PPD PROGRESSION

using biomarkers

Rashed Alkanawi, Ezgi Booth, Phil Lonsdale, Emily Pompa, Marc Roca

Introduction

Doctors use your medical history and physical examination to diagnose Parkinson's Disease (PD). No blood test, brain scan or other test can be used to make a definitive diagnosis of PD and its progression.

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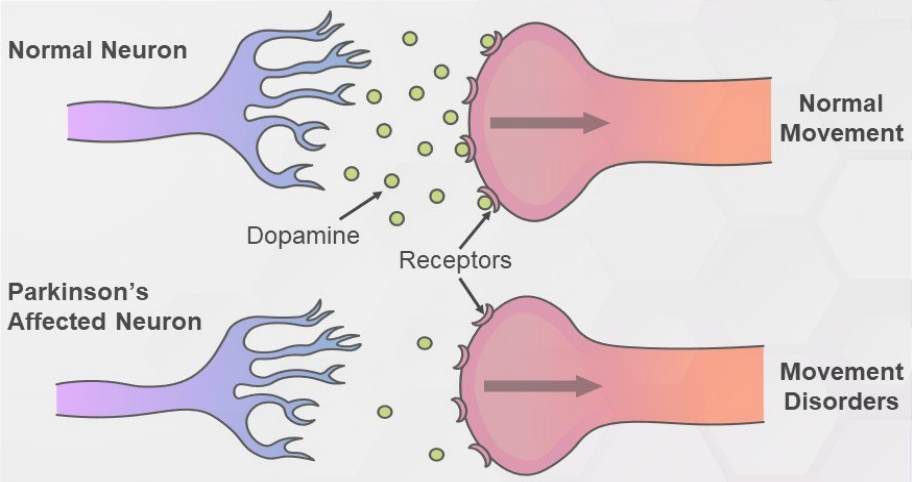
Disease

About the disease

- Second most common neurological illness, impacting 2-3% of adults over the age of 65.
- Brain cells that make dopamine, a chemical that coordinates movement, stop working or die.
- PD is a lifelong and progressive disease, which means that symptoms slowly worsen over time.
- There is no cure for PD, treatments focused on managing symptoms



Prevalence

6 million
Worldwide

1 million
US

02

Symptoms

Symptoms of the disease

Motor Skills

Rigidity & walking difficulties

Bradykinesia & tremors

Vocal symptoms

Non-motor Skills

Mental & behavioral issues

Sense of smell & gastrointestinal issues

Melanoma & joint pain

Diagnosis

How is PD progression currently assessed?

UPDRS Assessment

(Unified Parkinson's Disease Rating Scale)

Part I: Non-Motor Aspects of Experiences of Daily Living

Behavior, mood, motivation

Part II: Motor Aspects of Experiences of Daily Living

Daily task completion

Part III: Motor Examination

Muscle related rigidity, posture/stability issues, tremor

Part IV: Motor Complications

Dyskinesias, dystonia, motor fluctuation

UPDRS

	Scale	Mild	Severe
Part I: Non-Motor Aspects of Experiences of Daily Living	0-52	=<10	=>22
Part II: Motor Aspects of Experiences of Daily Living	0-52	=<12	=>30
Part III: Motor Examination	0-132	=<32	=>59
Part IV: Motor Complications	0-24	=<4	=>13

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Data

Datasets Used

01

Train_peptides

Data on amount of peptides found in patient

02

Train_proteins

Data on amount of protein found in patient

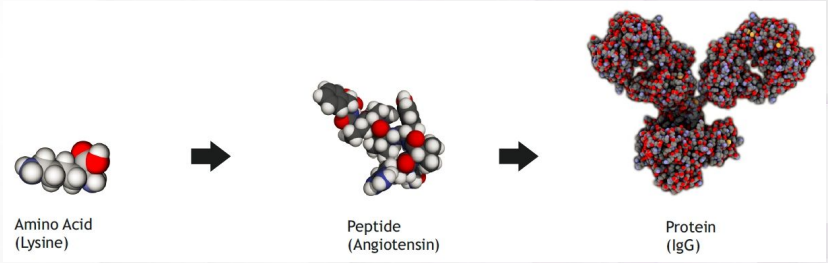
03

Train_clinical_data

Data scores of the patients evaluations

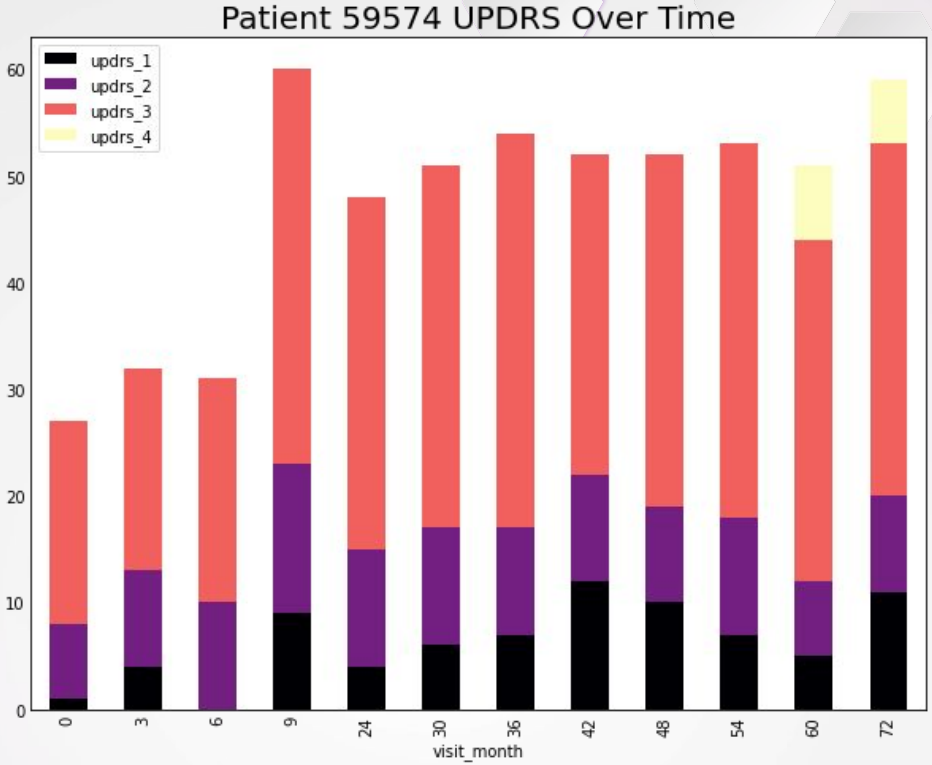
Understanding Data

- Parkinson Disease is caused by environmental and genetic factors
- Proteins gather together to form clumps that interfere with brain functions
- Protein is made up of amino acids. A group of amino acids is called peptide



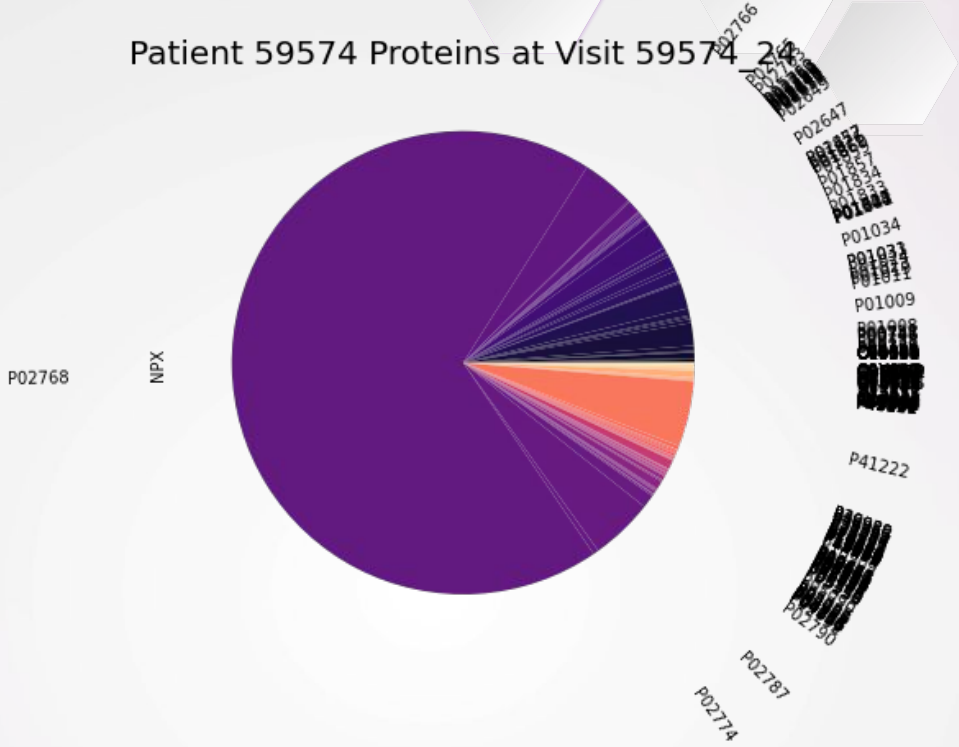
Example

- Random.choice is used to select one patient from the data
- That patient's UPDRS scores are plotted over the course of their visits
- We can see how the disease progresses over time and which impacts are most severe



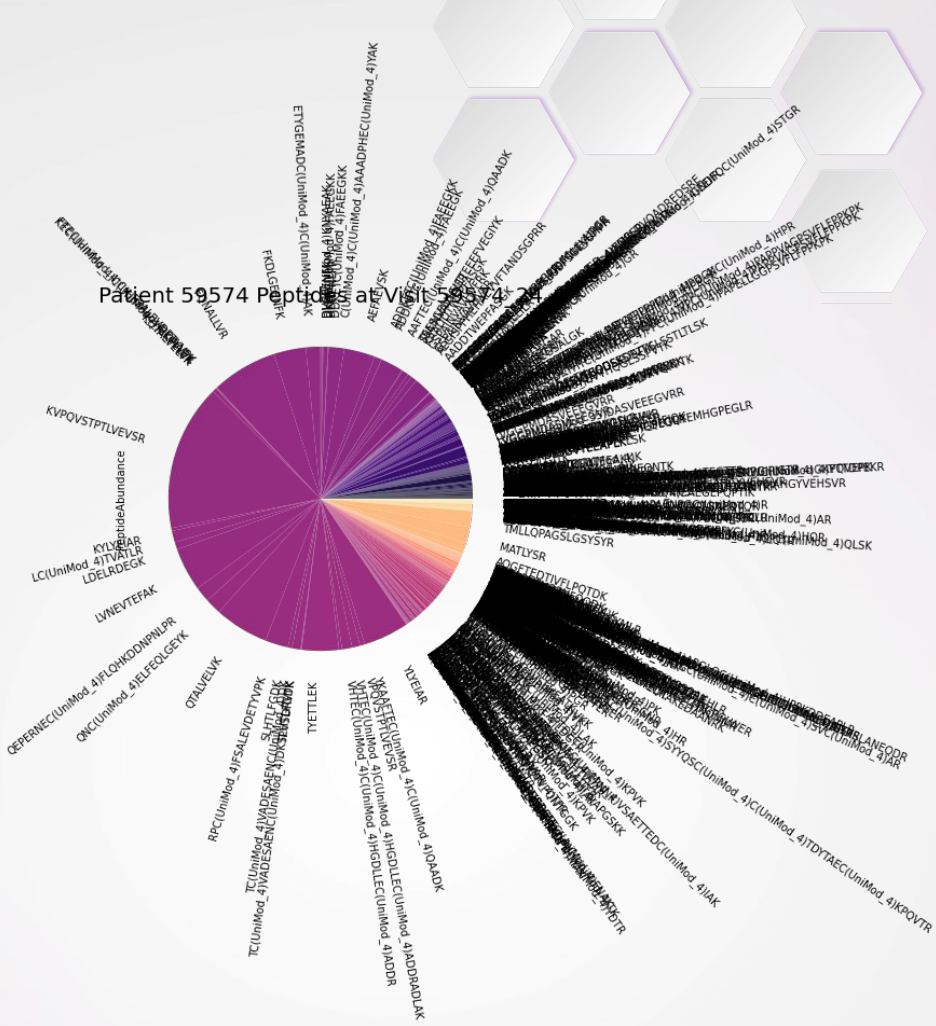
Example

- Random.choice is used to select one visit from our example patient's data
- We visualize that patient's proteins and peptides measured at the visit in a pie chart



Example

- There are dozens of proteins and hundreds of peptides present in every sample
- We will try to use the power of machine learning to determine the influence of these biomarkers in disease progression



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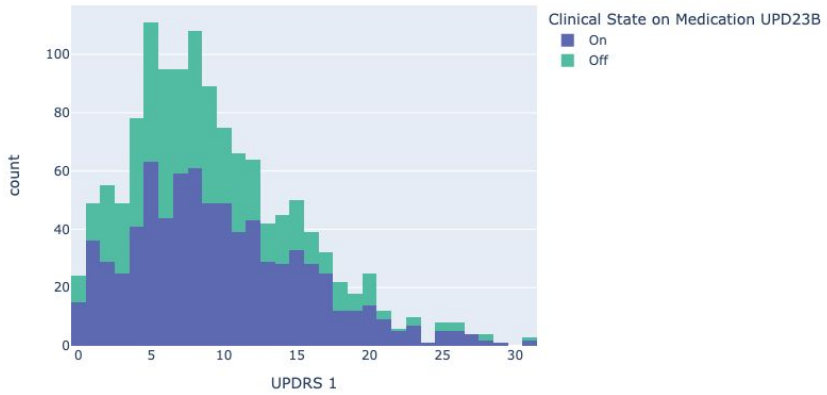
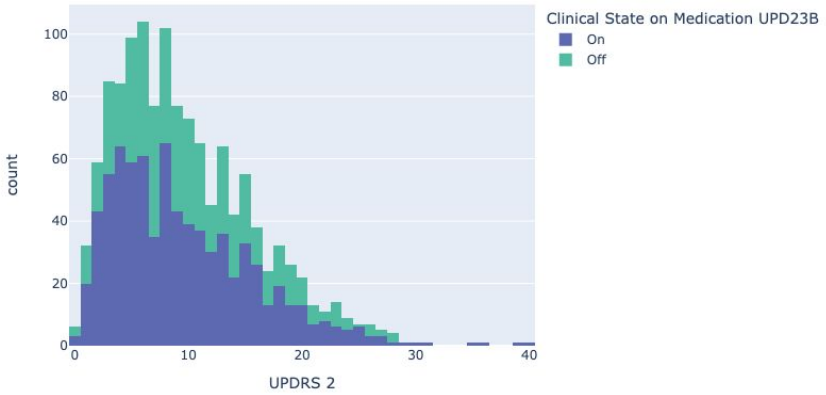
Analysis

Are there differences in the UPDR scores of PD patients receiving medication versus those who do not receive medication?

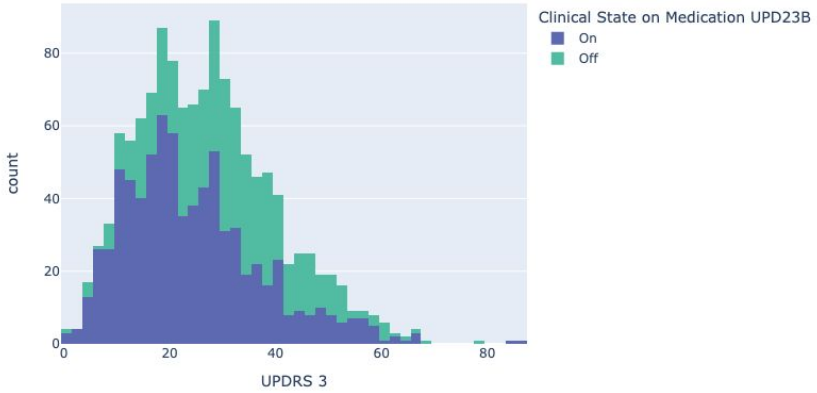
Count of UPDR 1 Scores of Parkinson's Disease Patients



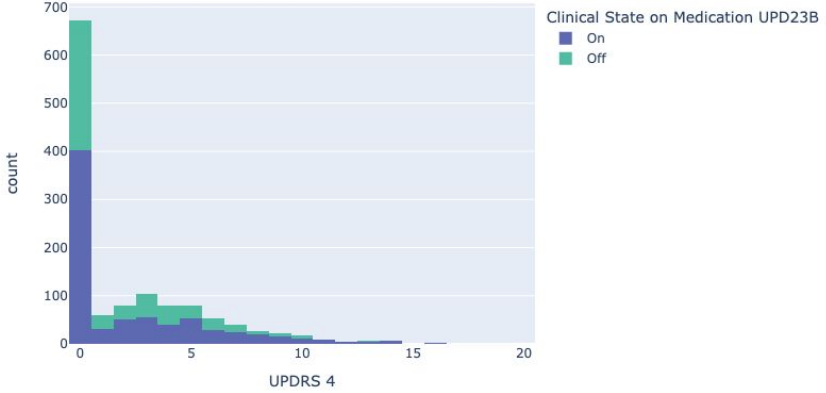
Count of UPDR 2 Scores of Parkinson's Disease Patients

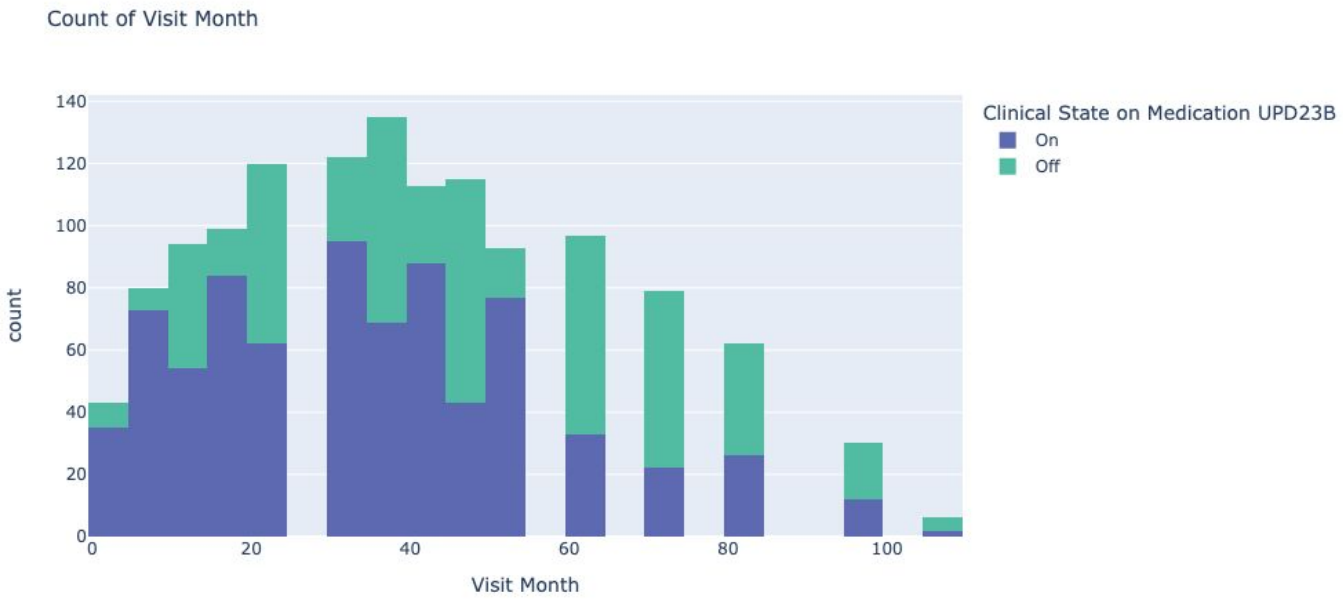


Count of UPDR 3 Scores of Parkinson's Disease Patients



Count of UPDR 4 Scores of Parkinson's Disease Patients

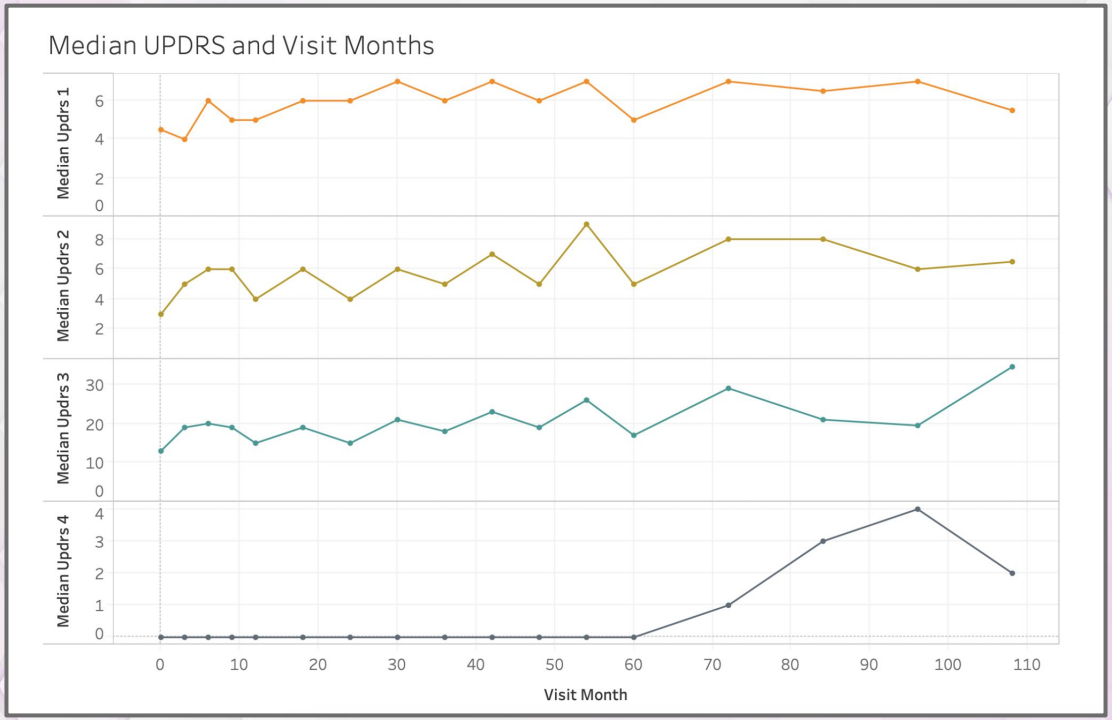




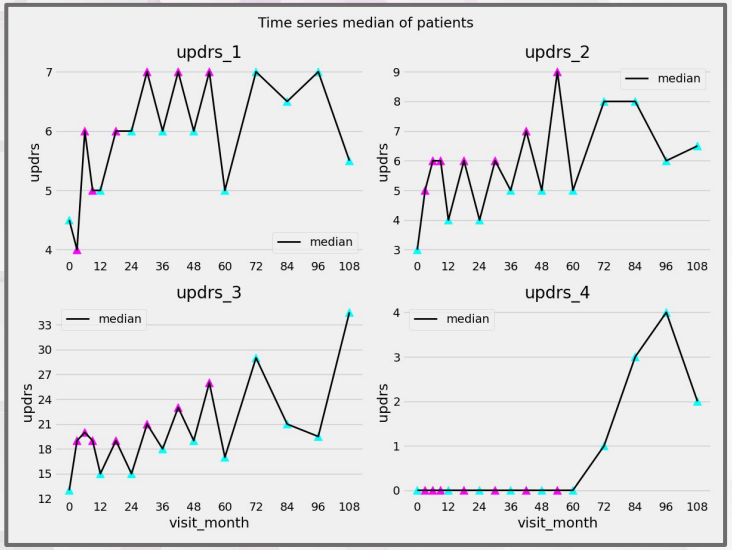
Patients of Parkinson’s Disease that are not on medication are visiting more than those who are on medication.

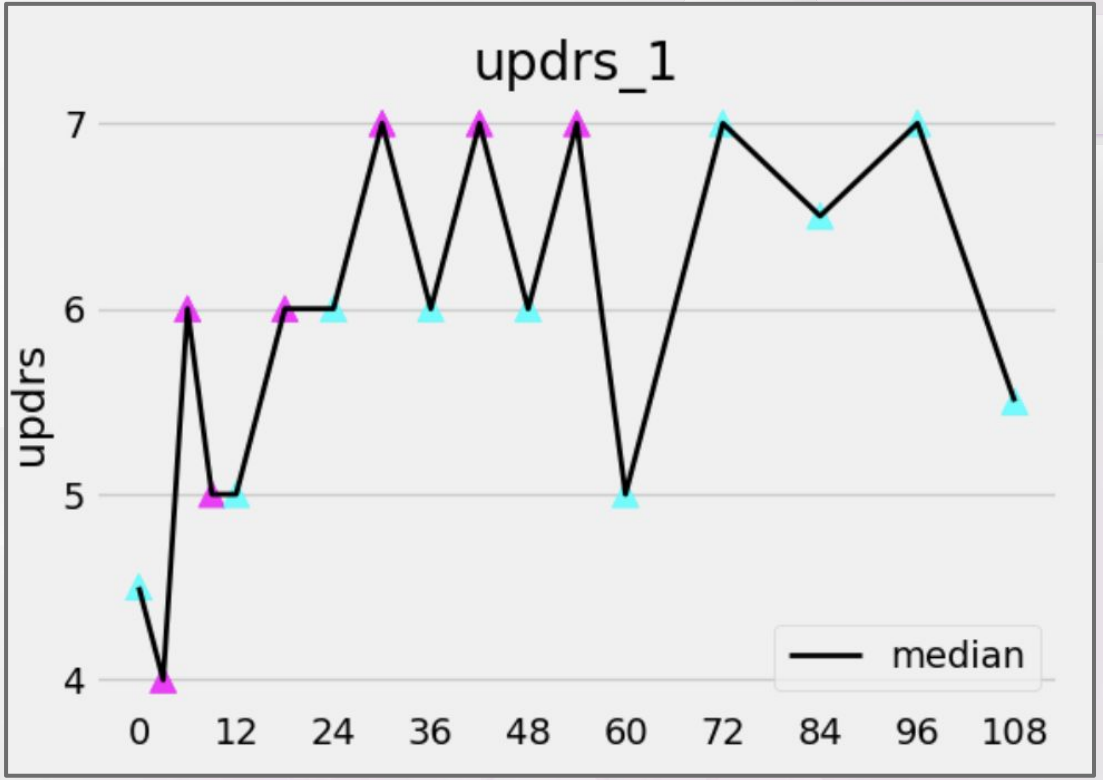
Analysis using months and updrs results.

Using only the Month data



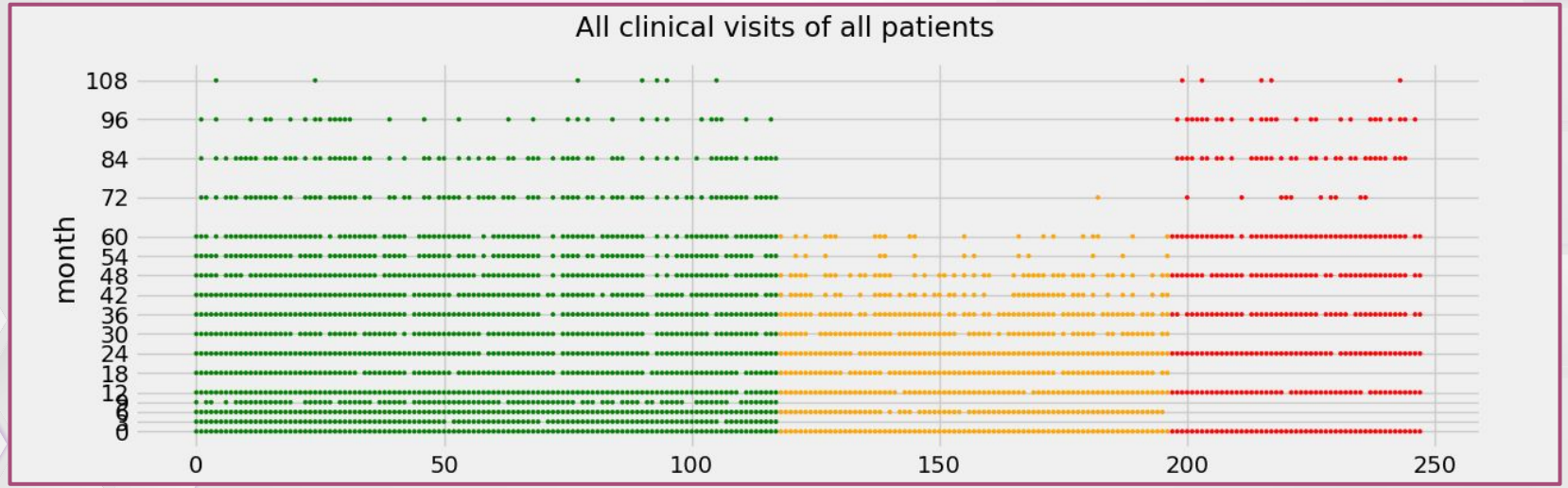
median updrs scores for every month

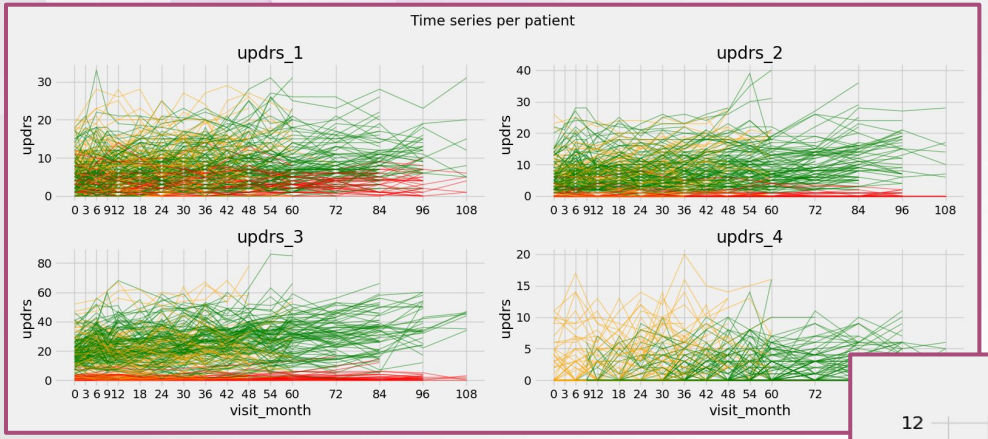




updrs scores over time of every patient

- The patients of the **green** group had their every 3 months
- The patients of the **orange** group had their every 6 months
- The patients of the **red** group had their every year.

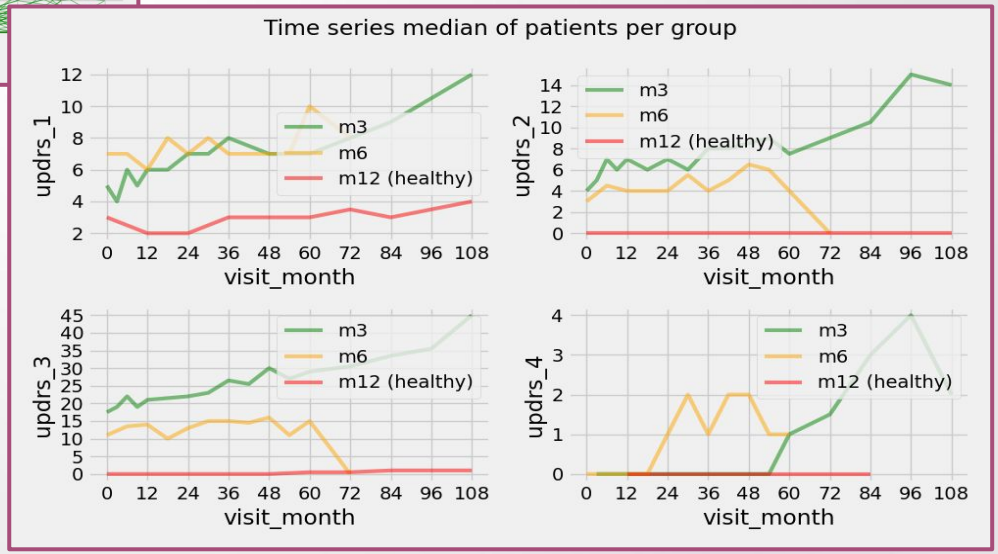




every 3 months

every 6 months

every 1 year

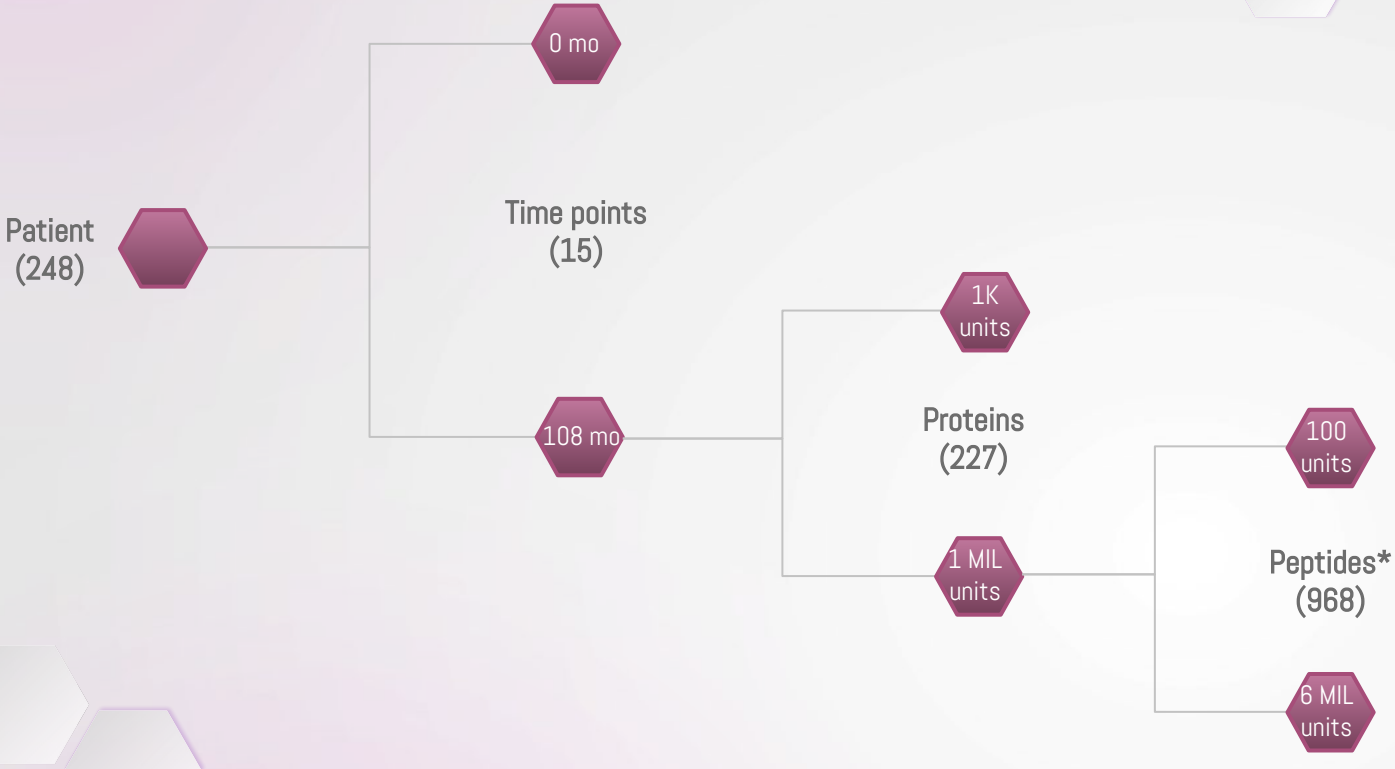


The red group in particular has the lowest updrs scores.


updrs_1
visit_month
unknown
ill
healthy
updrs_2
visit_month
unknown
ill
healthy
updrs_3
visit_month
unknown
ill
healthy
updrs_4
visit_month
unknown
ill
healthy

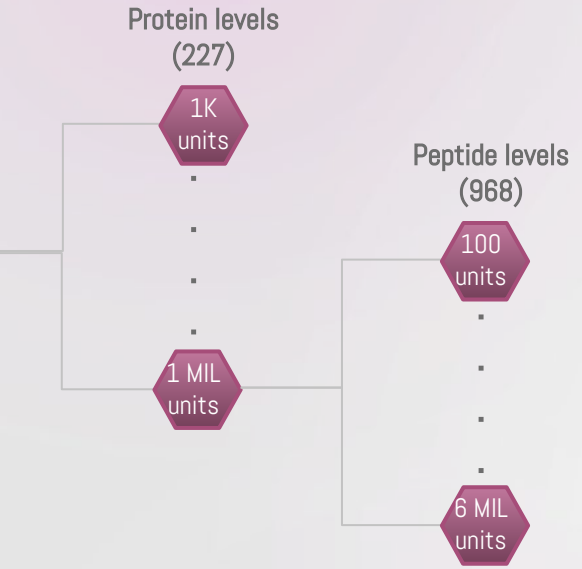
Analysis using Peptides and Proteins.

Data Overview



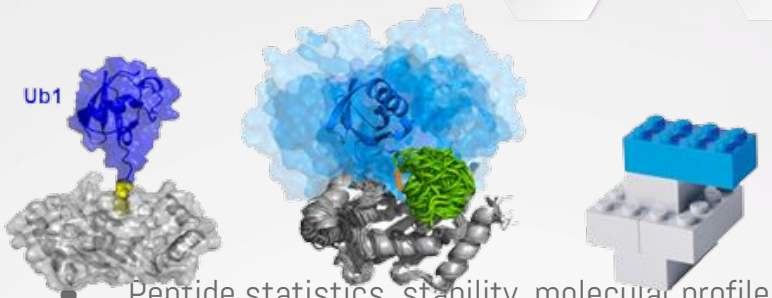
** Each protein is made up of 2-50 peptides*

Peptides levels

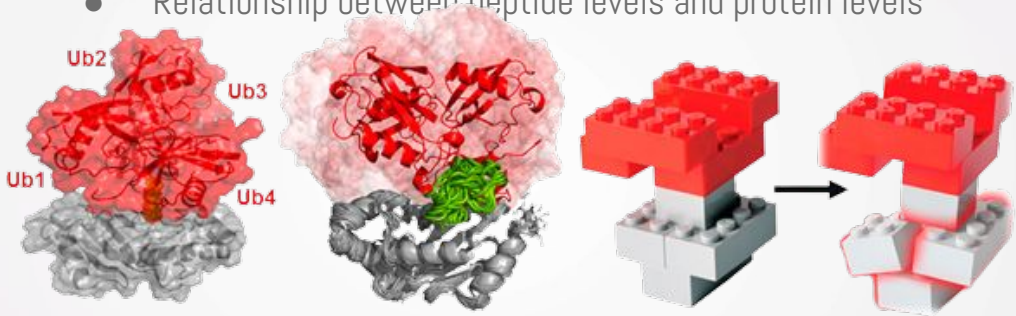


peptides 0.3.2

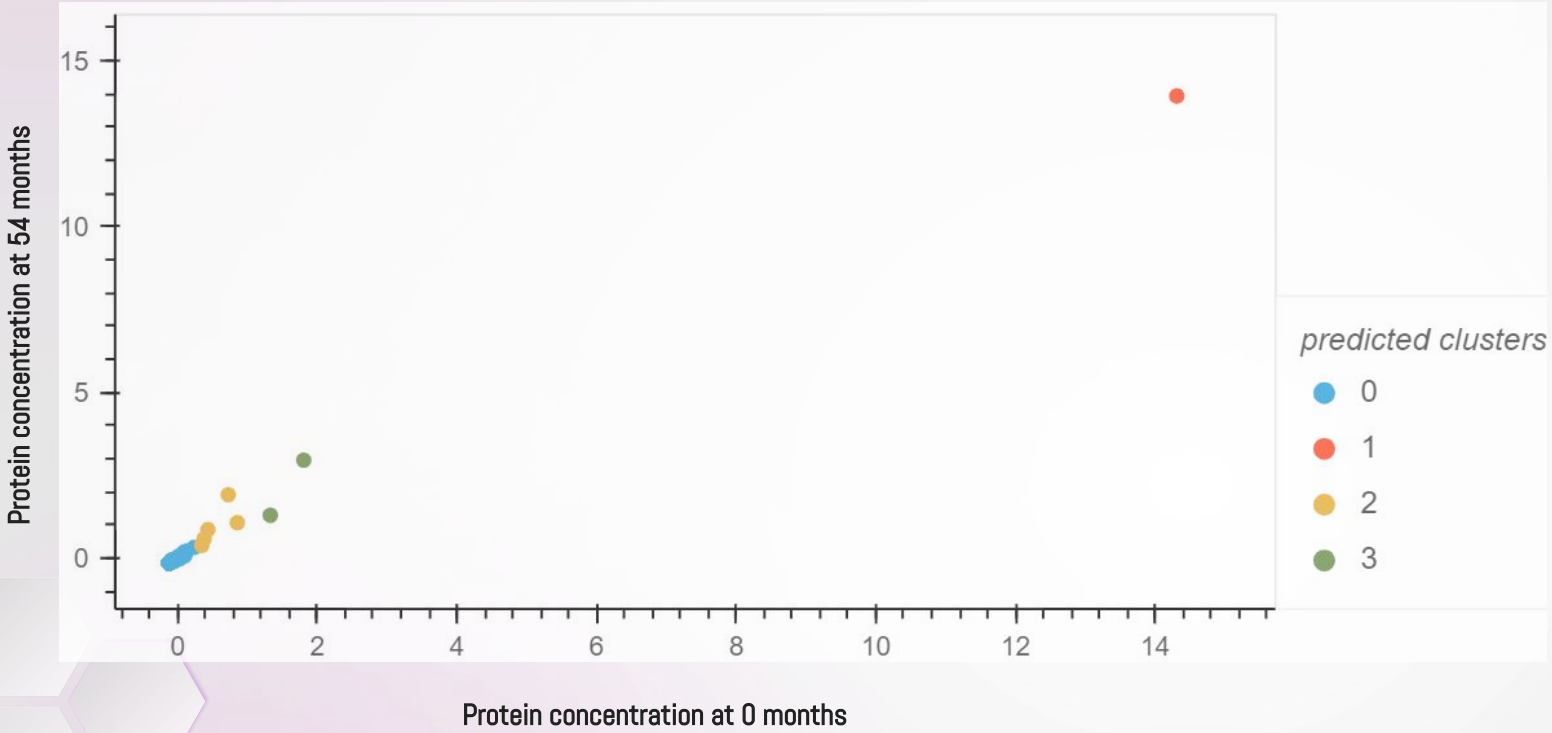
```
pip install peptides
```



- Peptide statistics, stability, molecular profile
- Relationship between stats and peptide expression
- Relationship between peptide levels and protein levels

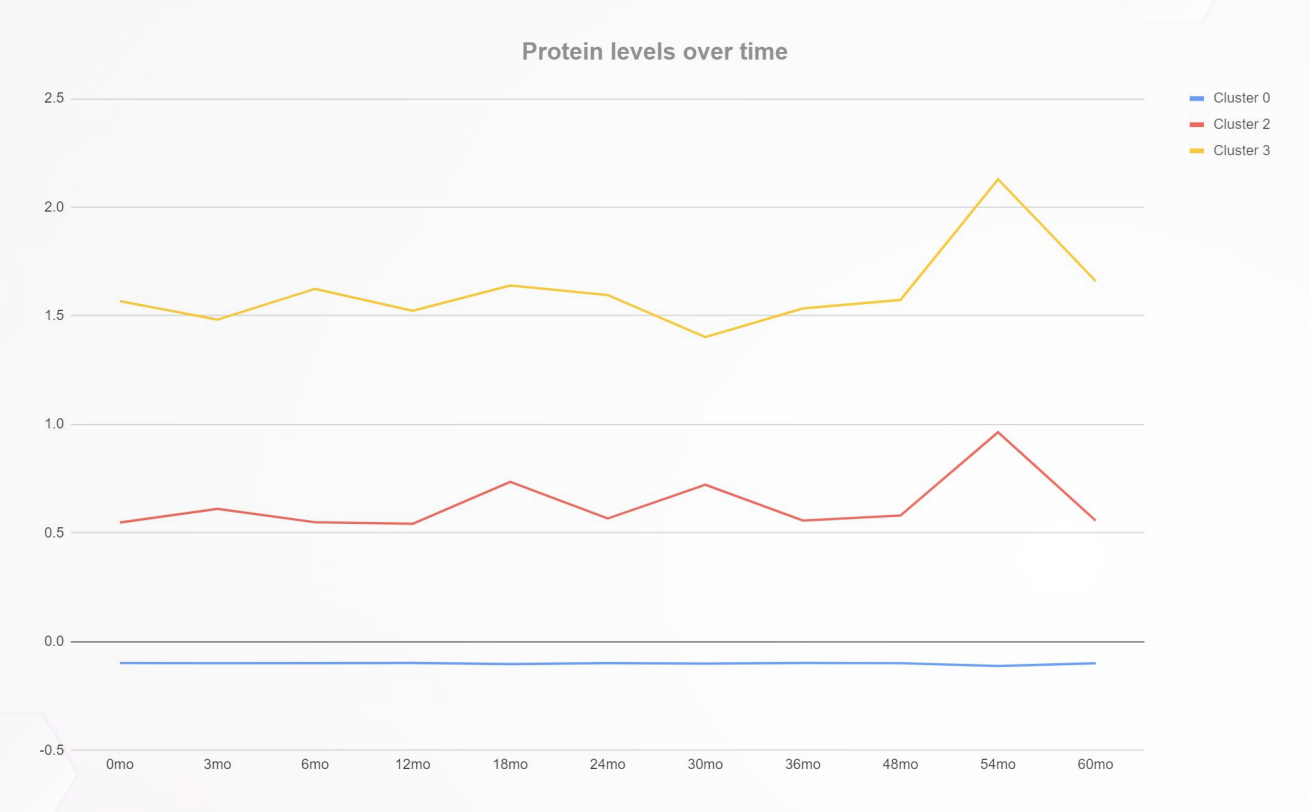


Protein clustering



Protein concentration over time

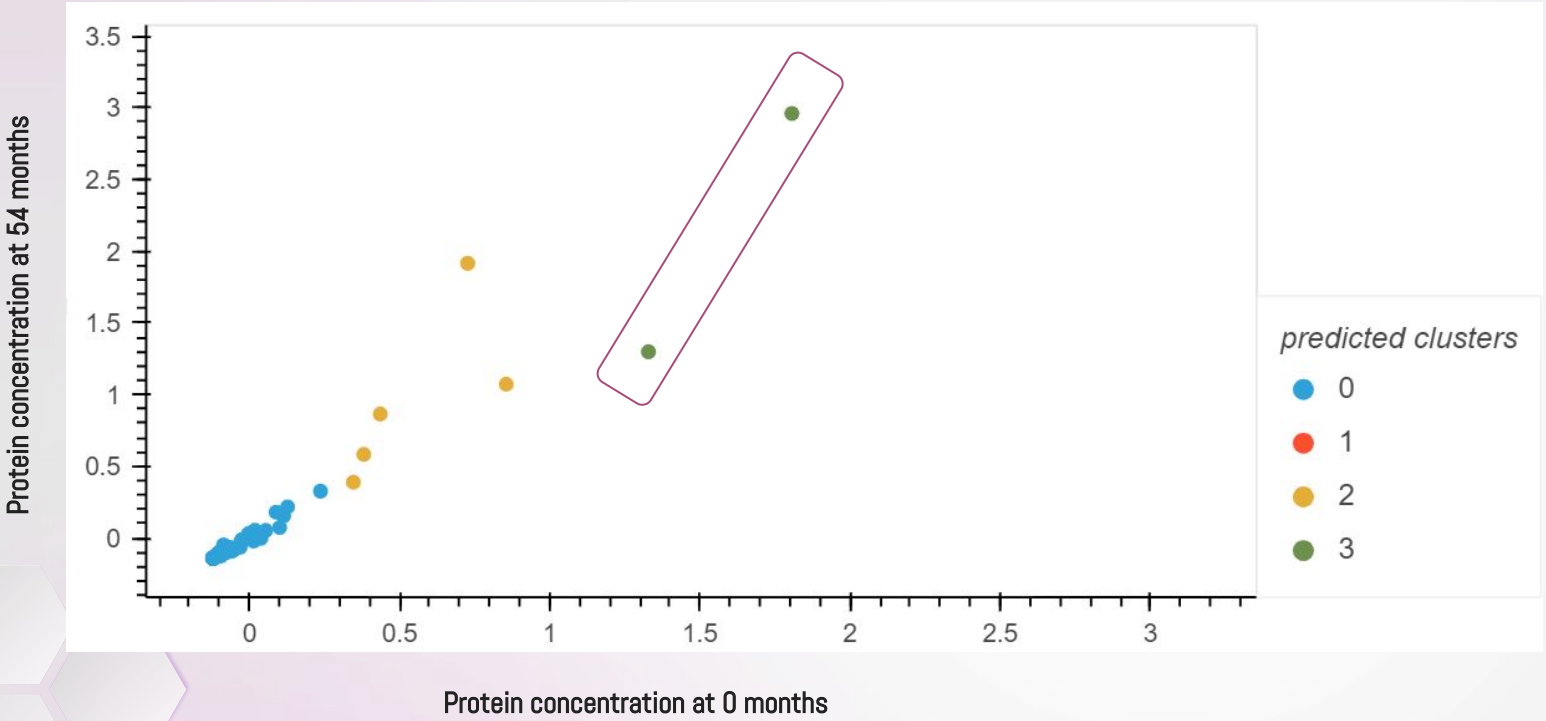
Protein concentration over time



Fluctuating Proteins

Cluster	Name	Expression location	Function
1	Albumin	plasma	LDL/HDL regulation
2	Cystatin-C	cerebrospinal fluid	potential biomarker for Alzheimer's like diseases
2	Transthyretin	serum and cerebrospinal fluid	thyroid hormone-binding protein, amyloidosis
2	Apolipoprotein	plasma HDL	transport of cholesterol from tissues to the liver
2	Alpha-1-antitrypsin	leukocytes and plasma	inhibit serine protease (cleave peptides)
2	Apolipoprotein E	astrocytes, in the cerebral cortex	regulator protein recycling in neurons
3	Prostaglandin	blood-brain barrier, cerebrospinal fluid	abnormal iron overload, indicated in Alzheimer's
3	Serotransferrin	liver and plasma	iron binding, involved in CNS functions, such as sedation/sleep, and may protect oligodendrocytes

Protein clustering



Fluctuating Proteins

Cluster	Name	T-test (p-value) (protein levels in patients with low vs. high PD scores)	Function
2	Cystatin-C	2.0E-04	potential biomarker for Alzheimer's like diseases
2	Transthyretin	0.062	thyroid hormone-binding protein, amyloidosis
2	Apolipoprotein	0.971	transport of cholesterol from tissues to the liver
2	Alpha-1-antitrypsin	0.003	inhibit serine protease (cleave peptides)
2	Apolipoprotein E	6.73E-05	regulator protein recycling in neurons
3	**Prostaglandin**	**1.62E-06**	**abnormal iron overload, indicated in Alzheimer's**
3	**Serotransferrin**	**4.52E-09**	**iron binding, involved in CNS functions, such as sedation/sleep, and may protect oligodendrocytes**

UPDRS 3 Prediction

kerastuneR

```
'activation': 'tanh',
'first_units': 6,
'num_layers': 1,
'units_0': 39,
'units_1': 5,
'units_2': 3,
'units_3': 17,
'units_4': 3,
'units_5': 17,
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'tuner/initial_epoch': 0,
'tuner/bracket': 1,
'tuner/round': 0}
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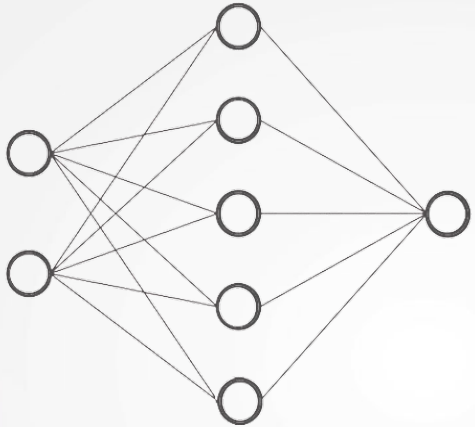

Prediction Accuracy: 0.7753

Conclusions

- Overall, PD patients on medication scored lower on the UPDRS scales
- Biological data is complex and noisy
- Clinical data is not uniform across patients and UPDRS 3 is a more reliable measurement compared to others
- Our model using Prostaglandin and Serotransferrin biomarkers is able to predict UPDRS 3 scores with 0.7753 accuracy

Next Steps

01

Peptides

Utilize peptide expression after sorting for protein frequency

02

Cluster 3 Proteins

Include more proteins implicated in PD-like processes in data training

03

UPDRS 1 & 2

Include for training and testing

04

Test

Using diverse patients & computational models

THANK YOU

Questions?