

Section VI: References

- Acharya, U. R., Fernandes, S. L., WeiKoh, J. E., Ciaccio, E. J., Fabell, M. K., Tanik, U. J., Rajinikanth, V., & Yeong, C. H. (2019). Automated detection of Alzheimer's disease using brain mri images– a study with various feature extraction techniques. *Journal of Medical Systems*, 43(9). <https://doi.org/10.1007/s10916-019-1428-9>
- Bellio, M., Oxtoby, N. P., Walker, Z., Henley, S., Ribbens, A., Blandford, A., Alexander, D. C., & Yong, K. X. (2020). Analyzing large alzheimer's disease cognitive datasets: Considerations and challenges. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, 12(1). <https://doi.org/10.1002/dad2.12135>
- Brooks, A. (2021, December 6). How much does an MRI cost without insurance in 2021? Mira. Retrieved January 27, 2022, from <https://www.talktomira.com/post/how-much-does-an-mri-cost-without-insurance-in-2021>
- Bunis, D. (2019, September 12). Numbers of Americans without health insurance grows. AARP. Retrieved October 25, 2021, from <https://www.aarp.org/health/health-insurance/info-2019/older-americans-not-insured.html>
- Centers for Disease Control and Prevention. (2020, October 26). What is alzheimer's disease? Centers for Disease Control and Prevention. Retrieved October 24, 2021, from <https://www.cdc.gov/aging/aginginfo/alzheimers.htm>
- Cardenas VA, Chao LL, Studholme C, Yaffe K, Miller BL, Madison C, Buckley ST, Mungas D, Schuff N, Weiner MW. Brain atrophy associated with baseline and longitudinal measures of cognition. *Neurobiol Aging*. 2011 Apr;32(4):572-80. doi:

10.1016/j.neurobiolaging.2009.04.011. Epub 2009 May 14. PMID: 19446370; PMCID: PMC2891686.

Christ, B. U., Combrinck, M. I., & Thomas, K. G. (2018). Both reaction time and accuracy measures of intraindividual variability predict cognitive performance in Alzheimer's disease. *Frontiers in Human Neuroscience*, 12. <https://doi.org/10.3389/fnhum.2018.00124>

Harrison, O. (2019, July 14). Machine learning basics with the k-nearest Neighbors ALGORITHM. Medium. <https://towardsdatascience.com/machine-learning-basics-with-the-k-nearest-neighbors-algorithm-6a6e71d01761>.

Maroco, J., Silva, D., Rodrigues, A., Guerreiro, M., Santana, I., & de Mendonça, A. (2011). Data mining methods in the prediction of dementia: A real-data comparison of the accuracy, sensitivity and specificity of linear discriminant analysis, logistic regression, neural networks, support vector machines, classification trees and random forests. *BMC Research Notes*, 4(1). <https://doi.org/10.1186/1756-0500-4-299>

Nawaz, A., Anwar, S. M., Liaqat, R., Iqbal, J., Bagci, U., & Majid, M. (2020). Deep Convolutional Neural Network based Classification of Alzheimer's Disease using MRI Data. 2020 IEEE 23rd International Multitopic Conference (INMIC). <https://doi.org/10.1109/inmic50486.2020.9318172>

Schaffer, J. D., & Chiofolo, C. M. (2016, June 14). Methods and systems for identifying patients with mild cognitive impairment at risk of converting to alzheimer's. (US 9367817 B2), United States Patent, <https://www.freepatentsonline.com/9367817.pdf>

Section VII: Appendices

Appendix A: Limitations and Assumptions

Limitations:

1. Unable to test on human participants
2. Trained with a machine learning method that did not use a deep learning algorithm
3. The database had a size of about 9,000 data points after pre-processing.

Assumptions:

1. The Mini-Mental Score provides a correlation to Alzheimer's status as researched and stated by the ADNI database.
2. Genetic factors do not play a role in further progression of Alzheimer's disease.

Appendix B: Sample of Data Set used in the Model

RID	VISCODE 2	ADNI_ME M	ADNI_E F	AGE	GENDE R	EDUCATIO N	MMSCOR E	ADDIAGNOS IS
2	0	0.486	0.091	74	1	16	28	0
2	6	0.581	0.088	75	1	16	28	0
2	36	0.405	0.088	77	1	16	29	0
2	60	0.352	-0.294	79	1	16	28	0
2	72	0.35	0.343	80	1	16	23	1
2	84	0.428	-0.274	81	1	16	24	1
2	96	0.325	-0.79	82	1	16	25	0
2	108	0.089	-0.75	83	1	16	28	0
2	120	0.384	-0.609	84	1	16	28	0
2	132	0.164	-0.711	85	1	18	24	1

Appendix C: LSTM Code

1. `from math import sqrt`
2. `from numpy import concatenate`
3. `from matplotlib import pyplot`
4. `from pandas import read_csv`
5. `from pandas import DataFrame`
6. `from pandas import concat`
7. `from sklearn.preprocessing import MinMaxScaler`
8. `from sklearn.preprocessing import LabelEncoder`
9. `from sklearn.metrics import mean_squared_error`
10. `from keras.models import Sequential`
11. `from keras.layers import Dense`
12. `from keras.layers import LSTM`
- 13.
14. `import tensorflow as tf`
15. `from google.colab import drive`
16. `drive.mount("/content/drive")`
17. `tf.config.list_physical_devices('GPU')`
- 18.
19. `dataset = read_csv("/content/drive/MyDrive/Datasets/Dataset.csv")`
20. `dataset.head()`
- 21.
22. `values = dataset.values`
23. `# specify columns to plot`

```
24. groups = [1, 2, 3, 5, 6]
25. i = 1
26. # plot each column
27. pyplot.figure()
28. for group in groups:
29.     pyplot.subplot(len(groups), 1, i)
30.     pyplot.plot(values[:, group])
31.     pyplot.title(dataset.columns[group], y=0.5, loc='right')
32.     i += 1
33. pyplot.show()
34.
35. # convert series to supervised learning
36. def series_to_supervised(data, n_in=1, n_out=1, dropnan=True):
37.     n_vars = 1 if type(data) is list else data.shape[1]
38.     df = DataFrame(data)
39.     cols, names = list(), list()
40.     # input sequence (t-n, ... t-1)
41.     for i in range(n_in, 0, -1):
42.         cols.append(df.shift(i))
43.         names += [('var%d(t-%d)' % (j+1, i)) for j in range(n_vars)]
44.     # forecast sequence (t, t+1, ... t+n)
45.     for i in range(0, n_out):
46.         cols.append(df.shift(-i))
```

```
47.         if i == 0:
48.             names += [('var%d(t)' % (j+1)) for j in range(n_vars)]
49.         else:
50.             names += [('var%d(t+%d)' % (j+1, i)) for j in range(n_vars)]
51.     # put it all together
52.     agg = concat(cols, axis=1)
53.     agg.columns = names
54.     # drop rows with NaN values
55.     if dropnan:
56.         agg.dropna(inplace=True)
57.     return agg
58.
59. # load dataset
60. dataset = read_csv("/content/drive/MyDrive/Datasets/Dataset.csv", header = 0, index_col
    = 0)
61. values = dataset.values
62. # integer encode direction
63. encoder = LabelEncoder()
64. values[:,4] = encoder.fit_transform(values[:,4])
65. # ensure all data is float
66. values = values.astype('float32')
67. # normalize features
68. scaler = MinMaxScaler(feature_range=(0, 1))
```

```
69. scaled = scaler.fit_transform(values)
70. # frame as supervised learning
71. reframed = series_to_supervised(scaled, 1, 1)
72. # drop columns we don't want to predict
73. reframed.drop(reframed.columns[[6,7,8,9,10]], axis=1, inplace=True)
74. print(reframed.head())
75.
76. # split into train and test sets
77. values = reframed.values
78. n_train_days = 300
79. train = values[:n_train_days, :]
80. test = values[n_train_days:, :]
81. # split into input and outputs
82. train_X, train_y = train[:, :-1], train[:, -1]
83. test_X, test_y = test[:, :-1], test[:, -1]
84. # reshape input to be 3D [samples, timesteps, features]
85. train_X = train_X.reshape((train_X.shape[0], 1, train_X.shape[1]))
86. test_X = test_X.reshape((test_X.shape[0], 1, test_X.shape[1]))
87. print(train_X.shape, train_y.shape, test_X.shape, test_y.shape)
88.
89. # design network
90. model = Sequential()
91. model.add(LSTM(8, input_shape=(train_X.shape[1], train_X.shape[2])))
```

```
92. model.add(Dense(1))

93. model.compile(loss='mae', optimizer='adam', metrics=['accuracy'])

94. # fit network

95. history = model.fit(train_X, train_y, epochs=8, batch_size=72, validation_data=(test_X,
    test_y), verbose=2, shuffle=False)

96. # plot history

97. pyplot.plot(history.history['loss'], label='train')

98. pyplot.plot(history.history['val_loss'], label='test')

99. pyplot.title('Training and Validation loss')

100. pyplot.xlabel('Epochs')

101. pyplot.ylabel('Loss')

102. pyplot.legend()

103. pyplot.show()

104.

105. pyplot.plot(history.history['accuracy'], label='train')

106. pyplot.plot(history.history['val_accuracy'], label='test')

107. pyplot.title('Training and Validation Accuracy')

108. pyplot.xlabel('Epochs')

109. pyplot.ylabel('Accuracy')

110. pyplot.legend()

111. pyplot.show()

112.

113. # make a prediction
```



```
114. yhat = model.predict(test_X)
115. test_X = test_X.reshape((test_X.shape[0], test_X.shape[2]))
116. # invert scaling for forecast
117. inv_yhat = concatenate((yhat, test_X[:, 1:]), axis=1)
118. inv_yhat = scaler.inverse_transform(inv_yhat)
119. inv_yhat = inv_yhat[:,0]
120. # invert scaling for actual
121. test_y = test_y.reshape((len(test_y), 1))
122. inv_y = concatenate((test_y, test_X[:, 1:]), axis=1)
123. inv_y = scaler.inverse_transform(inv_y)
124. inv_y = inv_y[:,0]
125. # calculate RMSE
126. rmse = sqrt(mean_squared_error(inv_y, inv_yhat))
127. print("Test RMSE: %.3f % rmse)
128.
129. loss_train = history.history['accuracy']
130. loss_val = history.history['val_accuracy']
131. epochs = range(1,11)
132. pyplot.plot(epochs, loss_train, 'g', label='Training accuracy')
133. pyplot.plot(epochs, loss_val, 'b', label='validation accuracy')
134. pyplot.title('Training and Validation accuracy')
135. pyplot.xlabel('Epochs')
136. pyplot.ylabel('Accuracy')
```

```
137. pyplot.legend()
```

```
138. pyplot.show()
```

```
139.
```

Appendix D: Code for Optimization Method

```
1. def optimizeParameters(df):
2.     acc = 0
3.     n = 0
4.     drop = 0;
5.     for d in range(30,70):
6.         df = tempdf
7.         for y in range(len(df)):
8.             if(df.MMSCORE[y] >= 27 and random.randint(1,100) <= d):
9.                 df.drop(y,inplace = True)
10.            X = df[["ADNI_MEM", "ADNI_EF"]]
11.            y = df[["MMSCORE"]]
12.            X_train, X_test, y_train, y_test = train_test_split(X, y, test_size=0.25)
13.            for x in range(15,80):
14.                knn_model = KNeighborsRegressor(n_neighbors=x)
15.                knn_model.fit(X_train, y_train)
16.                test_preds = knn_model.predict(X_test)
17.                if (metrics.r2_score(y_test,test_preds) > acc):
18.                    acc = metrics.r2_score(y_test,test_preds)
```

```

19.     n = x
20.     drop = d
21.     print(acc)
22.     print(n)
23.     print(drop)
24.

```

Appendix E: Decision Matrix Comparing Different Machine Learning Methods

Criteria	Max Points	Multi Variate Regression	LSTM + kNN
1. Predicts next value for an inputted time step (required)	10	6	10
2. Prediction Accuracy above 75%	9	4	7
3. Classifies Alzheimer's using MM	8	7	8

score with RMSE below 4			
Total	27	17	25
Percent	100%	63%	93%

- Multi Variate Regression: A model that simply uses a linear regression model to create parametric equations to produce a predicted value; not as accurate to training set
- LSTM + kNN: A model that uses a neural network to predict future cognitive values and then classify using the kNN