Kagle_Submission

December 13, 2020

1 Mechanisms of Action (MoA) Prediction

Predicting multiple targets of the Mechanism of Action (MoA) response(s) of different samples (sig_id), given various inputs such as gene expression data and cell viability data.

1.1 Some of the important terms used in the headings of the tables are presented here:

```
g - : signifies gene expression data
c - : signifies cell expression data
cp_type : indicates samples treated with a compound (cp_vehicle) or with a control perturbatio
NOTE: (samples with control perturbations don't have MoAs)
cp_time - treatment duration (24,48,72) Hours
cp_dose - Dosage - HIGH or LOW
```

[1]:
```
# Importing the multi label stratified k-fold
# cross validator
import sys
sys.path.append('../input/iterative-stratification/
 ↪iterative-stratification-master')
from iterstrat.ml_stratifiers import MultilabelStratifiedKFold

# Initial random imports
import random
import os
import copy
import warnings
# warnings.filterwarnings('ignore')

# Importing numpy
import numpy as np

# Importing pandas
import pandas as pd

# Importing matplotlib
import matplotlib.pyplot as plt
```

```
# Importing seaborn
import seaborn as sns

# Importing sklearn
from sklearn import preprocessing
from sklearn.metrics import log_loss
from sklearn.preprocessing import StandardScaler
from sklearn.decomposition import PCA
from sklearn.feature_selection import VarianceThreshold

# Importing pytorch
import torch
import torch.nn as nn
import torch.nn.functional as F
import torch.optim as optim
```

2 Using GPU if available

[2]:
```
# using GPU if available
if torch.cuda.is_available():
    device_code = 'cuda'
else:
    device_code = 'cpu'
```

[3]:
```
# setting the seed, so that every time the seed is started from the same number

def set_seed_characteristics(seed=55):
    # Setting a random seed value

    random.seed(seed)

    # for guaranteering the reproducability of numbers by setting seed for NumPy

    np.random.seed(seed)

    # for setting the seed for cuda or cpu

    torch.manual_seed(seed)

    # To ensure that Pytorch doesnt just switch to the fastest possible␣
 ↪algorithm but
    # ensures that it selects a deterministic algorithm

    torch.backends.cudnn.deterministic = True
```

3 Reading the CSV Files

[4]:
```
training_features = pd.read_csv('input/lish-moa/train_features.csv')
# Reading the head rows and columns of train features
training_features_head = training_features.head()

training_targets_scored = pd.read_csv('input/lish-moa/train_targets_scored.csv')
# Reading the head rows and columns of train targets scored
training_targets_scored_head = training_targets_scored.head()

testing_features = pd.read_csv('input/lish-moa/test_features.csv')
# Reading the head rows and columns of train targets non-scored
testing_features_head = testing_features.head()
```

[5]:
```
# Printing the head - training features
training_features_head
```

[5]:

	sig_id	cp_type	cp_time	cp_dose	g-0	g-1	g-2	g-3	\
0	id_000644bb2	trt_cp	24	D1	1.0620	0.5577	-0.2479	-0.6208	
1	id_000779bfc	trt_cp	72	D1	0.0743	0.4087	0.2991	0.0604	
2	id_000a6266a	trt_cp	48	D1	0.6280	0.5817	1.5540	-0.0764	
3	id_0015fd391	trt_cp	48	D1	-0.5138	-0.2491	-0.2656	0.5288	
4	id_001626bd3	trt_cp	72	D2	-0.3254	-0.4009	0.9700	0.6919	

	g-4	g-5	…	c-90	c-91	c-92	c-93	c-94	c-95	\
0	-0.1944	-1.0120	…	0.2862	0.2584	0.8076	0.5523	-0.1912	0.6584	
1	1.0190	0.5207	…	-0.4265	0.7543	0.4708	0.0230	0.2957	0.4899	
2	-0.0323	1.2390	…	-0.7250	-0.6297	0.6103	0.0223	-1.3240	-0.3174	
3	4.0620	-0.8095	…	-2.0990	-0.6441	-5.6300	-1.3780	-0.8632	-1.2880	
4	1.4180	-0.8244	…	0.0042	0.0048	0.6670	1.0690	0.5523	-0.3031	

	c-96	c-97	c-98	c-99
0	-0.3981	0.2139	0.3801	0.4176
1	0.1522	0.1241	0.6077	0.7371
2	-0.6417	-0.2187	-1.4080	0.6931
3	-1.6210	-0.8784	-0.3876	-0.8154
4	0.1094	0.2885	-0.3786	0.7125

[5 rows x 876 columns]

[6]:
```
# Printing the head - train targets scored
training_targets_scored_head
```

[6]:

	sig_id	5-alpha_reductase_inhibitor	11-beta-hsd1_inhibitor	\
0	id_000644bb2	0	0	
1	id_000779bfc	0	0	
2	id_000a6266a	0	0	

```
3  id_0015fd391                            0                       0
4  id_001626bd3                            0                       0

   acat_inhibitor  acetylcholine_receptor_agonist  \
0               0                               0
1               0                               0
2               0                               0
3               0                               0
4               0                               0

   acetylcholine_receptor_antagonist  acetylcholinesterase_inhibitor  \
0                                  0                               0
1                                  0                               0
2                                  0                               0
3                                  0                               0
4                                  0                               0

   adenosine_receptor_agonist  adenosine_receptor_antagonist  \
0                           0                              0
1                           0                              0
2                           0                              0
3                           0                              0
4                           0                              0

   adenylyl_cyclase_activator  …  tropomyosin_receptor_kinase_inhibitor  \
0                           0  …                                      0
1                           0  …                                      0
2                           0  …                                      0
3                           0  …                                      0
4                           0  …                                      0

   trpv_agonist  trpv_antagonist  tubulin_inhibitor  \
0             0                0                  0
1             0                0                  0
2             0                0                  0
3             0                0                  0
4             0                0                  0

   tyrosine_kinase_inhibitor  ubiquitin_specific_protease_inhibitor  \
0                          0                                      0
1                          0                                      0
2                          0                                      0
3                          0                                      0
4                          0                                      0

   vegfr_inhibitor  vitamin_b  vitamin_d_receptor_agonist  wnt_inhibitor
0                0          0                           0              0
```

```
1                0          0                          0              0
2                0          0                          0              0
3                0          0                          0              0
4                0          0                          0              0

[5 rows x 207 columns]
```

[7]:
```
# Printing the head - test features
testing_features_head
```

[7]:
```
         sig_id      cp_type  cp_time cp_dose     g-0     g-1     g-2     g-3  \
0  id_0004d9e33       trt_cp       24      D1 -0.5458  0.1306 -0.5135  0.4408
1  id_001897cda       trt_cp       72      D1 -0.1829  0.2320  1.2080 -0.4522
2  id_002429b5b  ctl_vehicle       24      D1  0.1852 -0.1404 -0.3911  0.1310
3  id_00276f245       trt_cp       24      D2  0.4828  0.1955  0.3825  0.4244
4  id_0027f1083       trt_cp       48      D1 -0.3979 -1.2680  1.9130  0.2057

      g-4     g-5  …    c-90    c-91    c-92    c-93    c-94    c-95  \
0  1.5500 -0.1644  …  0.0981  0.7978 -0.1430 -0.2067 -0.2303 -0.1193
1 -0.3652 -0.3319  … -0.1190 -0.1852 -1.0310 -1.3670 -0.3690 -0.5382
2 -1.4380  0.2455  … -0.2261  0.3370 -1.3840  0.8604 -1.9530 -1.0140
3 -0.5855 -1.2020  …  0.1260  0.1570 -0.1784 -1.1200 -0.4325 -0.9005
4 -0.5864 -0.0166  …  0.4965  0.7578 -0.1580  1.0510  0.5742  1.0900

     c-96    c-97    c-98    c-99
0  0.0210 -0.0502  0.1510 -0.7750
1  0.0359 -0.4764 -1.3810 -0.7300
2  0.8662  1.0160  0.4924 -0.1942
3  0.8131 -0.1305  0.5645 -0.5809
4 -0.2962 -0.5313  0.9931  1.8380

[5 rows x 876 columns]
```

4 Dataset classes, training and testing functions

[8]:
```
# Pytorch data loader implementation of MoA dataset
class MoADataset:
    def __init__(self, features, targets):
        self.features = features
        self.targets = targets

    def __len__(self):
        return (self.features.shape[0])

    def __getitem__(self, idx):
```

```
        train_tensor_dictionary = {
            'x' : torch.tensor(self.features[idx, :], dtype=torch.float),
            'y' : torch.tensor(self.targets[idx, :], dtype=torch.float)
        }
        return train_tensor_dictionary

# Pytorch data loader implementation of test dataset
class TestDataset:
    def __init__(self, features):
        self.features = features

    def __len__(self):
        return (self.features.shape[0])

    def __getitem__(self, idx):
        test_tensor_dictionary = {
            'x' : torch.tensor(self.features[idx, :], dtype=torch.float)
        }
        return test_tensor_dictionary
```

[9]:
```
# Pytorch model for the MoA determination

class Model(nn.Module):

    # Instantiaing all the models before utilizing
    # them later in the forward function.
    def __init__(self, num_features, num_targets, hidden_size):

        # super keyword used to access data from the parent
        # pytorch.nn.Module class
        super(Model, self).__init__()
        # Applying batch normalization. This is done to standardize
        # the input for each mini batches and will help reduce the
        # number of epochs for which the training is done. This limits
        # the covariate shift (this is the value by which the hidden
        # layer values shift around) and allows to learn from a more
        # stable set of data. Sometimes, it also allows for a
        # higher learning rate.This is also used for regularization
        # and helps reduce over fitting. Generally, if batch
        # normalization is used, you can use a smaller dropout,
        # which in turn means that lesser layers can be lost
        # in every step.
        self.batch_normalization_1 = nn.BatchNorm1d(num_features)
        # For regularization purposes the dropout is set
        # This is done by setting a probablity. Random
        # neural networks are picked at a probablity, say p
        # or dropped at a probablity of 1-p. This is essential
```

```
        # to prevent overfitiing of the model and also reduces
        # the computation time. A fully connected neural network, if
        # run without dropout will start forming dependancies between
        # each other and this can lead to over-fitting.
        self.dropoutlayer_1 = nn.Dropout(0.2)
        # nn.utils.weight_norm : This is weight normalization. Usually,
        #                        faster than batch normalization
        # nn.Linear : Applying linear transform to the incoming data
        #             and creates a single layer feed forward network.
        # input size : num_features
        # output size : hidden_size
        self.denselayer_1 = nn.utils.weight_norm(nn.Linear(num_features,␣
↪hidden_size))

        self.batch_normalization_2 = nn.BatchNorm1d(hidden_size)
        self.dropoutlayer_2 = nn.Dropout(0.2)
        # input size : hidden_size
        # output size : hidden_size
        self.denselayer_2 = nn.utils.weight_norm(nn.Linear(hidden_size,␣
↪hidden_size))

        self.batch_normalization_3 = nn.BatchNorm1d(hidden_size)
        self.dropoutlayer_3 = nn.Dropout(0.1)
        # input size : hidden_size
        # output size : hidden_size
        self.denselayer_3 = nn.utils.weight_norm(nn.Linear(hidden_size,␣
↪hidden_size))

        self.batch_normalization_4 = nn.BatchNorm1d(hidden_size)
        self.dropoutlayer_4 = nn.Dropout(0.1)
        # input size : hidden_size
        # output size : hidden_size
        self.denselayer_4 = nn.utils.weight_norm(nn.Linear(hidden_size,␣
↪hidden_size))


        self.batch_normalization_5 = nn.BatchNorm1d(hidden_size)
        self.dropoutlayer_5 = nn.Dropout(0.1)
        # input size : hidden_size
        # output size : num_targets
        self.denselayer_5 = nn.utils.weight_norm(nn.Linear(hidden_size,␣
↪num_targets))

    # The forward function basically defines the model
    def forward(self, forward_x):

        forward_x = self.batch_normalization_1(forward_x)
```

```
        forward_x = self.dropoutlayer_1(forward_x)
        forward_x = F.relu(self.denselayer_1(forward_x))

        forward_x = self.batch_normalization_2(forward_x)
        forward_x = self.dropoutlayer_2(forward_x)
        forward_x = F.relu(self.denselayer_2(forward_x))

        forward_x = self.batch_normalization_3(forward_x)
        forward_x = self.dropoutlayer_3(forward_x)
        forward_x = self.denselayer_3(forward_x)

        forward_x = self.batch_normalization_4(forward_x)
        forward_x = self.dropoutlayer_4(forward_x)
        forward_x = self.denselayer_4(forward_x)

        forward_x = self.batch_normalization_5(forward_x)
        forward_x = self.dropoutlayer_5(forward_x)
        forward_x = self.denselayer_5(forward_x)

        return forward_x
```

[10]:
```
# Function to train the model
def trainingFunction(model, optimizer, scheduler, lossFunction, trainloader,␣
↪device_code):
    model.train()
    training_loss = 0
    for training_data in trainloader:
        optimizer.zero_grad()
        inputs, targets = training_data['x'].to(device_code),␣
↪training_data['y'].to(device_code)
        outputs = model(inputs)
        loss = lossFunction(outputs, targets)
        loss.backward()
        optimizer.step()
        scheduler.step()
        training_loss += loss.item()
    training_loss /= len(trainloader)
    return training_loss
```

[11]:
```
# Function to validate the model
def validationFunction(model, lossFunction, validationloader, device_code):
    model.eval()
    validation_loss = 0
    validation_predictions = []
    for validation_data in validationloader:
        inputs, targets = validation_data['x'].to(device_code),␣
↪validation_data['y'].to(device_code)
```

```
        outputs = model(inputs)
        loss = lossFunction(outputs, targets)
        validation_loss += loss.item()
        validation_predictions.append(outputs.sigmoid().detach().cpu().numpy())
    validation_loss /= len(validationloader)
    validation_predictions = np.concatenate(validation_predictions)
    return validation_loss, validation_predictions
```

[12]:
```
# Adding the inference function
def inferenceFunction(model, inferenceloader, device_code):
    model.eval()
    inferences = []
    for data in inferenceloader:
        inputs = data['x'].to(device_code)
        with torch.no_grad():
            outputs = model(inputs)
        inferences.append(outputs.sigmoid().detach().cpu().numpy())
    inferences = np.concatenate(inferences)
    return inferences
```

[13]:
```
# Adding dummy inserts to the cp_time and cp_dose columns
# Usually done to categorical variables
def addDummies(data):
    dummy_data = pd.get_dummies(data, columns=['cp_time','cp_dose'])
    return dummy_data
```

5 Preparing the dataset

[14]:
```
set_seed_characteristics(seed=55)
```

[15]:
```
# Seperating out the Gene expression Column and Cell Viability Column

gene_expression = [g for g in training_features.columns if g.startswith('g-')]
cell_viability = [c for c in training_features.columns if c.startswith('c-')]
```

[16]:
```
# Since our dimensions are really high, we can resort to
# using PCA for dimensionality reduction, but is still able
# to capture the characteristics of the data.

# Now, this can be done by choosing a random dimension, and
# having the same random state as before. By doing this
# we observe that we do not encounter
# any 'nan' errors during training.

# Doing PCA for the Gene expression data
```

```
# can choose any random number here
random_pca_dimension_genes = 20

# Concatenating the training and test set
data = pd.concat([pd.DataFrame(training_features[gene_expression]), pd.
 ↪DataFrame(testing_features[gene_expression])])

# Performing PCA and converting to a random_pca_dimension_genes number of␣
 ↪columns
pca_genes = PCA(n_components = random_pca_dimension_genes, random_state=55)

# Fitting the PCA transform
data_pca = pca_genes.fit_transform(data[gene_expression])

# Splitting the training and test columns
train_pca_genes = data_pca[:training_features.shape[0]]
test_pca_genes = data_pca[-testing_features.shape[0]:]

# Converting training and testing  into Pandas data frame shape
train_pca_genes = pd.DataFrame(train_pca_genes, columns=[f'pca_G-{i}' for i in␣
 ↪range(random_pca_dimension_genes)])
test_pca_genes = pd.DataFrame(test_pca_genes, columns=[f'pca_G-{i}' for i in␣
 ↪range(random_pca_dimension_genes)])

# Concatenating these back to the original features
training_features = pd.concat((training_features, train_pca_genes), axis=1)
testing_features = pd.concat((testing_features, test_pca_genes), axis=1)
```

[17]:
```
# Doing PCA for the Cell Viability Data

# can choose any random number here
random_pca_dimension_cells = 32

# Concatenating the training and test set
data = pd.concat([pd.DataFrame(training_features[cell_viability]), pd.
 ↪DataFrame(testing_features[cell_viability])])

# Performing PCA and converting to a random_pca_dimension_cells number of␣
 ↪columns
pca_cells = PCA(n_components = random_pca_dimension_cells, random_state=55)

# Fitting the PCA transform
data_pca = pca_cells.fit_transform(data[cell_viability])

# Splitting the training and test columns
```

```
train_pca_cells = data_pca[:training_features.shape[0]]
test_pca_cells = data_pca[-testing_features.shape[0]:]

# Converting training and testing  into Pandas data frame shape
train_pca_cells = pd.DataFrame(train_pca_cells, columns=[f'pca_C-{i}' for i in␣
 ↪range(random_pca_dimension_cells)])
test_pca_cells = pd.DataFrame(test_pca_cells, columns=[f'pca_C-{i}' for i in␣
 ↪range(random_pca_dimension_cells)])

# Concatenating these back to the original features
training_features = pd.concat((training_features, train_pca_cells), axis=1)
testing_features = pd.concat((testing_features, test_pca_cells), axis=1)
```

[18]:
```
# Setting a desired threshold to calculate the VarianceThreshold.
# As per the math all the Features with a training-set variance
# lower than this threshold will be removed.
variancethreshold = VarianceThreshold(threshold=0.7)

# Combining training and test features to create a single dataset
combined_data = training_features.append(testing_features)

# Fits to the data, before transforming it
combined_data_transformed = variancethreshold.fit_transform(combined_data.iloc[:
 ↪, 4:])

# Extracting the training and the testing data out of the
# transformed data
training_features_transformed = combined_data_transformed[ : training_features.
 ↪shape[0]]
testing_features_transformed = combined_data_transformed[-testing_features.
 ↪shape[0] : ]
```

[19]:
```
# Extracting the training features in a suitable
# pandas dataset format and numbering the columns
# after the labels of 'sig_id', 'cp_type', 'cp_time', 'cp_dose'.
training_features = pd.
 ↪DataFrame(training_features[['sig_id','cp_type','cp_time','cp_dose']].values.
 ↪reshape(-1, 4), columns=['sig_id','cp_type','cp_time','cp_dose'])
training_features = pd.concat([training_features, pd.
 ↪DataFrame(training_features_transformed)], axis=1)

# Extracting the testing features in a suitable
# pandas dataset format and numbering the columns
# after the labels of 'sig_id', 'cp_type', 'cp_time', 'cp_dose'.
```

```
testing_features = pd.
 ↪DataFrame(testing_features[['sig_id','cp_type','cp_time','cp_dose']].values.
 ↪reshape(-1, 4), columns=['sig_id','cp_type','cp_time','cp_dose'])
testing_features = pd.concat([testing_features, pd.
 ↪DataFrame(testing_features_transformed)], axis=1)
```

[20]:
```
# Merging the columns

train = training_features.merge(training_targets_scored, on='sig_id')

# Removing rows with cp_type as ctl_vehicle
# since control perturbations have no MoAs
# We are also manually setting the drop type as
# true because we do not want to include them back
# as a new column.

train = train[train['cp_type']!='ctl_vehicle'].reset_index(drop=True)

# Naturally, we have to get rid of them from the test dataset
# as well

test = testing_features[testing_features['cp_type']!='ctl_vehicle'].
 ↪reset_index(drop=True)
```

[21]:
```
# Extracting the columns of the drugs that are sold from
# the train pandas dataframe

target = train[training_targets_scored.columns]

# Now that the ctl_vehicle drugs have been removed, we do not need
# cp_type. So we can go ahead and remove that columns as well.

train = train.drop('cp_type', axis=1)
test = test.drop('cp_type', axis=1)

# extracting the columns in the targets

target_columns = target.drop('sig_id', axis=1).columns.values.tolist()
```

6 Dataset preparation complete

[22]:
```
# multilabel stratified K Fold import causes a small warning and we do not want
# to show that in the notebook.
warnings.filterwarnings('ignore')
```

```
folds = train.copy()
number_of_folds = 3

# creating a 3 fold multilabel stratified K Fold
multilabel_k_fold = MultilabelStratifiedKFold(n_splits = number_of_folds)

# Standard k fold splitting. Here we are splitting into number_of_folds folds

for fol, (train_folds, validation_folds) in enumerate(multilabel_k_fold.
 ↪split(X=train, y=target)):
    folds.loc[validation_folds, 'kfold'] = int(fol)

folds['kfold'] = folds['kfold'].astype(int)

# Isolating out the feature columns. This is done by first
# Isolating the columns that are not present in the target
# followed by extracting the columns except the sig_id and
# kfold.

feature_columns = [c for c in addDummies(folds).columns if c not in␣
 ↪target_columns]
feature_columns = [c for c in feature_columns if c not in ['kfold','sig_id']]
```

7 Declaring the HyperParameters

[23]:
```
BATCH_SIZE = 128
max_epochs = 16
# When training neural networks, it is common to use
# weight decay where after each update, the weights
# are multiplied by a factor slightly less than 1
weight_decay = 1e-5
# deciding the initial learning rate
# It controls how quickly or slowly a neural
# network model can learn a model or a problem.
lr = 1e-3
# Boolean to decide on stopping early when the
# validation_loss > best_loss
bool_early_stop = True
# steps to execute before early stopping
steps_early_stopping= 10
# number of features corresponding to the columns in the
# targets
num_features=len(feature_columns)
# number of targets corresponding to the columns in the
# features
```

```
num_targets=len(target_columns)
# in between neural netwrok size
hidden_size=1024
```

8 Declaring the training functions and performing the training

[24]:
```
# to plot validation loss
valid_loss_list = []
# to plot the training loss
train_loss_list = []
# to plot the best recorded loss
best_loss_list = []
```

[25]:
```
def run_training(fold, seed):
    # declaring the list as global to plot validation loss
    global valid_loss_list
    # declaring the training loss list as global to plot
    # the training loss
    global train_loss_list
    # declaring the best loss list as global to plot the
    # best losses recorded
    global best_loss_list

    # setting the seed to start from the same number as
    # explained previously
    set_seed_characteristics(seed)

    # adding dummy variables to the training set
    train = addDummies(folds)

    # extracting the validating rows numbers for the
    # respective k fold values
    val_idx = train[train['kfold'] == fold].index

    # Dropping all the rows from the training set
    # that does not belong to this kth fold
    train_necessary_rows = train[train['kfold'] != fold].reset_index(drop=True)
    # Dropping all the rows from the valiadtion set
    # that does not belong to this kth fold
    valid_necessary_rows = train[train['kfold'] == fold].reset_index(drop=True)

    # splitting the x and y values for training set
    train_features, train_targets  = train_necessary_rows[feature_columns].
↪values, train_necessary_rows[target_columns].values
    # splitting the x and y values for test set
```

```
    validation_features, validation_targets = ␣
↪valid_necessary_rows[feature_columns].values,␣
↪valid_necessary_rows[target_columns].values

    # Converting the training data to standard pytorch
    # dataset class format
    train_dataset = MoADataset(train_features, train_targets)

    # Converting the validation data to standard pytorch
    # dataset class format
    valid_dataset = MoADataset(validation_features, validation_targets)

    # calling the pytorch data loading utility for the
    # training set
    trainloader = torch.utils.data.DataLoader(train_dataset,␣
↪batch_size=BATCH_SIZE, shuffle=True)
    # calling the pytorch data loading utility for the
    # validation set
    validloader = torch.utils.data.DataLoader(valid_dataset,␣
↪batch_size=BATCH_SIZE, shuffle=False)

    # Declaring the model and can be tuned here
    # using the hyper parameters
    model = Model(
        num_features=num_features,
        num_targets=num_targets,
        hidden_size=hidden_size,
    )

    # moving the model to GPU if available,
    # else will run it on CPU itself
    model.to(device_code)

    # A standard optimizer. Adam optimizer is widely used
    # because it combines the advantages of the Adaptive gradient
    # algorithm and the root mean square propogation. Basically, it does
    # not stick to one learning rate and adapts it to the problem.
    # It is widely known to offer good results really fast.
    optimizer = torch.optim.Adam(model.parameters(), lr=lr,␣
↪weight_decay=weight_decay)

    # We use a learning rate scheduler to converge to the lowest
    # loss faster. This is also seen to provide higher accuracy.
    # This can be tuned.
    # Some of the optimizers I tried here are
    # optim.lr_scheduler.OneCycleLR
    # optim.lr_scheduler.StepLR
```

```
   # scheduler = optim.lr_scheduler.StepLR(optimizer, step_size=1, gamma=0.1)
   scheduler = optim.lr_scheduler.OneCycleLR(optimizer=optimizer, pct_start=0.
↪05, div_factor=1.5e3,
                                             max_lr=1e-2, epochs=max_epochs,␣
↪steps_per_epoch=len(trainloader))

   # after research I saw that the Binary cross
   # entropy loss with sigmoid layer works well
   lossFunction = nn.BCEWithLogitsLoss()

   # stops when the error starts increaseing. Setting the counter
   # to track this
   steps_before_early_stop = 0
   # general out of fold array shape
   out_of_fold = np.zeros((len(train), target.iloc[:, 1:].shape[1]))
   # declaring a very high value as an
   # initial loss for each kth fold
   best_loss = np.inf

   # looping through the epochs
   for epoch in range(max_epochs):

       # training the model
       training_loss = trainingFunction(model, optimizer,scheduler,␣
↪lossFunction, trainloader, device_code)
       print('epoch : ',epoch,'>> training_loss : ',training_loss)
       train_loss_list.append(training_loss)
       validation_loss, validation_predictions = validationFunction(model,␣
↪lossFunction, validloader, device_code)
       print('epoch : ',epoch,'>> validation : ',validation_loss)
       valid_loss_list.append(validation_loss)

       # checking if the loss is decreasing
       if validation_loss < best_loss:
           best_loss = validation_loss
           best_loss_list.append(best_loss)
           # Updating the out of fold predictions
           out_of_fold[val_idx] = validation_predictions
           # saving the model and data for this kth fold
           torch.save(model.state_dict(), f"FOLD{fold}_.pth")

       # Handling the increasing loss by calling
       # early stopping
       elif(bool_early_stop == True):

           # breaks out of the loop when this happens
```

```
            steps_before_early_stop += 1
            if (steps_before_early_stop >= steps_early_stopping):
                break
    # adding dummy variables to the test set
    test_ = addDummies(test)

    # extracting the x_test
    x_test = test_[feature_columns].values
    testdataset = TestDataset(x_test)
    testloader = torch.utils.data.DataLoader(testdataset,␣
↪batch_size=BATCH_SIZE, shuffle=False)

    model = Model(num_features=num_features,num_targets=num_targets,
        hidden_size=hidden_size,
    )

    # uploading the saved data for this kth fold
    model.load_state_dict(torch.load(f"FOLD{fold}_.pth"))
    # again uploading the model to GPU, if available
    model.to(device_code)

    predictions = np.zeros((len(test_), target.iloc[:, 1:].shape[1]))
    # evaluates the model
    predictions = inferenceFunction(model, testloader, device_code)

    return out_of_fold, predictions
```

[26]:
```
def executeKFold(number_of_folds, seed):
    # standard size for the out of fold predictions
    out_of_fold = np.zeros((len(train), len(target_columns)))
    # same size for all of the predictions
    predictions = np.zeros((len(test), len(target_columns)))

    for each_k_fold in range(number_of_folds):
        print('Fold Number : ', each_k_fold)
        out_of_fold_, pred_ = run_training(each_k_fold, seed)

        # adding all the predictions
        predictions += pred_ / number_of_folds
        # adding all the out of fold predictions
        out_of_fold += out_of_fold_
        print("------------------------")

    k_th_prediction = predictions
    return out_of_fold, k_th_prediction
```

[27]:
```
# setting a standard seed number
SEED = [55]
# general out of fold array shape
out_of_fold = np.zeros((len(train), len(target_columns)))
# general predictions array shape
predictions = np.zeros((len(test), len(target_columns)))

# for seed in SEED:
out_of_fold_, predictions_ = executeKFold(number_of_folds, SEED[0])
out_of_fold += out_of_fold_ / len(SEED)
predictions += predictions_ / len(SEED)

train[target_columns] = out_of_fold
test[target_columns] = predictions
```

```
Fold Number :  0
epoch :  0 >> training_loss :  0.2788736069979875
epoch :  0 >> validation :  0.021623456240471066
epoch :  1 >> training_loss :  0.020091968256494272
epoch :  1 >> validation :  0.01922281719101914
epoch :  2 >> training_loss :  0.019972266159627747
epoch :  2 >> validation :  0.01886744482506966
epoch :  3 >> training_loss :  0.019043210343174313
epoch :  3 >> validation :  0.018996690303601068
epoch :  4 >> training_loss :  0.018774466394730235
epoch :  4 >> validation :  0.018413769980442935
epoch :  5 >> training_loss :  0.01869301253362842
epoch :  5 >> validation :  0.01853232747264977
epoch :  6 >> training_loss :  0.01865103912094365
epoch :  6 >> validation :  0.018168202376571196
epoch :  7 >> training_loss :  0.018572327146387617
epoch :  7 >> validation :  0.01888334468520921
epoch :  8 >> training_loss :  0.018362585228422414
epoch :  8 >> validation :  0.018195184943234098
epoch :  9 >> training_loss :  0.018180621188619864
epoch :  9 >> validation :  0.01839715341941036
epoch :  10 >> training_loss :  0.017992399317090926
epoch :  10 >> validation :  0.017737267185644858
epoch :  11 >> training_loss :  0.01772677853865468
epoch :  11 >> validation :  0.017560527595723498
epoch :  12 >> training_loss :  0.017529506098641002
epoch :  12 >> validation :  0.01734824900932867
epoch :  13 >> training_loss :  0.017258823679193208
epoch :  13 >> validation :  0.01717964628839801
epoch :  14 >> training_loss :  0.01701616107121758
epoch :  14 >> validation :  0.01715383331837325
epoch :  15 >> training_loss :  0.016877019105722074
```

```
epoch :  15 >> validation :  0.01710507392497926
------------------------
Fold Number :  1
epoch :  0 >> training_loss :  0.2791394925635794
epoch :  0 >> validation :  0.021501707748092454
epoch :  1 >> training_loss :  0.02014602518276028
epoch :  1 >> validation :  0.019920575047104525
epoch :  2 >> training_loss :  0.019292888320658518
epoch :  2 >> validation :  0.020500779746036077
epoch :  3 >> training_loss :  0.01898241023654523
epoch :  3 >> validation :  0.019408218819519568
epoch :  4 >> training_loss :  0.01884553834957921
epoch :  4 >> validation :  0.018803634969838733
epoch :  5 >> training_loss :  0.018704059833417767
epoch :  5 >> validation :  0.01929768891041649
epoch :  6 >> training_loss :  0.018495980099491452
epoch :  6 >> validation :  0.018345469753418504
epoch :  7 >> training_loss :  0.018502545138092144
epoch :  7 >> validation :  0.0183179613748758
epoch :  8 >> training_loss :  0.01830926013543554
epoch :  8 >> validation :  0.018034464246111697
epoch :  9 >> training_loss :  0.01814349767468546
epoch :  9 >> validation :  0.018158412088864838
epoch :  10 >> training_loss :  0.01796842050617156
epoch :  10 >> validation :  0.017744970556091647
epoch :  11 >> training_loss :  0.017735546859710113
epoch :  11 >> validation :  0.01759479866074077
epoch :  12 >> training_loss :  0.01754570741854284
epoch :  12 >> validation :  0.017433413593419666
epoch :  13 >> training_loss :  0.017299547661905702
epoch :  13 >> validation :  0.017249190232491697
epoch :  14 >> training_loss :  0.017085145907881467
epoch :  14 >> validation :  0.017144549509574628
epoch :  15 >> training_loss :  0.01694276431656402
epoch :  15 >> validation :  0.01715218401032275
------------------------
Fold Number :  2
epoch :  0 >> training_loss :  0.28062024895587695
epoch :  0 >> validation :  0.021831682176682455
epoch :  1 >> training_loss :  0.019925031827195832
epoch :  1 >> validation :  0.02110225957786215
epoch :  2 >> training_loss :  0.019255759826172954
epoch :  2 >> validation :  0.01923344059494035
epoch :  3 >> training_loss :  0.01897560269774302
epoch :  3 >> validation :  0.01963105608291667
epoch :  4 >> training_loss :  0.01888560847905667
epoch :  4 >> validation :  0.018987211848384346
epoch :  5 >> training_loss :  0.018881849539668663
```

```
epoch :  5 >> validation :  0.019087364800788206
epoch :  6 >> training_loss :  0.01880092287193174
epoch :  6 >> validation :  0.018451588421032346
epoch :  7 >> training_loss :  0.01856426177141459
epoch :  7 >> validation :  0.018233612982620453
epoch :  8 >> training_loss :  0.018412961470692053
epoch :  8 >> validation :  0.018018708034450638
epoch :  9 >> training_loss :  0.018320308147889118
epoch :  9 >> validation :  0.01789587644603232
epoch :  10 >> training_loss :  0.018012238172409326
epoch :  10 >> validation :  0.017706910565752406
epoch :  11 >> training_loss :  0.01781968524598557
epoch :  11 >> validation :  0.01754140906870879
epoch :  12 >> training_loss :  0.017585085947876392
epoch :  12 >> validation :  0.017338143388644374
epoch :  13 >> training_loss :  0.01736602078637351
epoch :  13 >> validation :  0.017160253085452933
epoch :  14 >> training_loss :  0.01719682110554498
epoch :  14 >> validation :  0.017085314712262357
epoch :  15 >> training_loss :  0.017056497793806635
epoch :  15 >> validation :  0.0171179612135065
------------------------
```

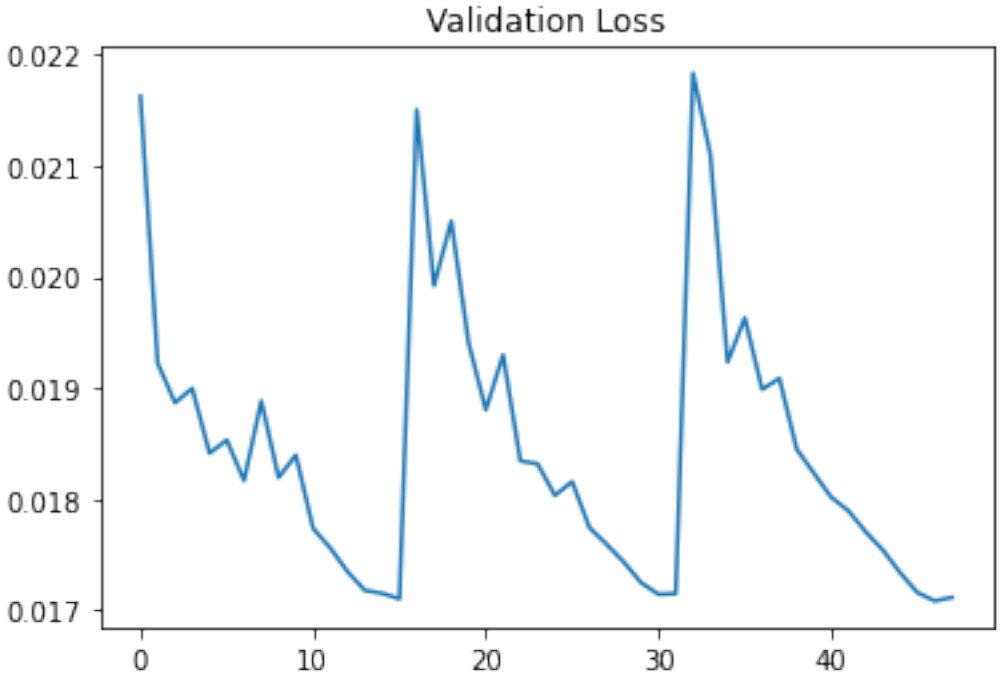
9 Evaluating the logarithmic loss function applied to each drug-MoA annotation pair.

[28]:
```
validation_df = training_targets_scored.drop(columns=target_columns).
 ↪merge(train[['sig_id']+target_columns], on='sig_id', how='left').fillna(0)
# True target values
true_target = training_targets_scored[target_columns].values
# Predicted target values
predicted_target = validation_df[target_columns].values
cross_validation_score = 0

# Now we can calculate the cross entropy loss

for i in range(len(target_columns)):
    cross_validation_score_target = log_loss(true_target[:, i],␣
 ↪predicted_target[:, i])
    cross_validation_score += cross_validation_score_target / target.shape[1]

print(" The Cross Validation loss is :>> ", cross_validation_score)
```

```
The Cross Validation loss is :>>  0.015734850054263057
```

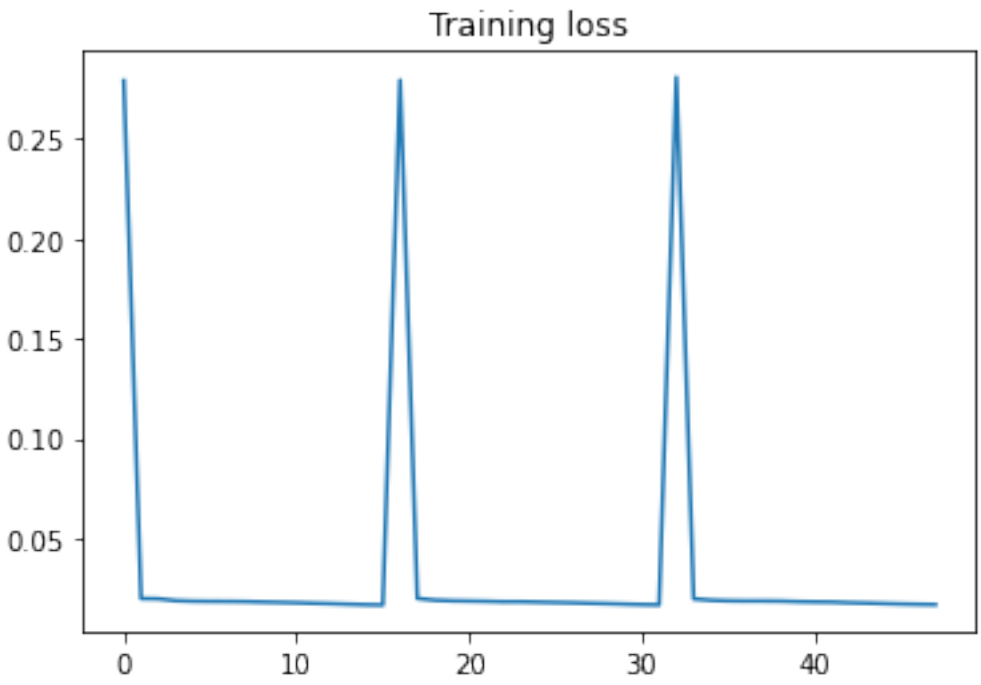
10 Plotting the Validation loss for each fold

[29]:
```
plt.plot(valid_loss_list)
plt.title('Validation Loss')
plt.savefig('valid_loss_list.png')
```



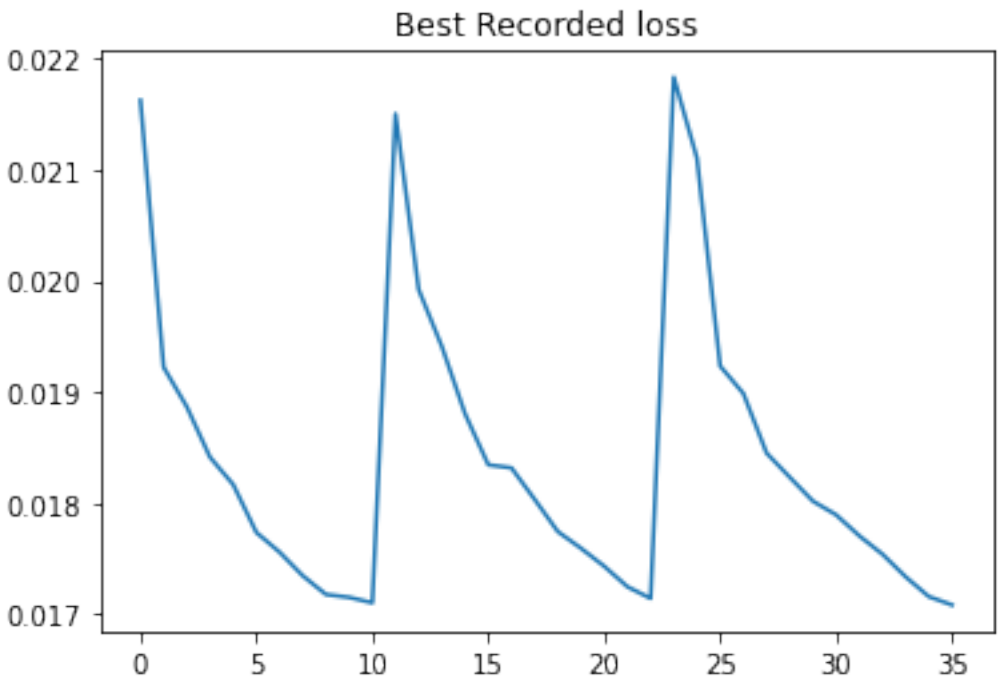
11 Plotting the Training loss for each fold

[30]:
```
plt.plot(train_loss_list)
plt.title('Training loss')
plt.savefig('train_loss_list.png')
```



12 Plotting the Best recorded loss for each fold

[31]:
```
plt.plot(best_loss_list)
plt.title('Best Recorded loss')
plt.savefig('best_loss_list.png')
```



[34]:
```
sample_submission = pd.read_csv('input/lish-moa/sample_submission.csv')
```

[35]:
```
sub = sample_submission.drop(columns=target_columns).
 ↪merge(test[['sig_id']+target_columns], on='sig_id', how='left').fillna(0)
sub.to_csv('submission.csv', index=False)
```

[ ]:
```

```

draft_1

Best Submission
✔ Successful
Submitted by Govind Ajith 34 minutes ago

Private Score	Public Score
0.01692	0.01924

Version 3 of 3

Notebook

Mechanisms Of Action (MoA) Prediction

Using GPU If Available

Reading The CSV Files

Dataset Classes, Training And Testing...

Preparing The Dataset

Dataset Preparation Complete

Declaring The HyperParameters

Declaring The Training Input (2)

Output

Execution Info

Log

Comments (0)

Mechanisms of Action (MoA) Prediction

Predicting multiple targets of the Mechanism of Action (MoA) response(s) of different samples (sig_id), given various inputs such as gene expression data and cell viability data.

Some of the important terms used in the headings of the tables are presented here:

```
g - : signifies gene expression data
c - : signifies cell expression data
cp_type : indicates samples treated with a compound (cp_vehicle) or with a control perturbat
ion (ctrl_vehicle)
NOTE: (samples with control perturbations don't have MoAs)
cp_time - treatment duration (24,48,72) Hours
cp_dose - Dosage - HIGH or LOW
```

In [1]:

```
# Importing the multi label stratified k-fold
# cross validator
```

ENPM808A Final Project Report

Govind Ajith Kumar
UID: 116699488

Introduction

The program is an exercise in developing a machine learning model that can Predict the multiple targets of the Mechanism of Action (MoA) response(s) of different samples, each identified by a different sig_id, given various inputs such as gene expression data and cell viability data.

The model is tested by finally evaluating the logarithmic loss function and applying this to each drug-MoA annotation pair. In this report, we go over the model used, the reasons for selections, and how the hyperparameters were chosen, followed by the results, plots, and conclusions.

Python Libraries and other requirements

- While the program can run on the CPU, it is much faster on GPU. Hence, please have your GPU/CUDA enabled.
- GPU Used: NVIDIA GTX950M
- Python 3.x
- Some of the libraries that are required are:
    a. PyTorch
    b. seaborn
    c. NumPy
    d. sklearn
    e. matplotlib
    f. pandas

Approach used

I decided to use a neural network for the assignment. We are going to leverage open libraries such as PyTorch to develop the neural network and configure them to predict the MoAs. PyTorch was used to do this because of the presence of

online support and the wide array of tool sets at its disposal. The steps used to solve is as follows:

1. Prepare the dataset
2. Select the model
3. Decide the Hyperparameters
4. Train the model
5. Test for the out of sample error
6. Plot the validation loss, training loss, and the best-recorded loss

Dataset preparation

The dataset is prepared by first separating the gene expression and cell viability columns. Now, on the Gene expression data, since our dimensions are really high, we can resort to using PCA for dimensionality reduction but is still able to capture the characteristics of the data. Now, this can be done by choosing a random dimension and having the same random state as before. After performing the PCA, we fir the PCA transform. We then split the data we have into training and test set. For readability, they are all converted to a pandas data frame format.
This process is repeated for the Cell viability data.
Now, we set the desired threshold to calculate the VarianceThreshold. As per the math, all the Features with a training-set variance lower than this threshold will be removed. This is followed by combining the training and testing features
We remove the unnecessary columns that do not contain numerical entries such as **'sig_id'**, **'cp_type'**.
Now we merge the training and training targets scored columns.
This is followed by removing the rows with **cp_type** as **ctl_vehicle** since control perturbations have no MoAs. The final train dataset after all the preparation looks like this:

	sig_id	cp_time	cp_dose	0	1	2	3	4	5	6	...	tropomyosin_receptor_kinase_inhibitor	trpv_agonist
0	id_000644bb2	24	D1	1.0620	-0.2479	-0.6208	-0.1944	-1.0120	-1.0220	-0.0326	...	0.000443	0.000663
1	id_000779bfc	72	D1	0.0743	0.2991	0.0604	1.0190	0.5207	0.2341	0.3372	...	0.000454	0.000860
2	id_000a6266a	48	D1	0.6280	1.5540	-0.0764	-0.0323	1.2390	0.1715	0.2155	...	0.000312	0.000446
3	id_0015fd391	48	D1	-0.5138	-0.2656	0.5288	4.0620	-0.8095	-1.9590	0.1792	...	0.000232	0.009057
4	id_001626bd3	72	D2	-0.3254	0.9700	0.6919	1.4180	-0.8244	-0.2800	-0.1498	...	0.000492	0.001390

5 rows × 1084 columns

Model

We are going to solve the problem by developing a 15 layer neural network that can help us with a wide variety of features we have in this problem. We are going to be using a simple feed-forward network. Using PyTorch we can easily model this.

We are going to pass this neural network model to our training function along with an optimizer and scheduler.

It is important to note that we have a lot of features and our dimensions are really large. In order to tackle this problem, we are going to deploy regularization techniques. The techniques of *regularization* that we are going to start with are:

Batch Normalization:

Applying batch normalization is done to standardize the input for each mini-batches and will help reduce the number of epochs for which the training is done. This limits the covariate shift (*this is the value by which the hidden layer values shift around*) and allows to learn from a more stable set of data. Sometimes, it also allows for a higher learning rate. This is also used for regularization and helps reduce overfitting. Generally, if batch normalization is used, you can use a smaller dropout, which in turn means that lesser layers can be lost in every step.

Using dropout layers:

For regularization purposes, the dropout is set by setting a probability. Random neural networks are picked at a probability, say ***p***, or dropped at a probability of ***1-p***. This is essential to prevent overfitting of the model and also reduces the computation time. A fully connected neural network, if run without dropout will start forming dependencies between each other and this can lead to over-fitting, which is not favorable.

PCA:

Besides this PCA is also applied during the dataset preparation, which can help with dimensionality reduction and can run the program faster. Doing PCA reduces the dimensions, but it can still capture the characteristics of the data.

We are going to be running this on an NVIDIA GTX950M GPU because of the exponentially fast running times as compared to running on a CPU.

Some of the other most important features linked to the training function are

In this training function, we are using Adam optimizer. This is a standard optimizer and is widely used because it combines the advantages of the Adaptive gradient algorithm and the root-mean-square propagation. Basically, it does not stick to one learning rate and adapts it to the problem. It is widely known to offer good results really fast. The Adam optimizer takes in a learning rate (here, 0.001) and a factor for weight decay. When training neural networks, it is common to use weight decay where after each update, the weights are multiplied by a factor. Here the factor is set to 0.00001.

Here we are also using a learning rate scheduler. We use a learning rate scheduler to converge to the lowest loss faster. This is also seen to provide higher accuracy. I tried using a StepLR scheduler. This works by decaying the learning rate of each parameter by a fixed constant called gamma and repeats the process every epoch. However, the trained model was not as good as the one that used OneCycleLR. OneCycleLR bounces the learning rate between a fixed maximum value and a fixed minimum value, which was set to 0.001, which is much lower than the maximum value, which was set to around 0.01.

Multiple loss functions are available through PyTorch, but we are using the Binary Cross Entropy loss with a sigmoid layer. After a trial and error with other losses, this was seen to offer better results.

Hyperparameters

Some of the most important hyperparameters that are used are shown in the table below:

Hyperparameter	Value	Notes
Batch size	64	Number of training samples used in one training iteration
Learning rate	0.001	It controls how quickly or slowly a neural network model can learn a model or a problem.
K folds	3	Creating a 3 fold multilabel stratified k fold
max_epochs	15	It is the number of times a training vector is used to update the weights. The value can be set through trial and error.
weight_decay	0.00005	When training neural networks, it is common to use weight decay where after each update, the weights are multiplied by a factor slightly less than 1
num_features	880	This is the number of features corresponding to the columns in the feature_columns
num_targets	206	This is the number of targets corresponding to the columns in the target_columns
hidden_size	1024	Can set by trial and error. This is the number of neuron layers in the middle.

Validation

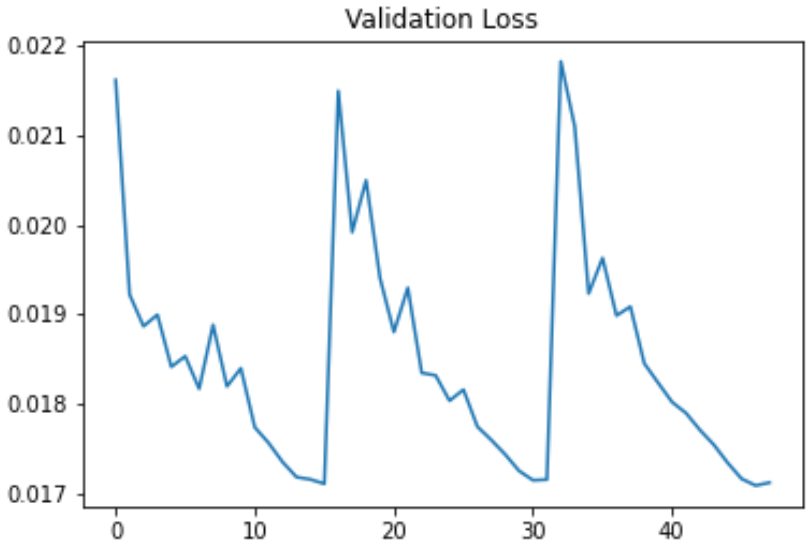
In each fold the trained model is validated by the batch that was not used to train, this process is called validation and the dataset that is used for this purpose is called the validation set.

Results

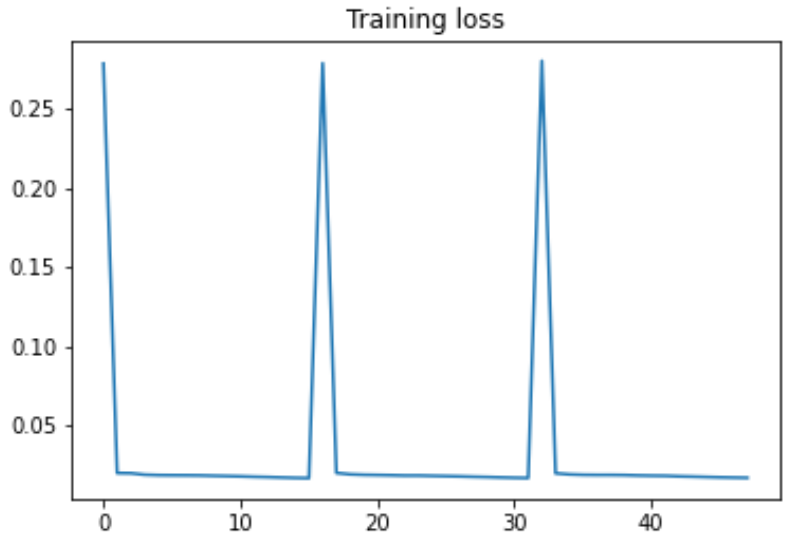
Various combinations were run and we finally obtained a cross-validation error over the test set was obtained. It was observed to be **0.015734850054263057**.

Graphs

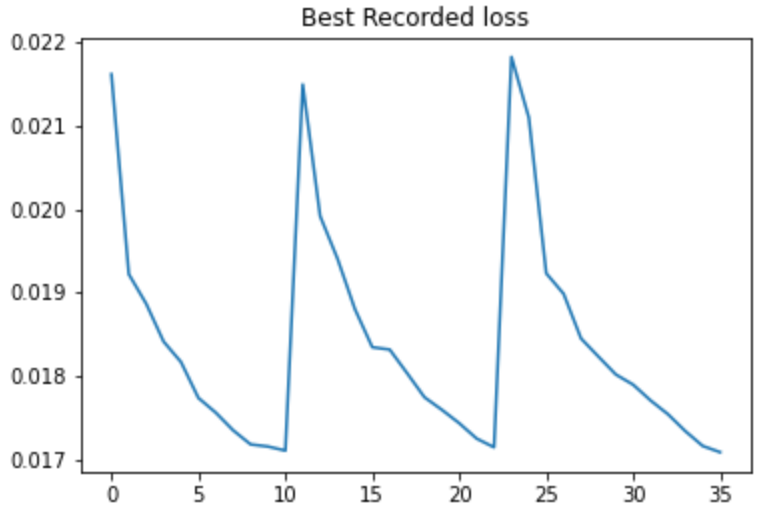
The plot for the validation loss over every Kth fold can be seen in the graph below:



The plot for the training loss over every Kth fold can be seen in the graph below:



The plot for the best-recorded loss over every Kth fold can be seen in the graph below:



ENPM 808A
Machine Learning

Final Project
Mechanisms of Action (MoA) Prediction

Govind Ajith Kumar - 116699488

Introduction

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- The model is tested by finally evaluating the logarithmic loss function and applying this to each drug-MoA annotation pair.

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  c. NumPy
  d. sklearn
  e. matplotlib
  f. pandas

Approach used

I decided to use a neural network for the assignment. We are going to leverage open libraries such as PyTorch to develop the neural network and configure them to predict the MoAs. PyTorch was used to do this because of the presence of online support and the wide array of tool sets at its disposal.

The steps used to solve is as follows:

1. Prepare the dataset
2. Select the model
3. Decide the Hyperparameters
4. Train the model
5. Test for the out of sample error
6. Plot the validation loss, training loss, and the best-recorded loss

Dataset Preparation

1. The dataset is prepared by first separating the gene expression and cell viability columns. Now, on the Gene expression data, since our dimensions are really high, we can resort to using PCA for dimensionality reduction but is still able to capture the characteristics of the data. Now, this can be done by choosing a random dimension and having the same random state as before.
2. After performing the PCA, we fir the PCA transform.
3. We then split the data we have into training and test set. For readability, they are all converted to a pandas dataframe format.
4. This process is repeated for the Cell viability data.
5. Now, we set the desired threshold to calculate the VarianceThreshold. As per the math, all the Features with a training-set variance lower than this threshold will be removed.
6. This is followed by combining the training and testing features
7. We remove the unnecessary columns that do not contain numerical entries such as **'sig_id'**, **'cp_type'**.
8. Now we merge the training and training targets scored columns.
9. This is followed by removing the rows with **cp_type** as **ctl_vehicle** since control perturbations have no MoAs.

Model Used

- We are going to solve the problem by developing a 15 layer neural network that can help us with a wide variety of features we have in this problem.
- We are going to be using a simple feed-forward network.
- These layers are
  - BatchNorm1d: This applies batch normalization over a 2D input.
  - Dropout: For regularization purposes
  - Weight_norm: For weight normalization (faster than batch normalization)
- Using PyTorch we can easily model this.
- We are going to pass this neural network model to our training function along with an optimizer and scheduler.

Regularization

It is important to note that we have a lot of features and our dimensions are really large. In order to tackle this problem, we are going to deploy regularization techniques. The techniques of *regularization* that we are going to start with are:

- **Batch Normalization:**

  Applying batch normalization is done to standardize the input for each mini-batches and will help reduce the number of epochs for which the training is done. This limits the covariate shift (*this is the value by which the hidden layer values shift around*) and allows to learn from a more stable set of data. Sometimes, it also allows for a higher learning rate. This is also used for regularization and helps reduce overfitting. Generally, if batch normalization is used, you can use a smaller dropout, which in turn means that lesser layers can be lost in every step.

Regularization contd...

- **Dropout layers:**

  For regularization purposes, the dropout is set by setting a probability. Random neural networks are picked at a probability, say ***p***, or dropped at a probability of ***1-p***. This is essential to prevent overfitting of the model and also reduces the computation time. A fully connected neural network, if run without dropout will start forming dependencies between each other and this can lead to overfitting, which is not favorable.

- **PCA:**

  Besides this PCA is also applied during the dataset preparation, which can help with dimensionality reduction and can run the program faster. Doing PCA reduces the dimensions, but it can still capture the characteristics of the data.

Hyperparameters

These parameters define the model and can be tuned in many different ways.

The detailed explanation of each of the parameter is provided in the project report.

Hyperparameter	Value
Batch size	64
Learning rate	0.001
K folds	3
max_epochs	15
weight_decay	0.00005
num_features	880
num_targets	206
hidden_size	1024

Results and Graphs

Various combinations were run and we finally obtained a cross-validation error over the test set was obtained. It was observed to be **0.015734850054263057**.

The following learning curves depict the reduction in loss over each fold.