project_data_exploration

April 28, 2023

1 Be/Bi 205 Course Project – Data exploration

1.0.1 From Therapeutics Data Commons, I've chosen to work on Gene-Disease association prediction task for this project.

https://tdcommons.ai/multi_pred_tasks/gdi/

The task uses data from DisGeNet (https://www.disgenet.org/) – the largest publicly available collection of genes and variants associated with human diseases curated from various catalogues, annotated with controlled vocabularies

TDC has curated a subset of data from DisGeNet and mapped disease ID to definition through MedGen (https://www.ncbi.nlm.nih.gov/medgen/), and Gene ID to uniprot (https://www.uniprot.org/) amino acid sequence. The task is to quantify the association between gene and disease given the disease description and gene amino acid sequence through regression.

Dataset statistics on TDC: 52476 gene-disease pairs, 7399 genes, 7095 diseases

1.0.2 Rationale behind the task (as I understand it)

Many diseases are caused by genetic variations, and for a given disease, its clinical presentation (phenotype) may vary among patients either due to reduced penetrance or variable expressivity or a combination of both, which makes the task of identifying therapeutic target genes difficult. Studies analyzing a disease try to identify genomic regions associated with the disease and then verify the function of genes in that region, ranking candidate genes for analysis following a "guilt-by-association" principle, i.e. associated genes would share common functionality and show common traits across different genomic data. But this is only useful to find candidate genes for diseases that already have a partial genetic basis identified.

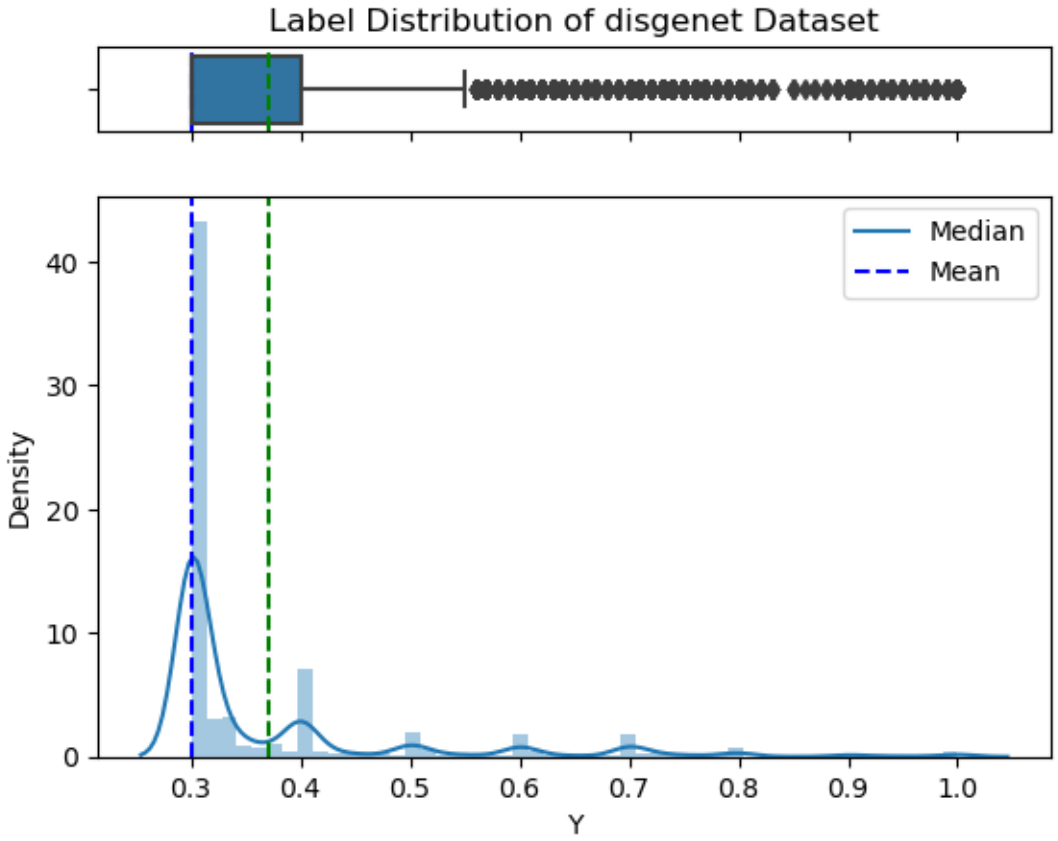
However, the guilt-by-association principle can be extended to phenotypically related diseases, i.e. genes associated with phenotypically related diseases could also share common traits and functionality. Thus, a GDA network is constructed to probe gene-disease mechanisms for pairs of multiple genes and diseases. Deep learning can be used to fill the gaps in GDA network by training on known gene-disease associations and then extrapolating to unknown pairs to identify candidate targets.

1.0.3 TDC data

[1]:
```
from tdc.multi_pred import GDA
data = GDA(name = 'DisGeNET')
split = data.get_split()
```

```
Found local copy...
Loading...
Done!
```

[2]:
```
data.label_distribution()
```



[3]:
```
import pandas as pd
import matplotlib.pyplot as plt
import numpy as np
```

[4]:
```
traindf = pd.DataFrame(split['train'])
valdf = pd.DataFrame(split['valid'])
testdf = pd.DataFrame(split['test'])
print('Training samples: ',len(traindf))
```

```
print('Validation samples: ',len(valdf))
print('Testing samples: ',len(testdf))
```

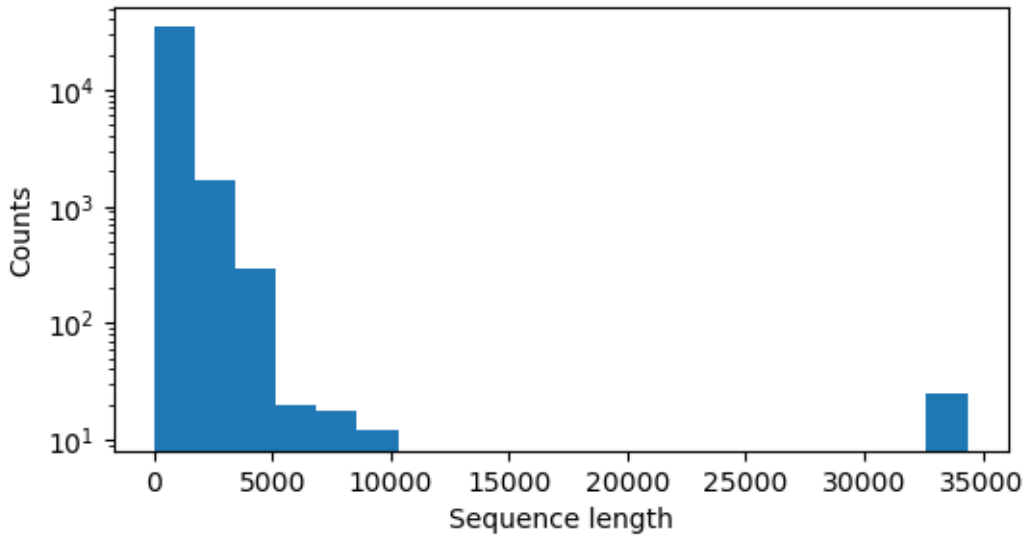
```
Training samples:  36733
Validation samples:  5248
Testing samples:  10495
```

[5]:
```
traindf.head()
```

[5]:

	Gene_ID	Gene	Disease_ID	Disease	Y
0	1	MSMLVVFLLLWGVTWGPVTEAAIFYETQPSLWAESESLLKPLANVT…	C0019209	Hepatomegaly: Abnormal enlargement of the liver.	0.3
1	1	MSMLVVFLLLWGVTWGPVTEAAIFYETQPSLWAESESLLKPLANVT…	C0036341	Schizophrenia: Schizophrenia is highly heritab…	0.3
2	2	MGKNKLLHPSLVLLLLVLLPTDASVSGKPQYMVLVPSLLHTETTEK…	C0002395	Alzheimer's Disease: Alzheimer disease is the …	0.5
3	2	MGKNKLLHPSLVLLLLVLLPTDASVSGKPQYMVLVPSLLHTETTEK…	C0011265	Presenile dementia: The presence of dementia i…	0.3
4	2	MGKNKLLHPSLVLLLLVLLPTDASVSGKPQYMVLVPSLLHTETTEK…	C0019202	Hepatolenticular Degeneration: Wilson disease …	0.3

[6]:
```
## Length of amino acid sequences
genelengths = [len(g) for g in traindf['Gene']]
plt.figure(figsize=(6,3))
_ = plt.hist(genelengths,bins=20,log=True)
plt.ylabel('Counts')
plt.xlabel('Sequence length')
plt.show()
## Not uniform
```



[7]:
```
## Amino acid sequence alphabet
alphabets = np.unique([item for g in traindf['Gene'] for item in list(set(g))])
alphabets
```

[7]:
```
array(['A', 'C', 'D', 'E', 'F', 'G', 'H', 'I', 'K', 'L', 'M', 'N', 'P',
       'Q', 'R', 'S', 'T', 'U', 'V', 'W', 'X', 'Y'], dtype='<U1')
```

[8]:
```
global alphabet_map
alphabet_map = {'A':1, 'C':2, 'D':3, 'E':4, 'F':5, 'G':6, 'H':7, 'I':8, 'K':9,␣
 ↪'L':10, 'M':11, 'N':12, 'P':13,
       'Q':14, 'R':15, 'S':16, 'T':17, 'U':18, 'V':19, 'W':20, 'X':21, 'Y':22}
```

[40]:
```
## Example disease description
traindf['Disease'][0]
```

[40]:
```
'Hepatomegaly: Abnormal enlargement of the liver.'
```

1.0.4 Data preprocessing

- Gene column would need to be converted to one-hot encoded arrays, and padded to make their lengths uniform
- Disease column would need to be converted to a uniform vector embedding using some NLP method

[31]:
```
import tensorflow as tf
import spacy
import en_core_web_md
from gensim.corpora.dictionary import Dictionary
from gensim.models.word2vec import Word2Vec
import gensim.downloader as api
```

```
2023-04-28 15:05:08.528867: E
tensorflow/compiler/xla/stream_executor/cuda/cuda_driver.cc:267] failed call to
cuInit: CUDA_ERROR_UNKNOWN: unknown error
```

- First dealing with sequences

[19]:
```
def convert_to_onehot(seq):
    ohe = np.zeros((len(seq),len(alphabet_map)+1))
    for i,s in enumerate(seq):
        ohe[i,alphabet_map[s]] = 1
    return ohe[:,1:]
```

[20]:
```
%%time
X = [convert_to_onehot(g) for g in traindf['Gene']]
```

```
CPU times: user 3.5 s, sys: 816 ms, total: 4.32 s
Wall time: 4.32 s
```

[28]:
```
traindf['X1'] = X
```

Since shape of X1 is not uniform (each sample is sequence_length x alphabet_length and sequence length varies), it will be padded before training

- Next dealing with disease descriptions

Looking at two approaches here, first to get word embeddings and use averaged word vectors to get sentence vector

[37]:
```
%%time
## Tokenize our disease descriptions
nlp = en_core_web_md.load()
tokens = []
removal= ['ADV','PRON','CCONJ','PUNCT','PART','DET','ADP','SPACE', 'SYM']
for disease in nlp.pipe(traindf['Disease']):
    tokens.append([token.lemma_ for token in disease if token.pos_ not in␣
 ↪removal])
```

```
CPU times: user 3min 39s, sys: 378 ms, total: 3min 39s
Wall time: 3min 40s
```

[38]:
```
traindf['tokens'] = tokens
```

[39]:
```
tokens[0]
```

[39]:
```
['hepatomegaly', 'abnormal', 'enlargement', 'liver']
```

[64]:
```
## Train gensim Word2vec model, it takes list of str tokens directly
model = Word2Vec(traindf['tokens'])
```

[73]:
```
model.wv.most_similar("hepatomegaly")
```

[73]:
```
[('lymphadenopathy', 0.6800524592399597),
 ('splenomegaly', 0.6631979942321777),
 ('hepatosplenomegaly', 0.6514338254928589),
 ('transaminase', 0.6323346495628357),
 ('iron', 0.6228795051574707),
 ('jaundice', 0.609259843826294),
 ('hypermetabolism', 0.5977323055267334),
 ('hyperlipidemia', 0.5799980163574219),
 ('storage', 0.5683786273002625),
 ('dehydration', 0.5414830446243286)]
```

[82]:
```
sentvecs = []
for sent in traindf['tokens']:
```

```
    sentvecs.append(np.mean([model.wv.word_vec(word) for word in sent if model.
↪wv.has_index_for(word)],axis=0))
```

[84]:
```
np.shape(sentvecs)
```

[84]:
```
(36733, 100)
```

[85]:
```
traindf['X2_1'] = sentvecs
```

[101]:
```
traindf['X2_1'][0]
```

[101]:
```
array([-0.52782047, -0.04894644,  0.76871836, -1.0649453 , -1.5059873 ,
       -0.6001269 ,  0.54573756, -0.45159644,  1.2727453 , -0.12144589,
        0.62991273,  1.5930324 , -1.5477872 , -0.7542422 ,  0.8003924 ,
        0.99251795, -0.72856915, -0.6127136 ,  0.7354403 ,  1.5507761 ,
        0.8774863 ,  0.06242841,  1.0365998 , -0.16637748, -0.08315891,
       -0.40897864,  0.54345566, -0.31396005, -0.22021526,  0.09733475,
       -0.6424665 , -0.86649257,  0.5254741 , -0.79103935,  1.3729737 ,
        0.44039637,  1.1916041 ,  0.13361013, -0.56389415,  1.0949733 ,
        1.0677724 ,  2.1772964 ,  0.42967787, -1.1127867 , -0.38290417,
       -0.7928448 , -0.15492609,  1.2799029 ,  0.7262238 ,  0.22973257,
       -0.7824364 , -1.1150577 , -1.2449121 ,  0.12956107, -0.63287103,
        0.66198504,  0.03185637,  0.17376429, -0.37552828, -0.5302457 ,
       -0.21630587,  1.3483291 , -0.9437089 ,  0.81244427,  0.615585  ,
        1.2106735 ,  0.43051308, -0.8922671 , -1.37398   ,  0.6830906 ,
       -0.7319294 ,  2.6390784 , -0.1944848 , -1.1533122 ,  1.2825685 ,
        0.9970237 ,  0.62600434,  0.7105643 ,  0.09987763,  0.3511719 ,
       -0.84860706,  0.32612827,  0.71036696, -0.34549165, -1.3603135 ,
       -0.1462045 , -0.608334  , -1.1225631 , -0.6654348 , -0.13957608,
        0.06209651, -0.1568076 , -1.0095336 , -1.2212346 , -0.39312035,
        0.2690161 ,  1.3230462 , -0.66000193, -0.1118302 , -1.8428149 ],
      dtype=float32)
```

Second approach - doc2vec embeddings

[86]:
```
from gensim.models.doc2vec import Doc2Vec, TaggedDocument
```

[96]:
```
dictionary = Dictionary(traindf['tokens'])
documents = [TaggedDocument(doc,dictionary.doc2idx(doc)) for doc in␣
↪traindf['tokens']]
```

[98]:
```
model = Doc2Vec(documents,vector_size=20)
```

[99]:
```
traindf['X2_2'] = [model.infer_vector(doc) for doc in traindf['tokens']]
```

[100]:
```
traindf['X2_2'][0]
```

[100]:
```
array([ 0.14122088, -0.06563216, -0.00734649, -0.2059837 ,  0.08993583,
        0.04964326, -0.03235229, -0.27719197, -0.20296392, -0.03021958,
       -0.06755918,  0.12062613,  0.07048996,  0.17293632,  0.00637513,
       -0.17755455, -0.00840605, -0.12333015, -0.02660876, -0.06621847],
      dtype=float32)
```

Visualize embeddings

[102]:
```
from sklearn.manifold import TSNE
import matplotlib.pyplot as plt
```

[103]:
```
tsne = TSNE(perplexity=40, n_components=2, init='pca', n_iter=2500,␣
 ↪random_state=23)
```

[107]:
```
tvals = tsne.fit_transform(list(traindf['X2_1']))
```

[108]:
```
traindf['tsne_x'] = tvals[:,0]
traindf['tsne_y'] = tvals[:,1]
```

[2]:
```
# %matplotlib inline
# import plotly.express as px
# px.scatter(traindf,x='tsne_x',y='tsne_y',color='Disease_ID')
```

[112]:
```
tsne2 = TSNE(perplexity=40, n_components=2, init='pca', n_iter=2500,␣
 ↪random_state=23)
tvals2 = tsne2.fit_transform(list(traindf['X2_2']))
```

[115]:
```
traindf['tsne_x2'] = tvals2[:,0]
traindf['tsne_y2'] = tvals2[:,1]
```

[116]:
```
px.scatter(traindf,x='tsne_x2',y='tsne_y2',color='Disease_ID')
```

Doc2Vec embedding looks better

[ ]:
```
```