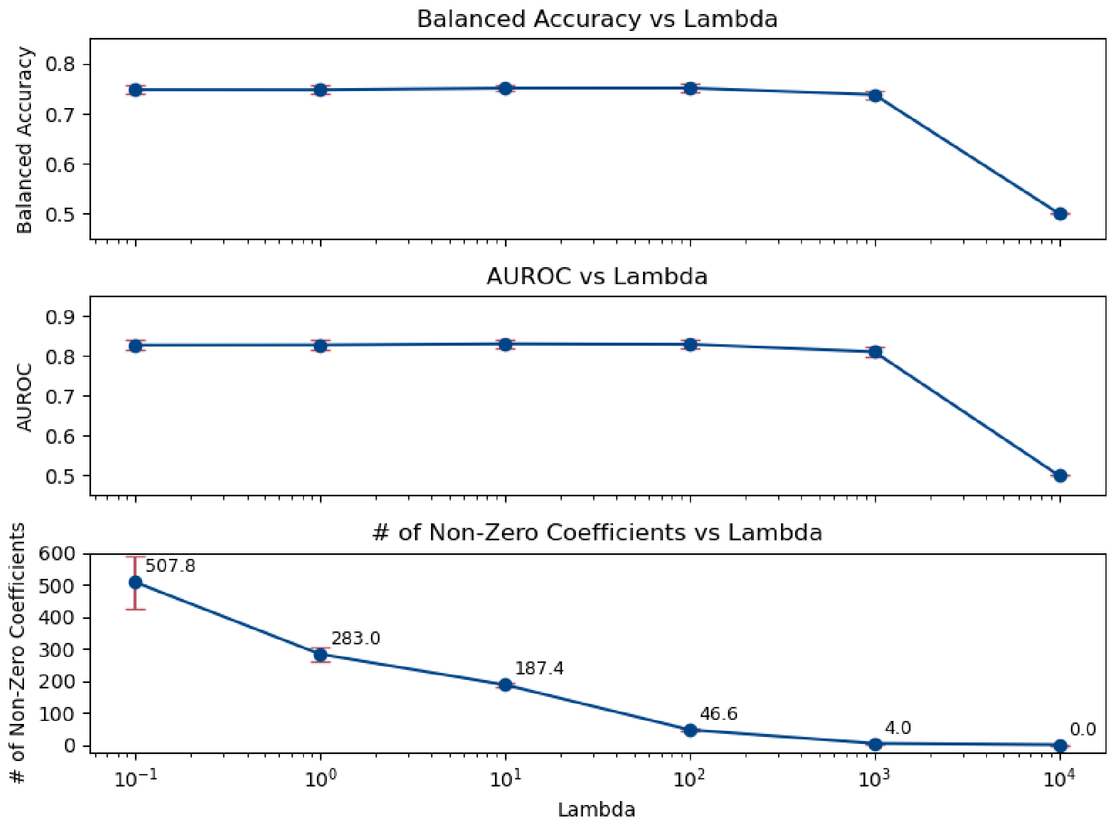
[7]:

```python
# sort the lambda values
lambda_vals                 = sorted(results_dict.keys())

# initialize lists to store the aggregated metric means and standard deviations
bal_acc_means, bal_acc_stds = [],[]
auroc_means, auroc_stds     = [],[]
nonzero_means, nonzero_stds = [],[]

# loop over each lambda and compute metrics
for lambda_val in lambda_vals:

    cv_results     = results_dict[lambda_val]

    # extract balanced accuracy and AUROC scores
    test_bal_acc   = cv_results['test_balanced_accuracy']
    test_roc_auc   = cv_results['test_roc_auc']

    # compute mean and standard deviation
    mean_bal_acc   = np.mean(test_bal_acc)
    std_bal_acc    = np.std(test_bal_acc, ddof=1)
    mean_roc_auc   = np.mean(test_roc_auc)
    std_roc_auc    = np.std(test_roc_auc, ddof=1)

    # compute number of non-zero coefficients for each fold
    nonzero_counts = [np.count_nonzero(estimator.coef_[0]) for estimator in␣
↪cv_results['estimator']]
    mean_nonzero   = np.mean(nonzero_counts)
    std_nonzero    = np.std(nonzero_counts, ddof=1)

    # Append the computed metrics to the corresponding lists
    bal_acc_means.append(mean_bal_acc)
    bal_acc_stds.append(std_bal_acc)
    auroc_means.append(mean_roc_auc)
    auroc_stds.append(std_roc_auc)
```

```python
    nonzero_means.append(mean_nonzero)
    nonzero_stds.append(std_nonzero)

# print summary information to screen
header = ("Lambda".ljust(12) + "Balanced Acc (mean ± std)".ljust(27) +
          "AUROC (mean ± std)".ljust(30) + "Non-zero Coeffs (mean ± std)")
print(header)

for i, lambda_val in enumerate(lambda_vals):
    nonzero_str = f"{nonzero_means[i]:10.1f} ± {nonzero_stds[i]:10.1f}"
    print(f"{lambda_val:10.4f}\t" f"{bal_acc_means[i]:0.3f} ± {bal_acc_stds[i]:
 ↪0.3f}\t\t"
          f"{auroc_means[i]:0.3f} ± {auroc_stds[i]:0.3f}\t\t" f"{nonzero_str}")

# create summary plots
plot_color  = "#004488"
error_color = "#BB5566"
fig, axes   = plt.subplots(3, 1, figsize=(8, 6), sharex=True)

# plot Balanced Accuracy
axes[0].errorbar(lambda_vals, bal_acc_means, yerr=bal_acc_stds, fmt='o-',␣
 ↪capsize=5, color=plot_color, ecolor=error_color)
axes[0].set_xscale('log')
axes[0].set_ylabel('Balanced Accuracy')
axes[0].set_title('Balanced Accuracy vs Lambda')
axes[0].set_ylim(0.45, 0.85)
axes[0].set_yticks([0.5, 0.6, 0.7, 0.8])

# plot AUROC
axes[1].errorbar(lambda_vals, auroc_means, yerr=auroc_stds, fmt='o-',␣
 ↪capsize=5, color=plot_color, ecolor=error_color)
axes[1].set_xscale('log')
axes[1].set_ylabel('AUROC')
axes[1].set_title('AUROC vs Lambda')
axes[1].set_ylim(0.45, 0.95)
axes[1].set_yticks([0.5, 0.6, 0.7, 0.8, 0.9])

# plot number of non-zero coefficients
axes[2].errorbar(lambda_vals, nonzero_means, yerr=nonzero_stds, fmt='o-',␣
 ↪capsize=5,color=plot_color, ecolor=error_color)
axes[2].set_xscale('log')
axes[2].set_ylabel('# of Non-Zero Coefficients')
axes[2].set_title('# of Non-Zero Coefficients vs Lambda')
axes[2].set_ylim(-25, 600)
axes[2].set_yticks([0, 100, 200, 300, 400, 500, 600])
axes[2].set_xlabel('Lambda')
```

```python
# annotate each point with the mean number of non-zero coefficients (to one␣
↪decimal)
for i, lambda_val in enumerate(lambda_vals):
    axes[2].annotate(f"{nonzero_means[i]:.1f}", (lambda_val, nonzero_means[i]),
                     textcoords="offset points", xytext=(5, 5), fontsize=9,␣
↪color='black')

plt.tight_layout()
plt.show()
```

```
Lambda      Balanced Acc (mean ± std)  AUROC (mean ± std)            Non-zero
Coeffs (mean ± std)
    0.1000      0.748 ± 0.008            0.826 ± 0.012              507.8 ±
81.8
    1.0000      0.748 ± 0.008            0.827 ± 0.011              283.0 ±
20.8
   10.0000      0.751 ± 0.005            0.830 ± 0.011              187.4 ±
5.6
  100.0000      0.751 ± 0.008            0.829 ± 0.011               46.6 ±
3.5
 1000.0000      0.738 ± 0.008            0.810 ± 0.011                4.0 ±
0.0
10000.0000      0.500 ± 0.000            0.500 ± 0.000                0.0 ±
0.0
```



- With LASSO, we get to choose our preferred trade off between number of non-zero features and performance.
- In this case, we can achieve strong performance with = 1,000 and have only 4 features to consider

1.1.6 Step 4 - Build & test the final model

- We can now construct the final model by training on all data except the holdout dataset with = 1000.
- After training the final model, we will test its performance on the unseen holdout set

[8]:
```
# choose our preferred value of lambda
final_lambda        = 1000.

# setup the model
final_model         = LogisticRegression(penalty="l1", solver="saga",␣
 ↪max_iter=max_iter, C=1/final_lambda)

# fit the model to the data
final_model.fit(X_train, y_train)
```

```python
# evaluate the final model on the holdout dataset
y_holdout_pred_prob = final_model.predict_proba(X_holdout)[:, 1]
y_holdout_pred      = final_model.predict(X_holdout)
holdout_auroc       = roc_auc_score(y_holdout, y_holdout_pred_prob)
holdout_bal_acc     = balanced_accuracy_score(y_holdout, y_holdout_pred)

print ("Performance on holdout data\n")
print("Holdout AUROC             :", '%.3f' %holdout_auroc)
print("Holdout Balanced Accuracy :", '%.3f' %holdout_bal_acc)

# extract the nonzero coefficients
coef                = final_model.coef_.flatten()
nonzero_indices     = coef != 0
nonzero_coefs       = coef[nonzero_indices]
nonzero_features    = X_train.columns[nonzero_indices]

# sort coefficients by absolute magnitude in descending order
sorted_indices      = abs(nonzero_coefs).argsort()[::-1]
sorted_features     = nonzero_features[sorted_indices]
sorted_coefs        = nonzero_coefs[sorted_indices]

# print nonzero coefficients
print("\nNonzero Coefficients (sorted by magnitude)\n")
for feature, value in zip(sorted_features, sorted_coefs):
    print(feature.ljust(26) + ": " + "%.5f" % value)
```

```
Performance on holdout data

Holdout AUROC             : 0.813
Holdout Balanced Accuracy : 0.739

Nonzero Coefficients (sorted by magnitude)

CN_exp                    : 0.46217
Theta_exp                 : 0.20938
SS7__Strand               : 0.12323
rsaa                      : -0.08388
Tau_exp                   : -0.01460
```

1.1.7 Step 5 - Assess the results

- We observe that there are five rather than four non-zero features - we expect some differences between this final model, parameterized based on the entire training set, and those trained during cross-validation
- These non-zero features can serve as the basis for hypothesis generation; for example:
  - Why is `CN_exp`, which represents the local packing density of a set of residues, important to our ability to predict the outcome?