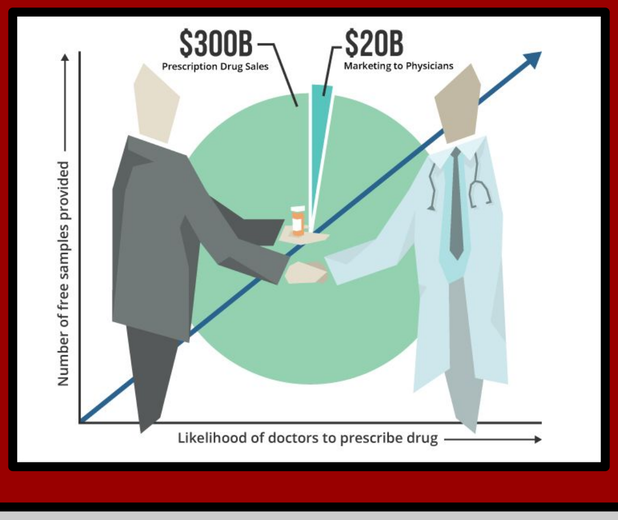
AI-Assisted Clinical Decision Making for PD Treatment Selection

"One in three patients with Parkinson's disease has been prescribed contraindicated drugs during hospitalization. Serious complications, mostly neuropsychiatric, have occurred in more than half of these patients." - US Pharmacy and Therapeutic Journal

Type of incident	Prescribing errors	
	n	%
Incorrect dosage	25	14.5
Incorrect timing	103	59.5
Omission error	26	15
Wrong medication	4	2.3
Wrong formulation	8	4.6
Wrong strength	7	4



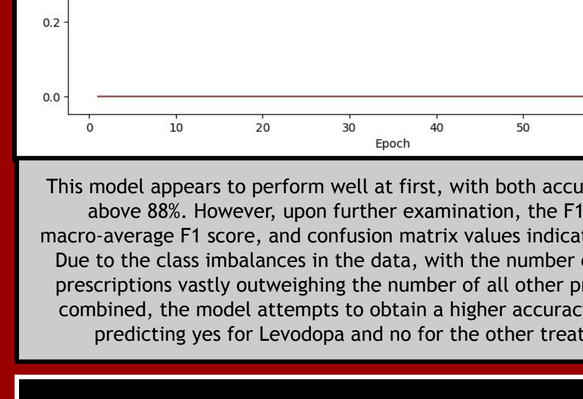
Parkinson's disease (PD) is a progressive neurodegenerative disease that causes numerous motor and non-motor dysfunction symptoms; some assessments for the severity or progression of PD in a patient are PD stage and MDS-UPDRS

Medication errors such as prescribing contraindicated drugs, incorrect timing, etc. in PD treatment are frequent, resulting in improper care and mismanagement of systems for patients with PD

Pharmaceutical companies, part of the prevalent pharmaceutical industry, incentivize the prescription of certain drugs and surgeries (even if they aren't as effective as others), perpetuating the problem of improper care for patients

Simulation Dataset Generation

Age (2015)		Prevalence estimates per 100.000	
	Global	Male	Female
30-39	2.9 (95% CI 1.8-4.45)	3.9 (95% CI 2.14-6.56)	1.9 (95% CI 0.73-3.96)
40-49	19.5 (95% CI 15.99-23.63)	25.7 (95% CI 19.98-32.51)	13.5 (95% CI 9.51-18.62)
50-59	91.6 (95% CI 82.71-101.29)	115.0 (95% CI 100.66-130.85)	70.1 (95% CI 59.46-82.16)
60-69	336.8 (95% CI 313.57-361.28)	408.8 (95% CI 371.70-448.61)	272.9 (95% CI 244.48-303.78)
70-79	1081.9 (95% CI 1019.27-1147.38)	1303.9 (95% CI 1200.95-1413.27)	906.5 (95% CI 830.36-987.84)
80-89	1786.1 (95% CI 1660.05-1919.19)	2236.9 (95% CI 2010.26-2482.16)	1508.6 (95% CI 1362.42-1666.26)
90+	1579.7 (95% CI 1305.37-1894.74)	1747.4 (95% CI 1269.68-2345.83)	1492.2 (95% CI 1167.58-1879.21)
All ages	157.92 (95% CI 152.25-163.43)	175.00 (95% CI 166.69-183.40)	141.91 (95% CI 134.85-149.24)



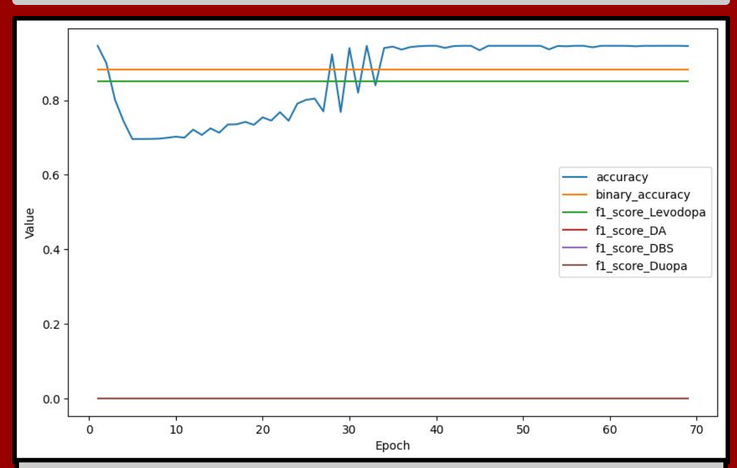
Features				Label	
Age	**Sex**	**Stage of PD**	**Potential Contraindications**	**Treatment(s)***	**Sources**
40-49 (0.4%)	Male: 65.6% Female: 34.4%	Stages 1-3: 96% Stage 4: 4%	In Male: 13.03% In Female: 19.36%	If $1 \leq$ PD Stage ≤ 2, Levo: 70.3%, DA: 15.5%, LevoDA: 14.2%; If $3 \leq$ PD Stage ≤ 4, Levo: 63.4%, DA: 29.7%, DBS: 10.0%, Duopa: 5.0%	(Orozco et al., 2020) (Willis et al., 2022) (Conti et al., 2022) (Rizek et al., 2016) (Houghton et al., 2019) (Medical Advisory Secretariat, 2005)
50-59 (1.9%)	Male: 62.1% Female: 37.9%	Stages 1-3: 91% Stage 4: 9%	In Male: 16.03% In Female: 22.36%	If $1 \leq$ PD Stage ≤ 2, Levo: 70.3%, DA: 15.5%, LevoDA: 14.2%; If $3 \leq$ PD Stage ≤ 4, Levo: 69.6%, DA: 29.7%, DBS: 30.0%, Duopa: 7.5%	
60-69 (6.9%)	Male: 60.0% Female: 40.0%	Stages 1-3: 89% Stages 4-5: 11%	In Male: 19.03% In Female: 25.36%	If $1 \leq$ PD Stage ≤ 2, Levo: 70.3%, DA: 15.5%, LevoDA: 14.2%; If $3 \leq$ PD Stage ≤ 5, Levo: 75.8%, DA: 29.7%, DBS: 30.0%, Duopa: 10.0%	
70-79 (22.1%)	Male: 59.0% Female: 41.0%	Stages 1-3: 83% Stages 4-5: 17%	In Male: 19.03% In Female: 25.36%	If $1 \leq$ PD Stage ≤ 2, Levo: 70.3%, DA: 15.5%, LevoDA: 14.2%; If $3 \leq$ PD Stage ≤ 5, Levo: 82.0%, DA: 24.7%, DBS: 24.0%, Duopa: 10.0%	
80-89 (36.5%)	Male: 59.7% Female: 40.3%	Stages 2-3: 77% Stages 4-5: 23%	In Male: 22.03% In Female: 28.36%	If $2 \leq$ PD Stage ≤ 3, Levo: 70.3%, DA: 15.5%, LevoDA: 14.2%; If $4 \leq$ PD Stage ≤ 5, Levo: 82.0%, DA: 19.7%, DBS: 22.0%, Duopa: 7.5%	
90-99 (32.2%)	Male: 53.9% Female: 46.1%	Stages 2-3: 74% Stages 4-5: 26%	In Male: 25.03% In Female: 31.36%	If $2 \leq$ PD Stage ≤ 3, Levo: 70.3%, DA: 15.5%, LevoDA: 14.2%; If $4 \leq$ PD Stage ≤ 5, Levo: 81.0%, DA: 14.7%, DBS: 20.0%, Duopa: 5.0%	
Rules	**1**	**2**	**3**		
	Levodopa and Duopa cannot both be assigned	If there is no potential presence of contraindication(s), at least one treatment should be assigned	If there is a potential presence of contraindication(s), no treatment should be assigned	*Note: · Levo is Levodopa · LevoDA is combination of Levodopa and DA · Other combinations are present, but their distributions will not be implemented due to absence of such data	

	Age	Sex	PD Stage	Contraindication(s)	Levodopa	DA	DBS	Duopa
0	83	Female	3	Yes	No	No	No	No
1	99	Female	2	Yes	No	No	No	No
2	75	Male	1	No	Yes	No	No	No
3	89	Male	4	No	Yes	Yes	No	No
4	81	Male	3	No	Yes	No	No	No
...	..	...	...	...	...	...	..	...
9995	93	Female	3	No	Yes	No	No	No
9996	84	Male	3	No	Yes	Yes	No	No
9997	64	Male	3	No	Yes	No	No	No
9998	60	Male	3	Yes	No	No	No	No
9999	94	Female	2	No	Yes	No	No	No

	Age	Sex	PD Stage	Contraindication(s)	Levodopa	DA	DBS	Duopa
0	0.728814	0	0.50	1	0	0	0	0
1	1.000000	0	0.25	1	0	0	0	0
2	0.593220	1	0.00	0	1	0	0	0
3	0.830508	1	0.75	0	1	1	0	0
4	0.694915	1	0.50	0	1	0	0	0
...	...	...	...	...	...	..	...	...
9995	0.898305	0	0.50	0	1	0	0	0
9996	0.745763	1	0.50	0	1	1	0	0
9997	0.406780	1	0.50	0	1	0	0	0
9998	0.338983	1	0.50	1	0	0	0	0
9999	0.915254	0	0.25	0	1	0	0	0

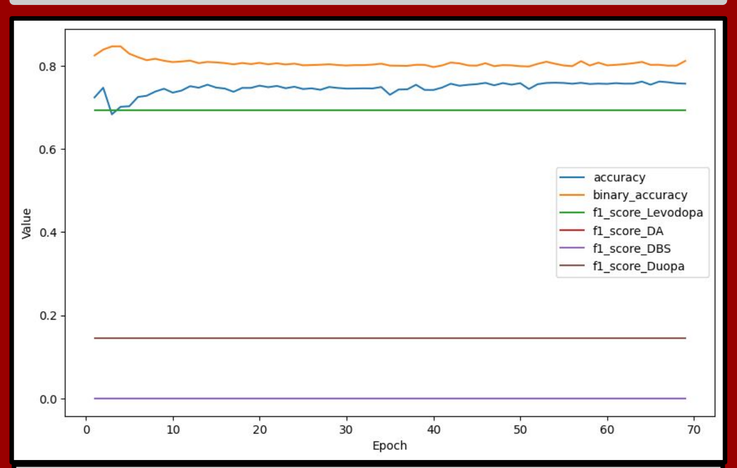
Designs

Prototype #1
Original ANN



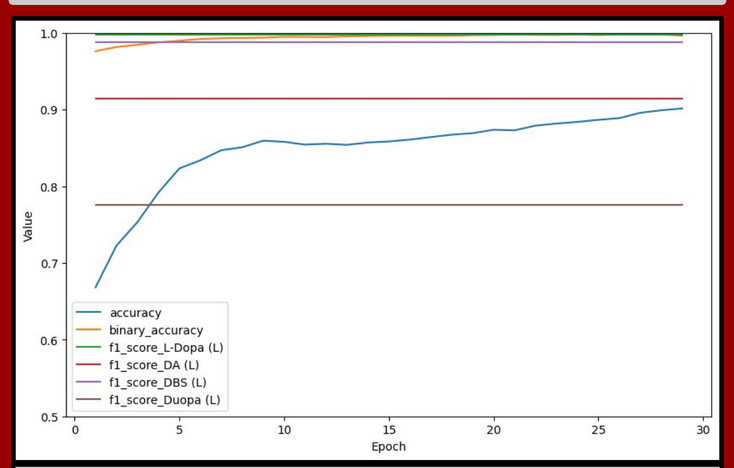
This model appears to perform well at first, with both accuracy metrics above 88%. However, upon further examination, the F1 scores, macro-average F1 score, and confusion matrix values indicate otherwise. Due to the class imbalances in the data, with the number of levodopa prescriptions vastly outweighing the number of all other prescriptions combined, the model attempts to obtain a higher accuracy by simply predicting yes for Levodopa and no for the other treatments.

Prototype #2
ANN with Class Weights



One method to suppress class imbalance, a major issue from Prototype #1, is adjusting class weights. Such adjustments penalize errors on the minority classes more heavily, encouraging the model to make better predictions for them. This model utilizes the ratio of levodopa prescriptions to a certain class prescriptions for the weights. Unfortunately, this change only slightly improves the F1 score and causes a significant decrease in both accuracy metrics. Moreover, the model continues to predict no every time for two classes, DA and DBS. Further efforts to enhance class balance must be made.

Prototype #3
ANN with Rules for Labels



This prototype alters the structure of the features and labels of the neural network, positively repurposing the model's application. The treatments produced from the dataset are considered features, or part of the simulated patient's medical history. The treatments that the neural network predicts, or the labels, are determined using a set of rules that can be established over time in a real world setting. This model is significantly more practical and effective than the previous prototypes, as evidenced by the high performance metrics from an example set of rules.

Prototype Comparison	Accuracy (%)	Binary Accuracy (%)	Average F1 Score (%)
Prototype 1 (Version 1)	94.40	88.54	21.07
Prototype 2 (Version 2)	79.05	82.98	21.48
Prototype 3 (Version 2)	87.35	99.59	92.48

Purpose

Today, Parkinson's disease (PD) negatively impacts the lives of more than 10 million people worldwide. Unfortunately, medication errors and adverse pharmaceutical industry influence are prevalent in treatment for PD, causing many patients with the disease to not be taken care of properly and to have prolonged or exacerbated symptoms.

A deep machine learning model can eradicate these issues or at least significantly reduce their harmful prominence in PD treatment. By considering various factors of an individual patient's medical history, the model can assign an effective treatment plan void of medication errors like contraindications, incorrect timing, etc. In addition, by being institutionalized as a requirement for providers to complete in order to aid their prescription decisions with unbiased input, this model has the potential to enhance the care of patients with PD worldwide.

Background Information

To the knowledge of this study, no programs have been previously made to assign treatments for patients with diseases, particularly PD, using an artificial neural network (ANN) machine learning model.

However, machine learning programs have been made that have attempted to generally tackle two of the problems mentioned: incorrect medications and incorrect medicine dosages. The programs that reduce incorrect medications implement a drug identification model, in which pictures of unknown medications are processed by a convolutional neural network to be identified. The primary aim of such programs is to eliminate the "look-alike and sound-alike" factor of medication administration errors.

A related topic in AI-assisted clinical decision making that is more relevant to the PD aspect of this study is diagnosis of PD or its severity. A correlation between phonetic features and early onset of PD was established, allowing models to utilize voice detection for diagnosis.

Ultimately, due to the novel nature of the program in this study and machine learning in general, there is minimal precedence to directly compare.

Design Plan

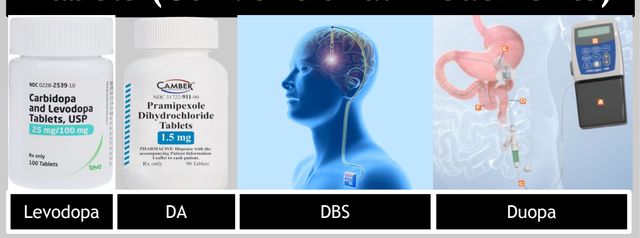
Simulation Dataset

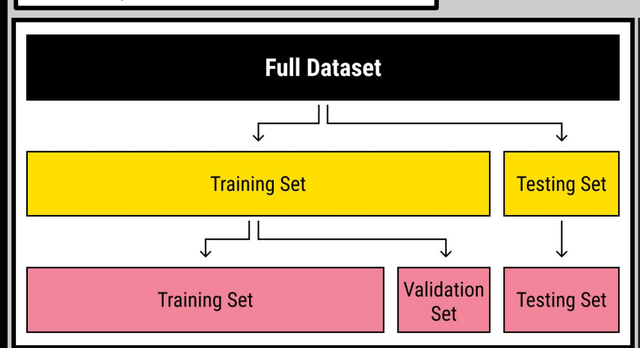
Patient # × 10000+*:

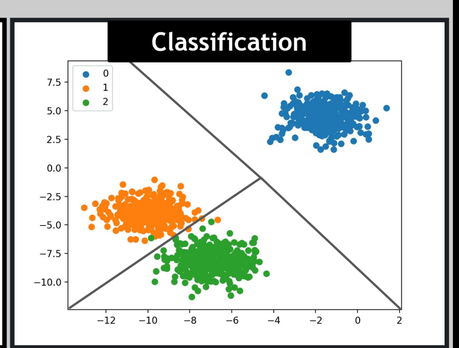
- Features
  - Age
  - Sex
  - Stage of PD
  - Contraindications (Presence or Absence)
- Labels
  - Optimal Treatment(s) (Levodopa, Dopamine Agonist (DA), Deep Brain Stimulation (DBS), Duopa)

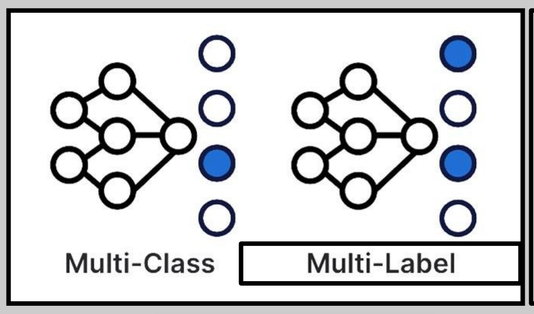
*Uses real world statistical distributions for all factors to simulate a representative dataset of patients with PD

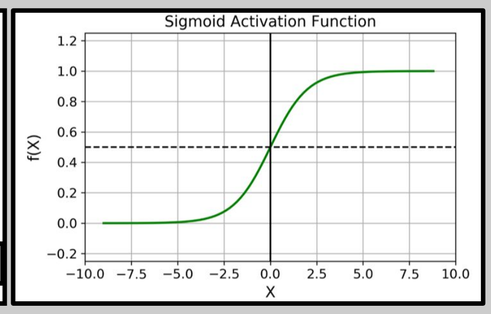
Labels (Conventional Treatments)

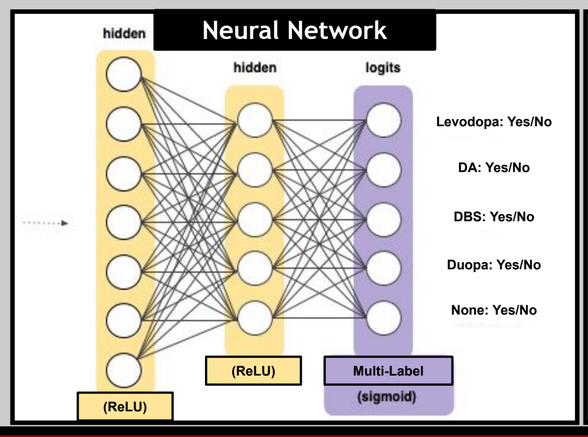


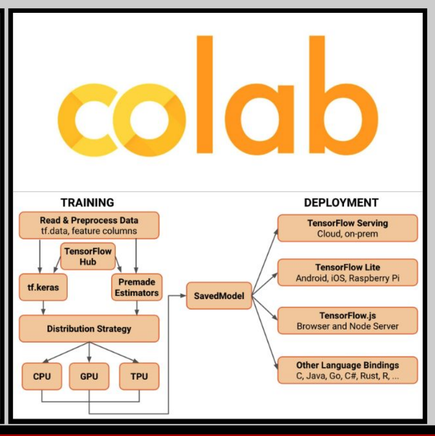












Performance Metrics

- **Confusion Matrix**
  - Tabular visualization of actual values versus model predictions
  - Foundation of all other performance metrics
- **Accuracy**
  - Number of correct predictions divided by total number of predictions, multiplied by 100
  - Percentage of times that model predicted most effective PD treatment(s)
- **Precision**
  - Ratio of true positives and total positives
  - Low precision score can mean high number of false positives and untuned model
- **Recall**
  - Ratio of true positives to true positives plus false negatives
  - Low recall score can mean high number of false negatives and untuned model
- **F1-score**
  - Combination of precision and recall
  - High F1-score indicates good balance between precision and recall

Confusion Matrix

	Actually Positive (1)	Actually Negative (0)
Predicted Positive (1)	True Positives (TPs)	False Positives (FPs)
Predicted Negative (0)	False Negatives (FNs)	True Negatives (TNs)

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN}$$

$$Precision = \frac{TP}{TP + FP}$$

$$Recall = \frac{TP}{TP + FN}$$

$$F_1 = 2 \cdot \frac{Precision \cdot Recall}{Precision + Recall}$$

Conclusion

This project aimed to create a revolutionary artificial neural network (ANN) model that accurately assigns the optimal treatment(s) for a patient with Parkinson's disease (PD) given multiple factors: age, sex, PD stage, and presence or absence of contraindications. Considering the high performance metrics of Prototype #3 particularly, the model was successful in accomplishing this goal.

However, in prototype progression, the application of this model altered slightly. The neural network began with hopes of being implemented directly with predictions from a simulated dataset. Upon testing with a realistic simulation dataset, this goal seemed rather impractical and somewhat ineffective due to constraints in simulation dataset acquisition, class imbalance, and natural randomness. Rather, a new approach was formed in the last prototype that separated the simulation dataset as the features and a set of rules as the labels, promoting rules-based predictions.

This updated model has no effect in its current proof-of-concept stage. Eventually, after tests and modifications in real world settings, a functional, elaborate set of rules will be formed that can be processed by the neural network and applied to all patients. In order to progress this promising program, the following steps should be taken: utilize data of PD patients from hospitals directly if possible (for the features) and conduct research for the creation of the set of rules (for the labels).

Ultimately, the purpose of this machine learning model in application was to eradicate certain medication errors including contraindications as well as reduce pharmaceutical industry influence in prescription decision making. With refinement of the model and just implementation in a hospital setting (impartial data collection and research, guidance for healthcare provider prescriptions, etc.), this purpose can be achieved.

Forms

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