Govind_MoA_Machine_Learning_Final_Project

November 22, 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

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 guaranteeing 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/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/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/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
```

[10]:
```
# 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
```

[11]:
```
# 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
```

[12]:
```
# 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
```

[13]:
```
# 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
```

[14]:
```
# 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

[15]:
```
set_seed_characteristics(seed=55)
```

[16]:
```
# 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-')]
```

[17]:
```
# 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)
```

[18]:
```
# 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)
```

[19]:
```
# 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] : ]
```

[20]:
```
# 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)
```

[21]:
```
# 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)
```

[22]:
```
# 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

[23]:
```
# 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

[24]:
```
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

[25]:
```
# to plot validation loss
valid_loss_list = []
# to plot the training loss
train_loss_list = []
# to plot the best recorded loss
best_loss_list = []
```

[26]:
```
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
```

[27]:
```
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
```

[28]:
```python
# 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
------------------------
```

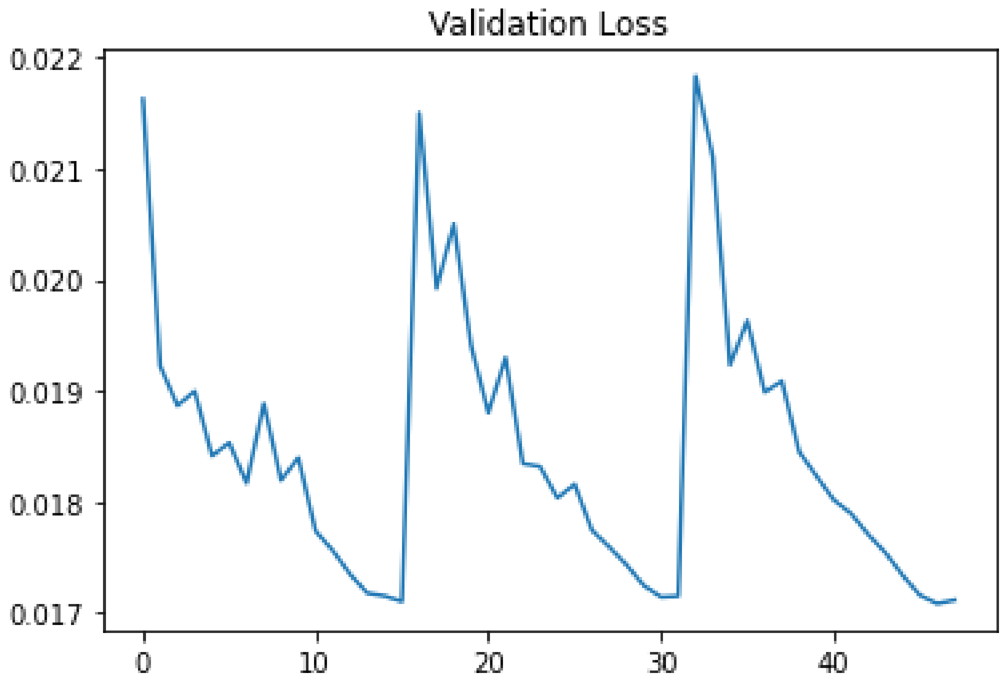
9 Evaluating the logarithmic loss function applied to each drug-MoA annotation pair.

[29]:
```
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
```

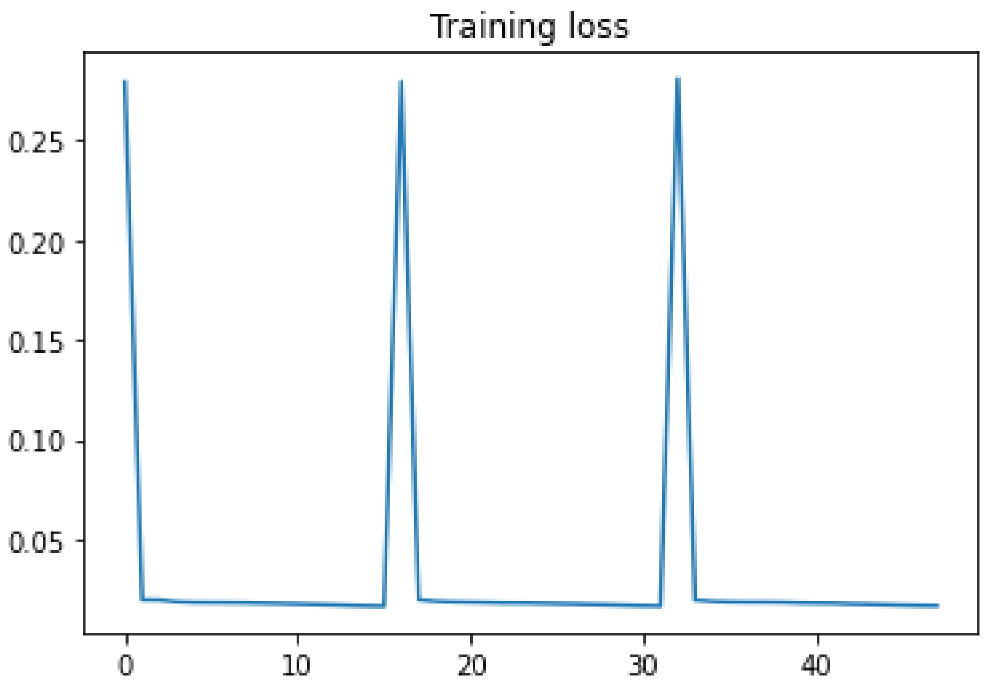
10 Plotting the Validation loss for each fold

[39]:
```python
plt.plot(valid_loss_list)
plt.title('Validation Loss')
plt.savefig('valid_loss_list.png')
```



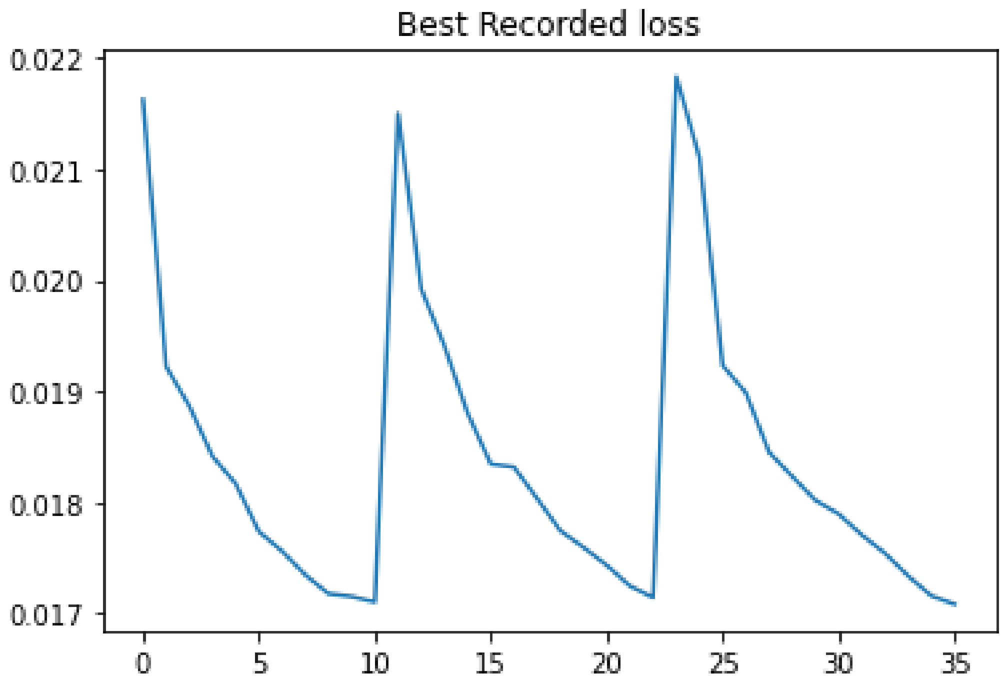
11 Plotting the Training loss for each fold

[40]:
```python
plt.plot(train_loss_list)
plt.title('Training loss')
plt.savefig('train_loss_list.png')
```



12 Plotting the Best recorded loss for each fold

[41]:
```
plt.plot(best_loss_list)
plt.title('Best Recorded loss')
plt.savefig('best_loss_list.png')
```


Best Recorded loss
0.022
0.021
0.020
0.019
0.018
0.017
0
5
10
15
20
25
30
35

```
[ ]:
```