



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.



Table of contents

01

Disease

02

Symptoms

03

Diagnosis

04

Data

05

Analysis

06

Conclusions

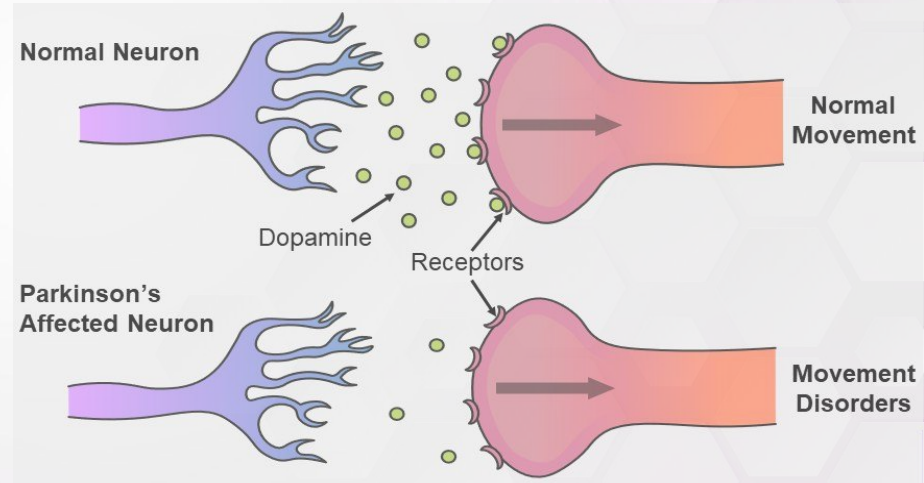
The background features a light gray hexagonal grid. A large, faint pink hexagon is centered on the page. Several smaller, solid maroon hexagons are placed at the corners and along the edges of the grid.

01

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



The background features a light gray hexagonal grid. A large, faint pink hexagon is centered on the page. Four smaller, solid maroon hexagons are positioned at the corners: top-left, top-right, bottom-left, and bottom-right. The number '02' is centered within the central pink hexagon.

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





03

Diagnosis

How is PD progression currently
assessed?

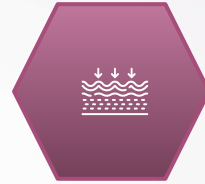
UPDRS Assessment

(Unified Parkinson's Disease Rating Scale)



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

Behavior, mood, motivation



Part III: Motor Examination

Muscle related rigidity, posture/stability issues, tremor



Part II: Motor Aspects of Experiences of Daily Living

Daily task completion



Part IV: Motor Complications

Dyskinesias, dystonia, motor fluctuation

UPDRS



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

Scale

0-52

Mild

=<10

Severe

=>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



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

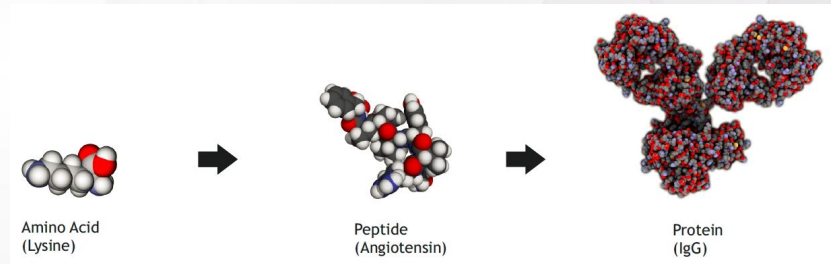
03

Train_clinical_data

Data scores of the
patients evaluations

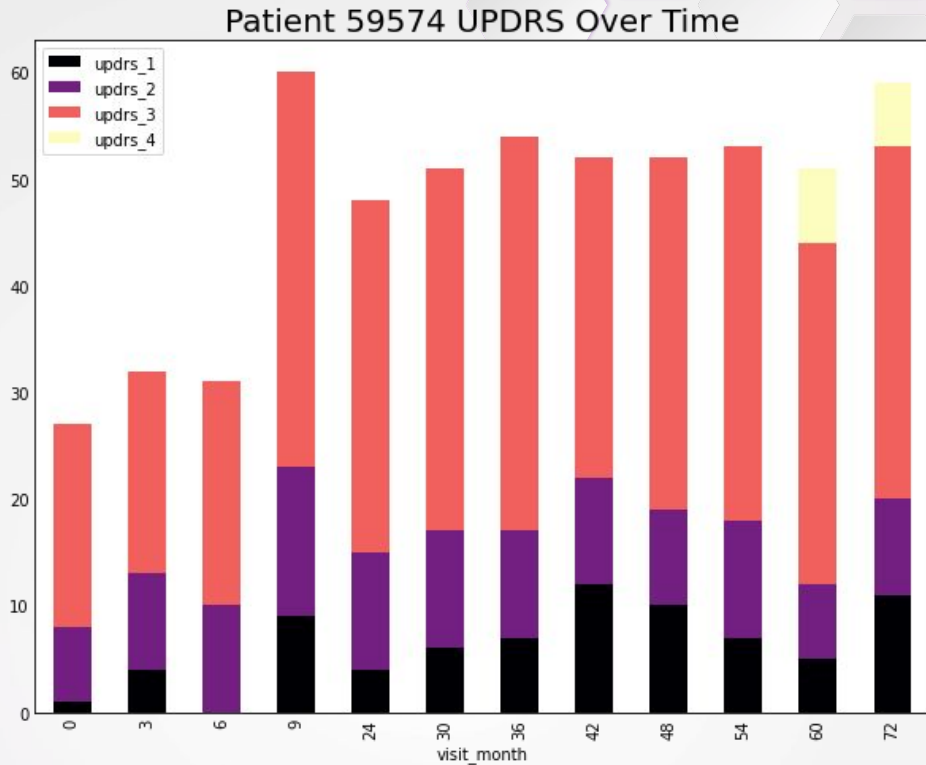
Understanding Data

- 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



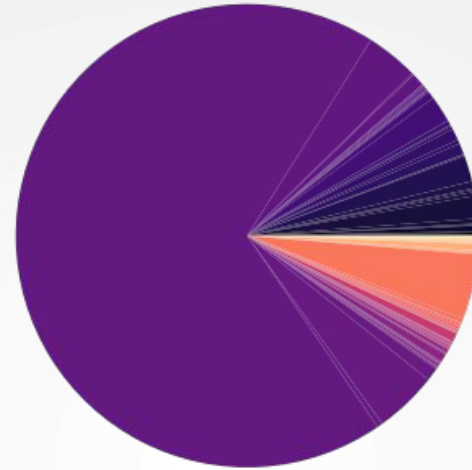
Example

- 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

Patient 59574 Proteins at Visit 59574_24

P02768

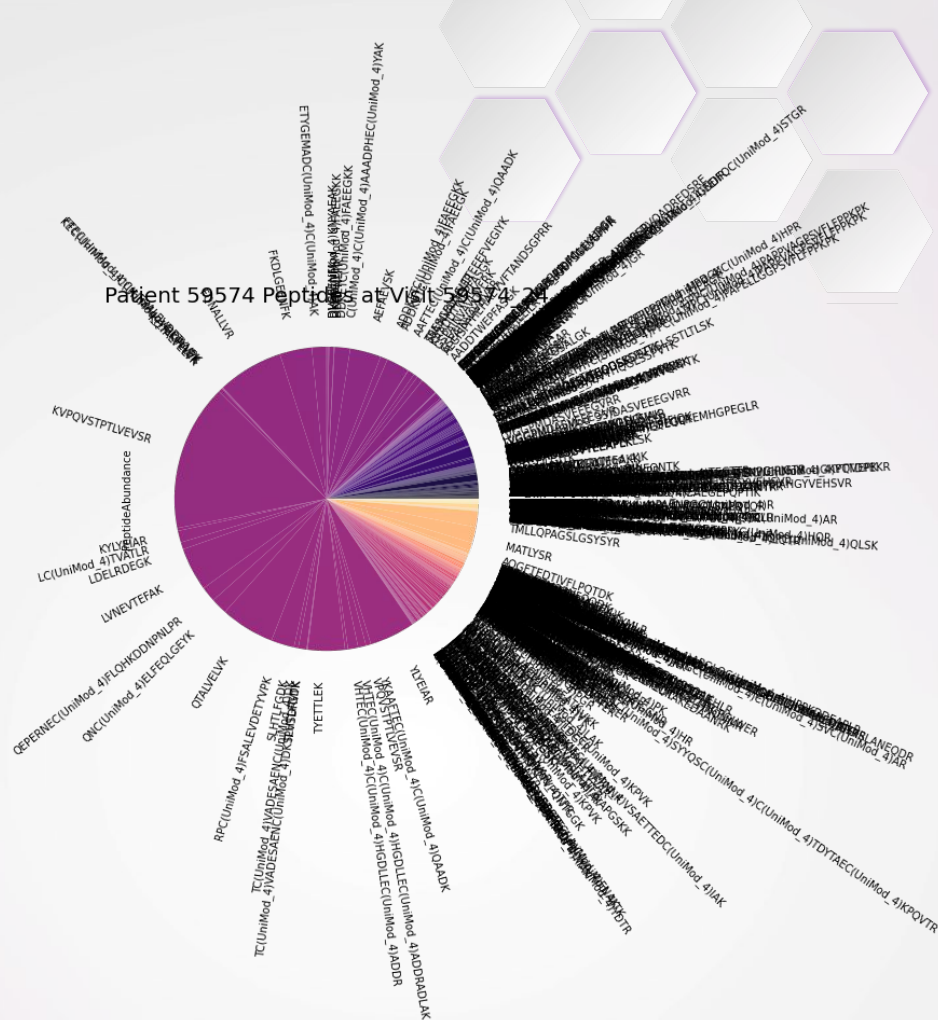
NPX



P02766
P02765
P02647
P01034
P01033
P01032
P01031
P01030
P01029
P01028
P01027
P01026
P01025
P01024
P01023
P01022
P01021
P01020
P01019
P01018
P01017
P01016
P01015
P01014
P01013
P01012
P01011
P01010
P01009
P01008
P01007
P01006
P01005
P01004
P01003
P01002
P01001
P01000
P00999
P00998
P00997
P00996
P00995
P00994
P00993
P00992
P00991
P00990
P00989
P00988
P00987
P00986
P00985
P00984
P00983
P00982
P00981
P00980
P00979
P00978
P00977
P00976
P00975
P00974
P00973
P00972
P00971
P00970
P00969
P00968
P00967
P00966
P00965
P00964
P00963
P00962
P00961
P00960
P00959
P00958
P00957
P00956
P00955
P00954
P00953
P00952
P00951
P00950
P00949
P00948
P00947
P00946
P00945
P00944
P00943
P00942
P00941
P00940
P00939
P00938
P00937
P00936
P00935
P00934
P00933
P00932
P00931
P00930
P00929
P00928
P00927
P00926
P00925
P00924
P00923
P00922
P00921
P00920
P00919
P00918
P00917
P00916
P00915
P00914
P00913
P00912
P00911
P00910
P00909
P00908
P00907
P00906
P00905
P00904
P00903
P00902
P00901
P00900
P00899
P00898
P00897
P00896
P00895
P00894
P00893
P00892
P00891
P00890
P00889
P00888
P00887
P00886
P00885
P00884
P00883
P00882
P00881
P00880
P00879
P00878
P00877
P00876
P00875
P00874
P00873
P00872
P00871
P00870
P00869
P00868
P00867
P00866
P00865
P00864
P00863
P00862
P00861
P00860
P00859
P00858
P00857
P00856
P00855
P00854
P00853
P00852
P00851
P00850
P00849
P00848
P00847
P00846
P00845
P00844
P00843
P00842
P00841
P00840
P00839
P00838
P00837
P00836
P00835
P00834
P00833
P00832
P00831
P00830
P00829
P00828
P00827
P00826
P00825
P00824
P00823
P00822
P00821
P00820
P00819
P00818
P00817
P00816
P00815
P00814
P00813
P00812
P00811
P00810
P00809
P00808
P00807
P00806
P00805
P00804
P00803
P00802
P00801
P00800
P00799
P00798
P00797
P00796
P00795
P00794
P00793
P00792
P00791
P00790
P00789
P00788
P00787
P00786
P00785
P00784
P00783
P00782
P00781
P00780
P00779
P00778
P00777
P00776
P00775
P00774
P00773
P00772
P00771
P00770
P00769
P00768
P00767
P00766
P00765
P00764
P00763
P00762
P00761
P00760
P00759
P00758
P00757
P00756
P00755
P00754
P00753
P00752
P00751
P00750
P00749
P00748
P00747
P00746
P00745
P00744
P00743
P00742
P00741
P00740
P00739
P00738
P00737
P00736
P00735
P00734
P00733
P00732
P00731
P00730
P00729
P00728
P00727
P00726
P00725
P00724
P00723
P00722
P00721
P00720
P00719
P00718
P00717
P00716
P00715
P00714
P00713
P00712
P00711
P00710
P00709
P00708
P00707
P00706
P00705
P00704
P00703
P00702
P00701
P00700
P00699
P00698
P00697
P00696
P00695
P00694
P00693
P00692
P00691
P00690
P00689
P00688
P00687
P00686
P00685
P00684
P00683
P00682
P00681
P00680
P00679
P00678
P00677
P00676
P00675
P00674
P00673
P00672
P00671
P00670
P00669
P00668
P00667
P00666
P00665
P00664
P00663
P00662
P00661
P00660
P00659
P00658
P00657
P00656
P00655
P00654
P00653
P00652
P00651
P00650
P00649
P00648
P00647
P00646
P00645
P00644
P00643
P00642
P00641
P00640
P00639
P00638
P00637
P00636
P00635
P00634
P00633
P00632
P00631
P00630
P00629
P00628
P00627
P00626
P00625
P00624
P00623
P00622
P00621
P00620
P00619
P00618
P00617
P00616
P00615
P00614
P00613
P00612
P00611
P00610
P00609
P00608
P00607
P00606
P00605
P00604
P00603
P00602
P00601
P00600
P00599
P00598
P00597
P00596
P00595
P00594
P00593
P00592
P00591
P00590
P00589
P00588
P00587
P00586
P00585
P00584
P00583
P00582
P00581
P00580
P00579
P00578
P00577
P00576
P00575
P00574
P00573
P00572
P00571
P00570
P00569
P00568
P00567
P00566
P00565
P00564
P00563
P00562
P00561
P00560
P00559
P00558
P00557
P00556
P00555
P00554
P00553
P00552
P00551
P00550
P00549
P00548
P00547
P00546
P00545
P00544
P00543
P00542
P00541
P00540
P00539
P00538
P00537
P00536
P00535
P00534
P00533
P00532
P00531
P00530
P00529
P00528
P00527
P00526
P00525
P00524
P00523
P00522
P00521
P00520
P00519
P00518
P00517
P00516
P00515
P00514
P00513
P00512
P00511
P00510
P00509
P00508
P00507
P00506
P00505
P00504
P00503
P00502
P00501
P00500
P00499
P00498
P00497
P00496
P00495
P00494
P00493
P00492
P00491
P00490
P00489
P00488
P00487
P00486
P00485
P00484
P00483
P00482
P00481
P00480
P00479
P00478
P00477
P00476
P00475
P00474
P00473
P00472
P00471
P00470
P00469
P00468
P00467
P00466
P00465
P00464
P00463
P00462
P00461
P00460
P00459
P00458
P00457
P00456
P00455
P00454
P00453
P00452
P00451
P00450
P00449
P00448
P00447
P00446
P00445
P00444
P00443
P00442
P00441
P00440
P00439
P00438
P00437
P00436
P00435
P00434
P00433
P00432
P00431
P00430
P00429
P00428
P00427
P00426
P00425
P00424
P00423
P00422
P00421
P00420
P00419
P00418
P00417
P00416
P00415
P00414
P00413
P00412
P00411
P00410
P00409
P00408
P00407
P00406
P00405
P00404
P00403
P00402
P00401
P00400
P00399
P00398
P00397
P00396
P00395
P00394
P00393
P00392
P00391
P00390
P00389
P00388
P00387
P00386
P00385
P00384
P00383
P00382
P00381
P00380
P00379
P00378
P00377
P00376
P00375
P00374
P00373
P00372
P00371
P00370
P00369
P00368
P00367
P00366
P00365
P00364
P00363
P00362
P00361
P00360
P00359
P00358
P00357
P00356
P00355
P00354
P00353
P00352
P00351
P00350
P00349
P00348
P00347
P00346
P00345
P00344
P00343
P00342
P00341
P00340
P00339
P00338
P00337
P00336
P00335
P00334
P00333
P00332
P00331
P00330
P00329
P00328
P00327
P00326
P00325
P00324
P00323
P00322
P00321
P00320
P00319
P00318
P00317
P00316
P00315
P00314
P00313
P00312
P00311
P00310
P00309
P00308
P00307
P00306
P00305
P00304
P00303
P00302
P00301
P00300
P00299
P00298
P00297
P00296
P00295
P00294
P00293
P00292
P00291
P00290
P00289
P00288
P00287
P00286
P00285
P00284
P00283
P00282
P00281
P00280
P00279
P00278
P00277
P00276
P00275
P00274
P00273
P00272
P00271
P00270
P00269
P00268
P00267
P00266
P00265
P00264
P00263
P00262
P00261
P00260
P00259
P00258
P00257
P00256
P00255
P00254
P00253
P00252
P00251
P00250
P00249
P00248
P00247
P00246
P00245
P00244
P00243
P00242
P00241
P00240
P00239
P00238
P00237
P00236
P00235
P00234
P00233
P00232
P00231
P00230
P00229
P00228
P00227
P00226
P00225
P00224
P00223
P00222
P00221
P00220
P00219
P00218
P00217
P00216
P00215
P00214
P00213
P00212
P00211
P00210
P00209
P00208
P00207
P00206
P00205
P00204
P00203
P00202
P00201
P00200
P00199
P00198
P00197
P00196
P00195
P00194
P00193
P00192
P00191
P00190
P00189
P00188
P00187
P00186
P00185
P00184
P00183
P00182
P00181
P00180
P00179
P00178
P00177
P00176
P00175
P00174
P00173
P00172
P00171
P00170
P00169
P00168
P00167
P00166
P00165
P00164
P00163
P00162
P00161
P00160
P00159
P00158
P00157
P00156
P00155
P00154
P00153
P00152
P00151
P00150
P00149
P00148
P00147
P00146
P00145
P00144
P00143
P00142
P00141
P00140
P00139
P00138
P00137
P00136
P00135
P00134
P00133
P00132
P00131
P00130
P00129
P00128
P00127
P00126
P00125
P00124
P00123
P00122
P00121
P00120
P00119
P00118
P00117
P00116
P00115
P00114
P00113
P00112
P00111
P00110
P00109
P00108
P00107
P00106
P00105
P00104
P00103
P00102
P00101
P00100
P00099
P00098
P00097
P00096
P00095
P00094
P00093
P00092
P00091
P00090
P00089
P00088
P00087
P00086
P00085
P00084
P00083
P00082
P00081
P00080
P00079
P00078
P00077
P00076
P00075
P00074
P00073
P00072
P00071
P00070
P00069
P00068
P00067
P00066
P00065
P00064
P00063
P00062
P00061
P00060
P00059
P00058
P00057
P00056
P00055
P00054
P00053
P00052
P00051
P00050
P00049
P00048
P00047
P00046
P00045
P00044
P00043
P00042
P00041
P00040
P00039
P00038
P00037
P00036
P00035
P00034
P00033
P00032
P00031
P00030
P00029
P00028
P00027
P00026
P00025
P00024
P00023
P00022
P00021
P00020
P00019
P00018
P00017
P00016
P00015
P00014
P00013
P00012
P00011
P00010
P00009
P00008
P00007
P00006
P00005
P00004
P00003
P00002
P00001

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



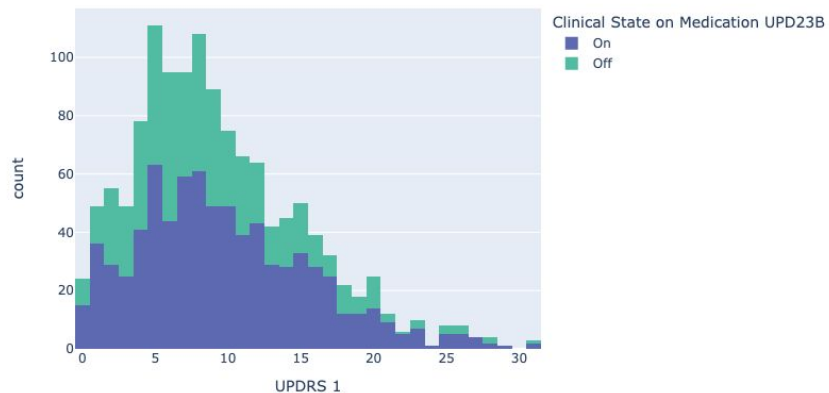


Analysis

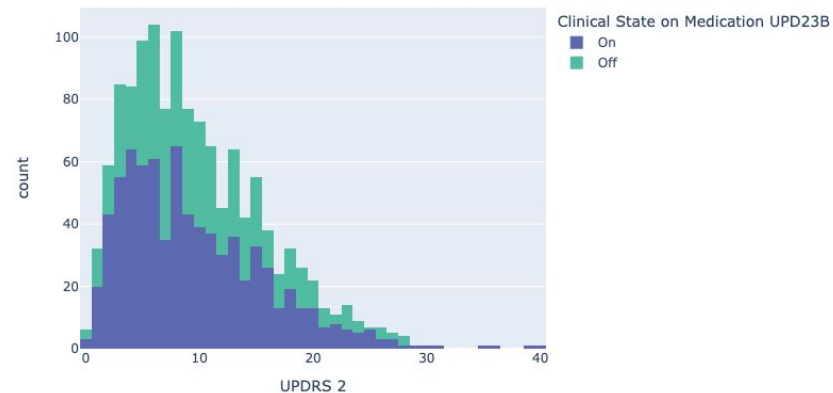
Are there differences in the UPDR scores of PD patients receiving medication versus those who do not receive medication?



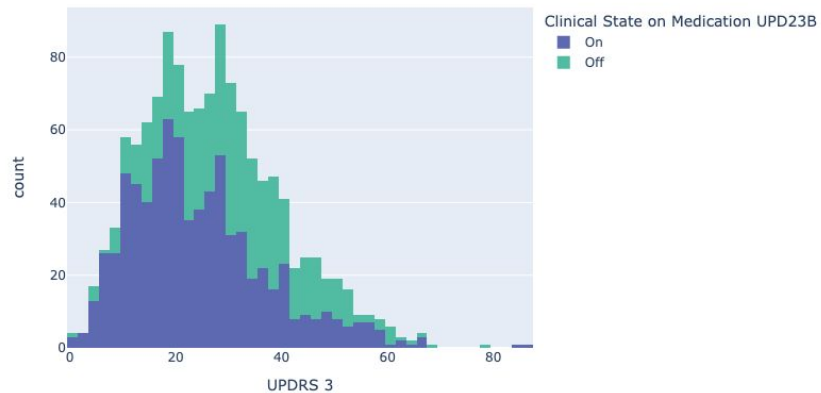
Count of UPDR 1 Scores of Parkinson's Disease Patients



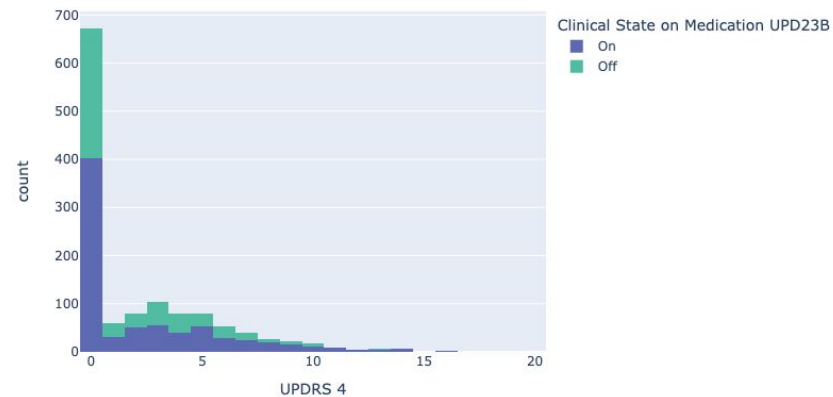
Count of UPDR 2 Scores of Parkinson's Disease Patients



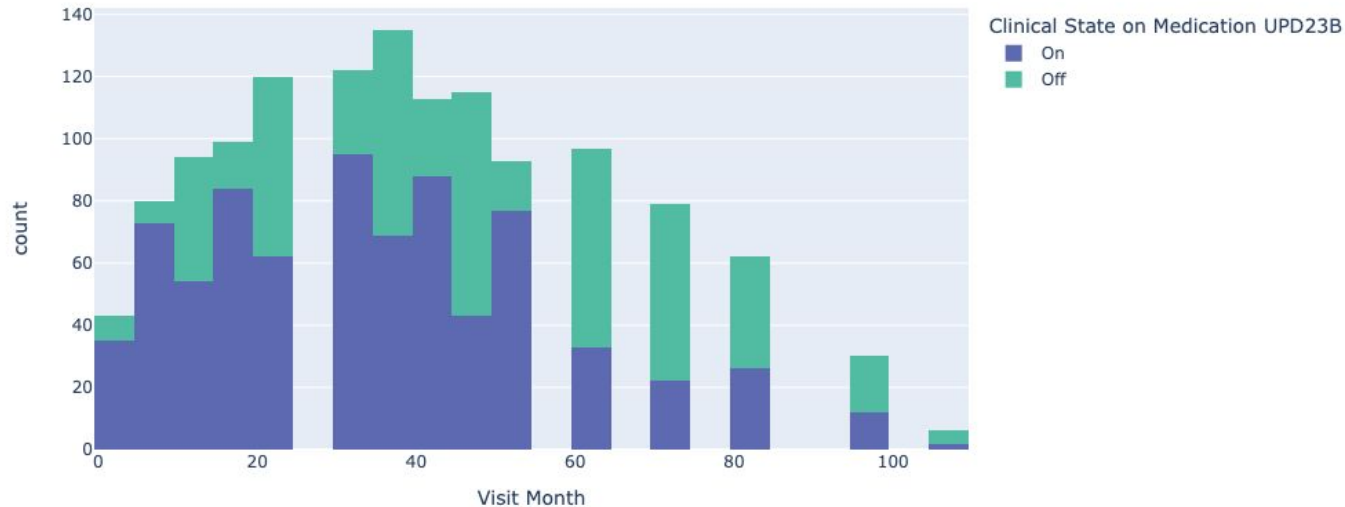
Count of UPDR 3 Scores of Parkinson's Disease Patients



Count of UPDR 4 Scores of Parkinson's Disease Patients



Count of Visit Month

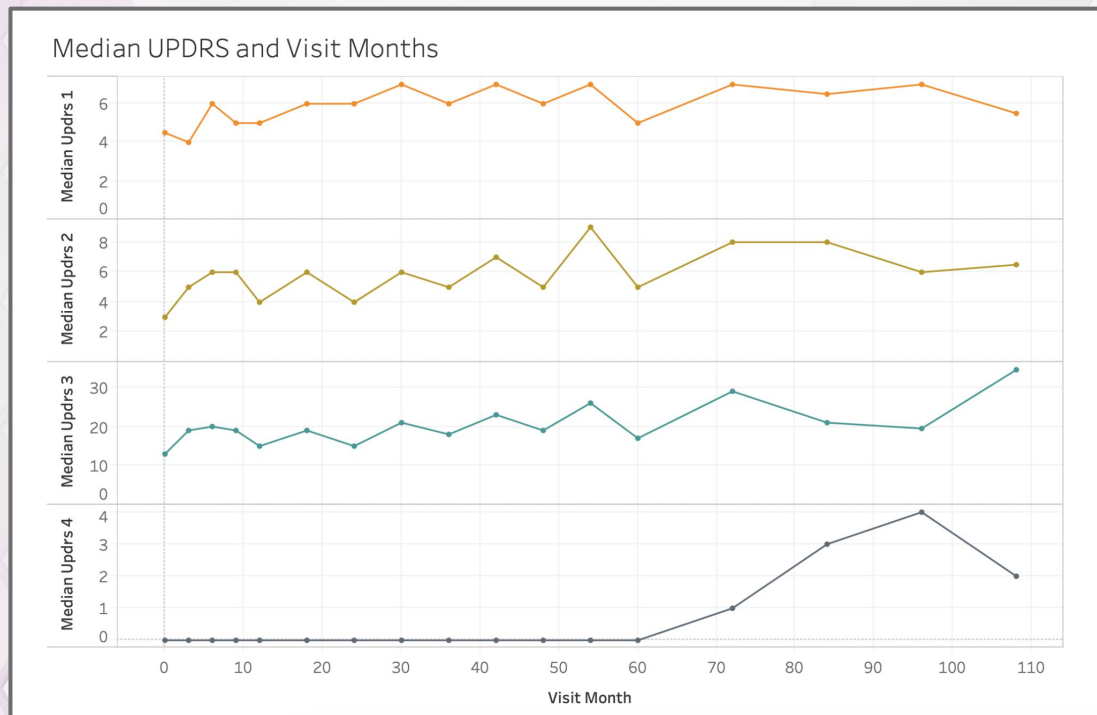


Patients of Parkinson's Disease that are not on medication are visiting more than those who are on medication.

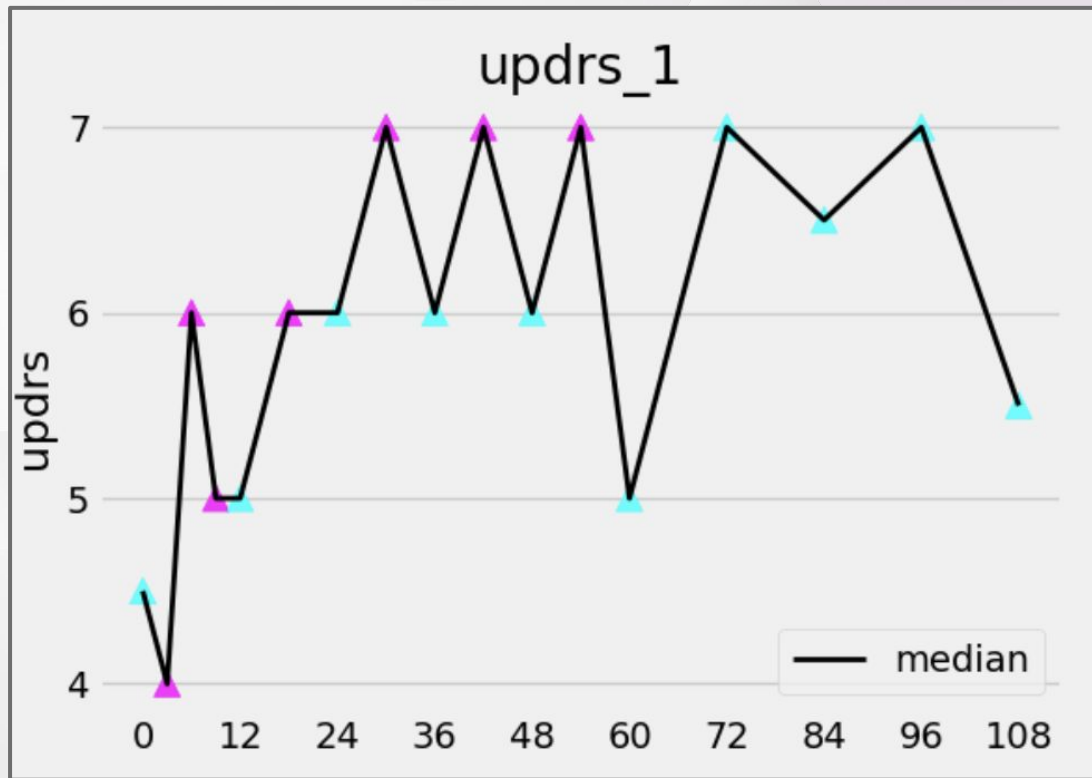
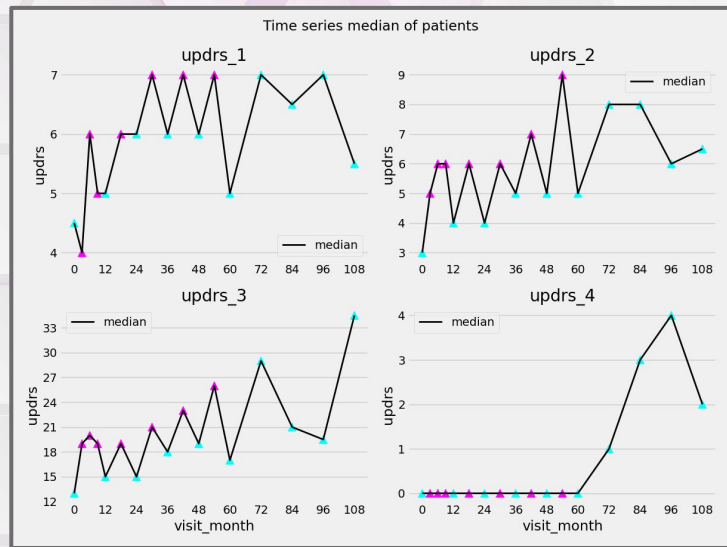


Analysis using months and
updrs results.

Using only the Month data

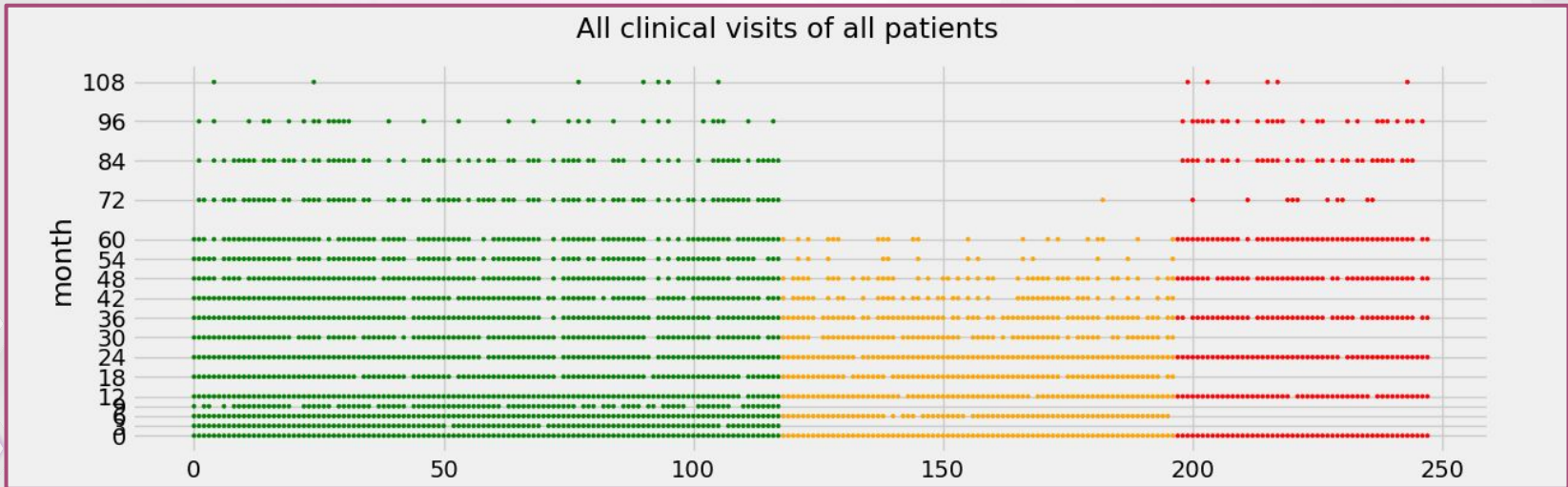


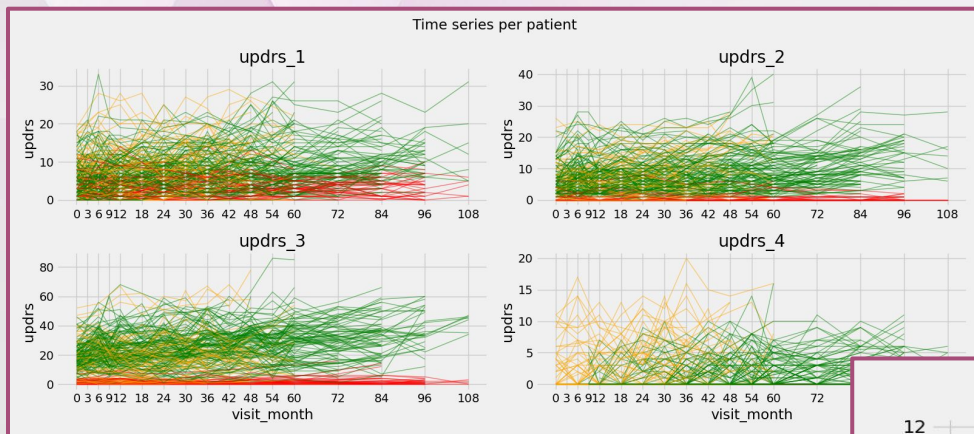
median updrs scores for every month



updrs scores over time of every patient

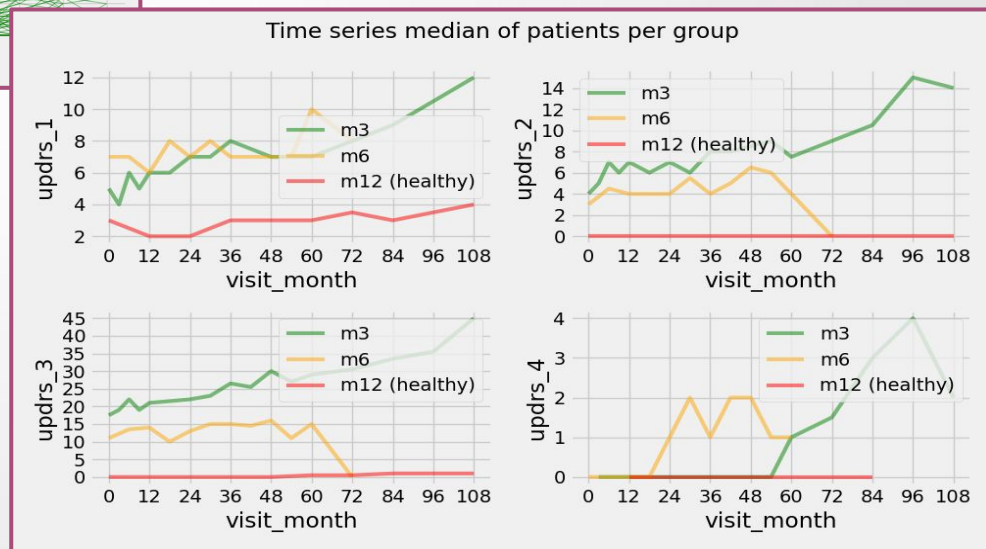
- The patients of the **green** group had their every 3 months
- The patients of the **orange** group had their every 6 months
- The patients of the **red** group had their every year.

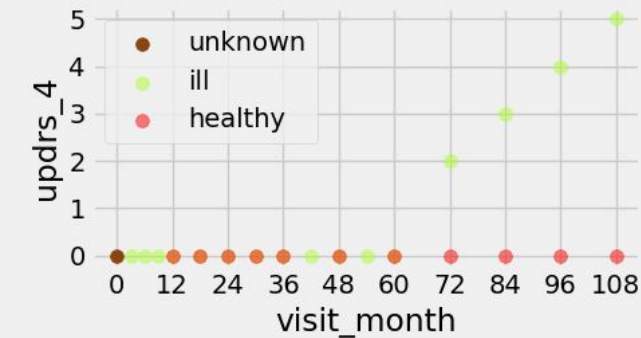
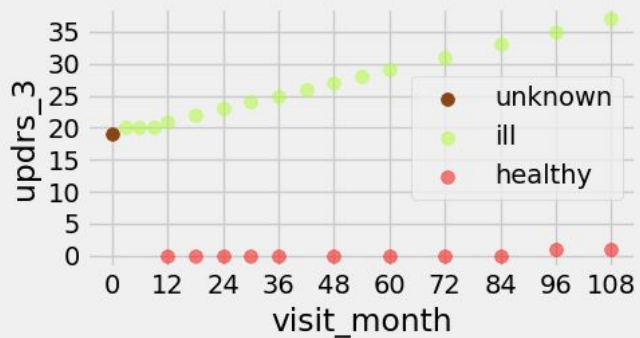
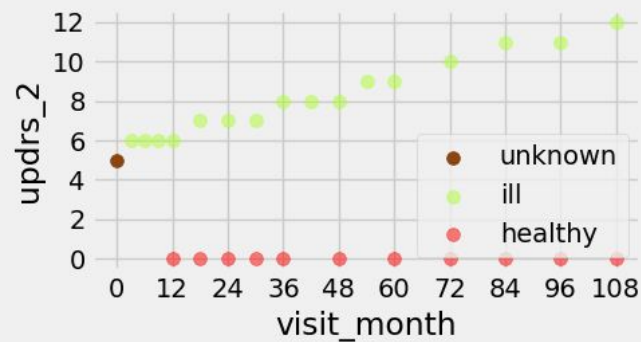
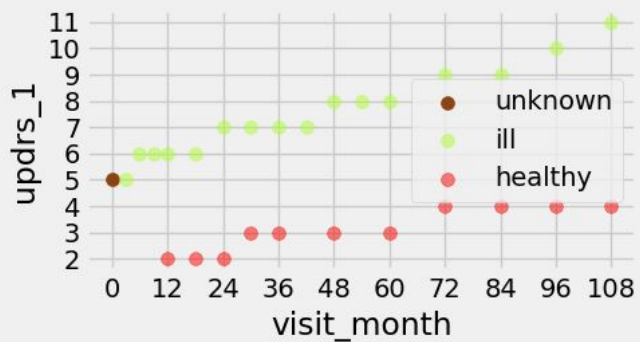




- every 3 months
- every 6 months
- every 1 year

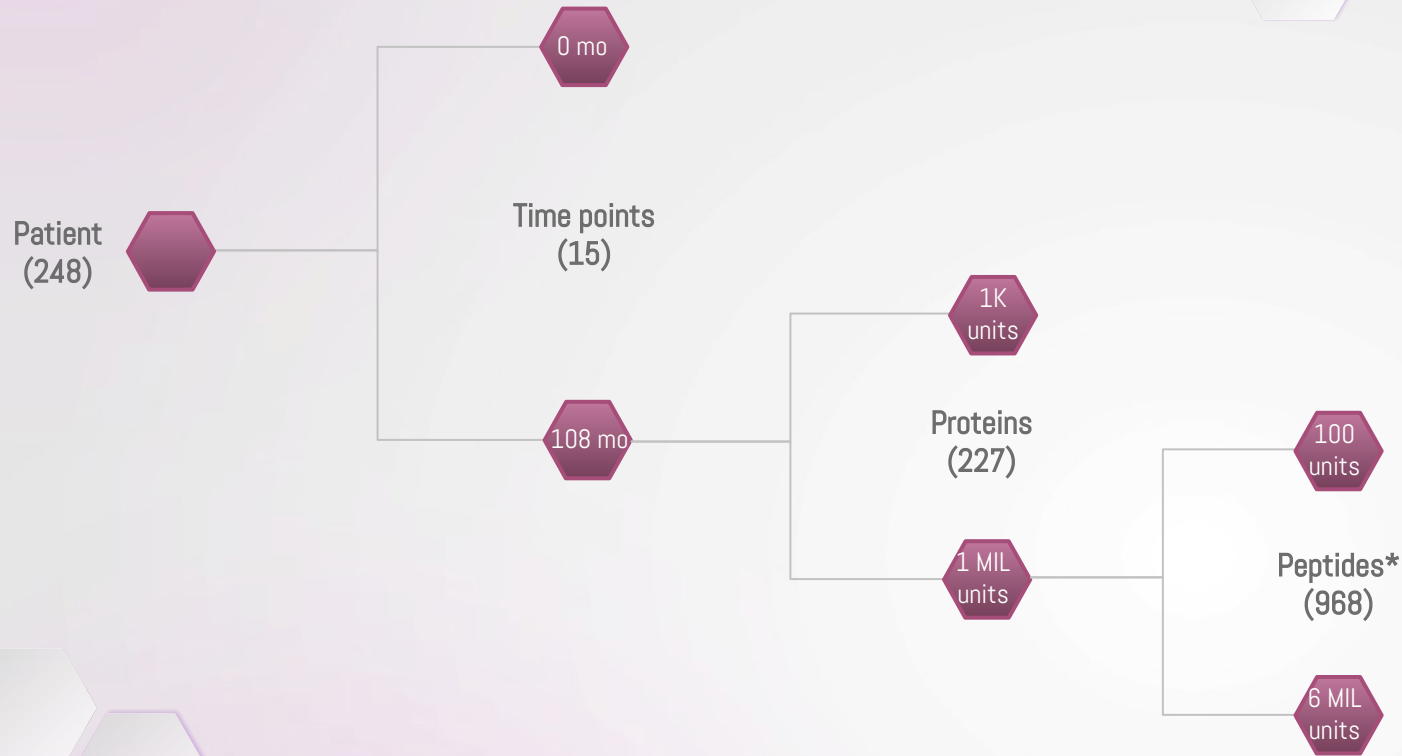
The red group in particular has the lowest updrs scores.





Analysis using Peptides and Proteins.

Data Overview



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

Peptides levels

Protein levels
(227)

1K
units

Peptide levels
(968)

100
units

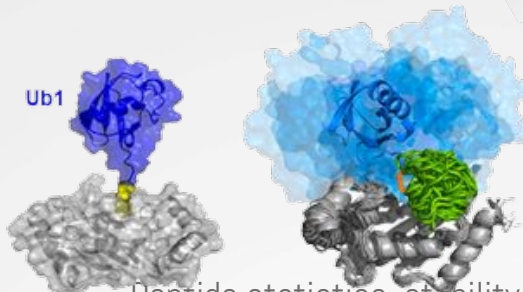
1 MIL
units

6 MIL
units

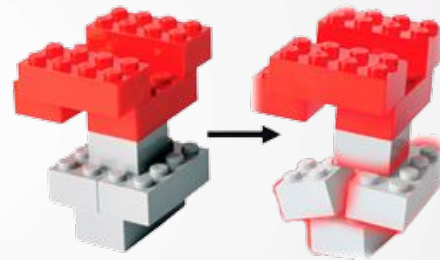
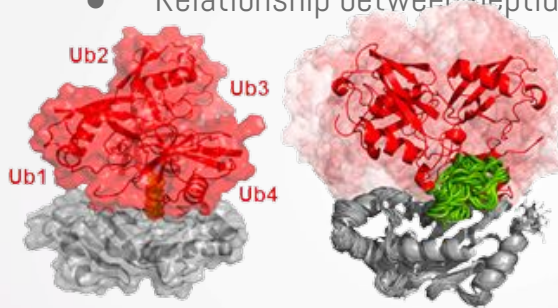
peptides 0.3.2

`pip install peptides`

Ub1



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



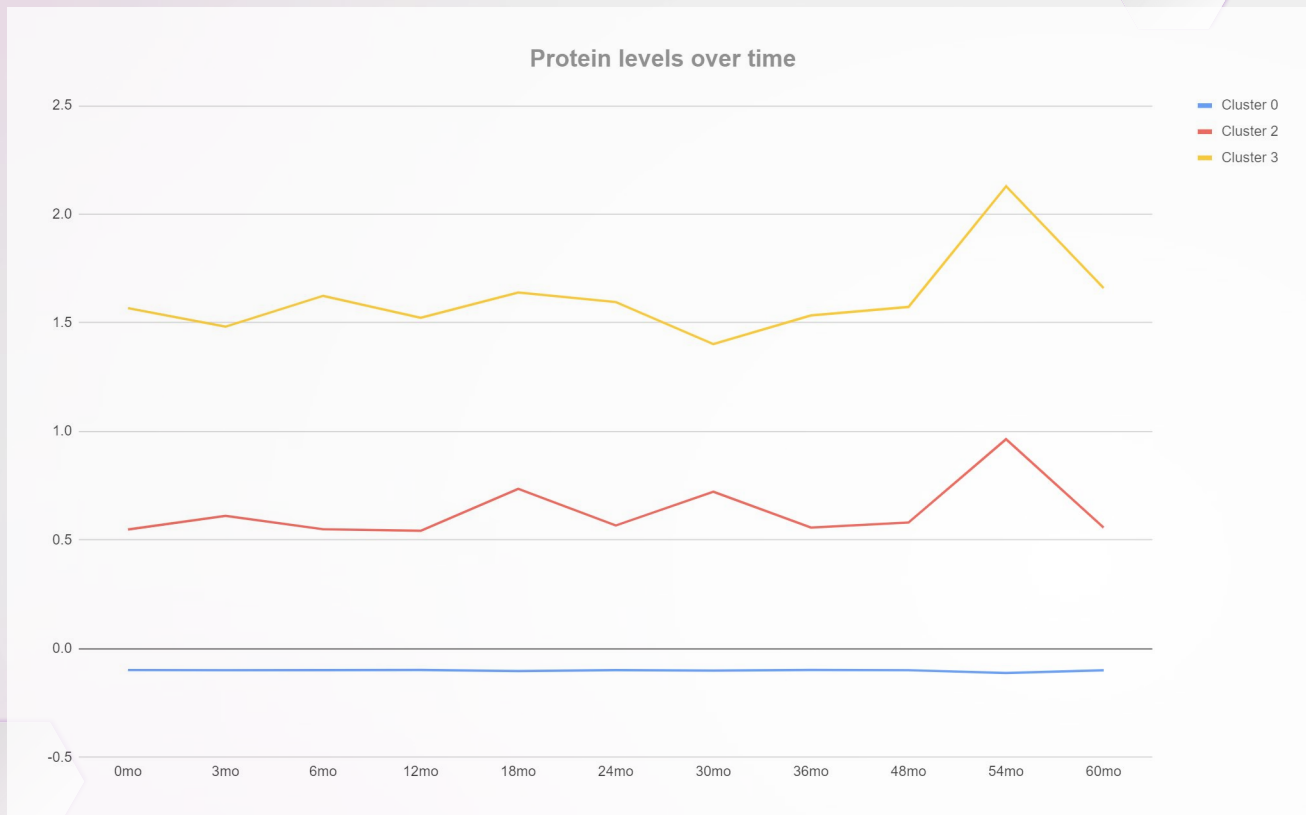
Protein clustering



Protein concentration over time



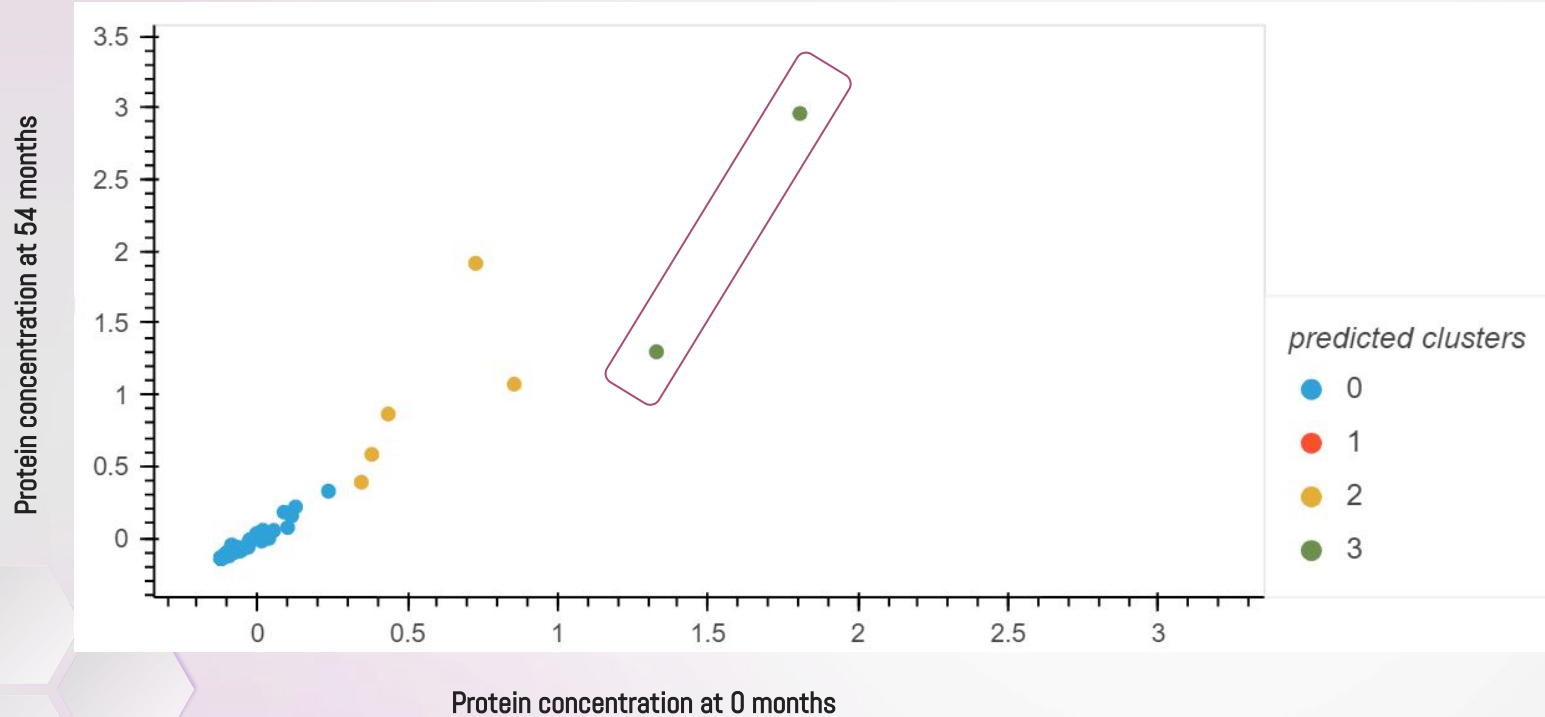
Protein concentration over time



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

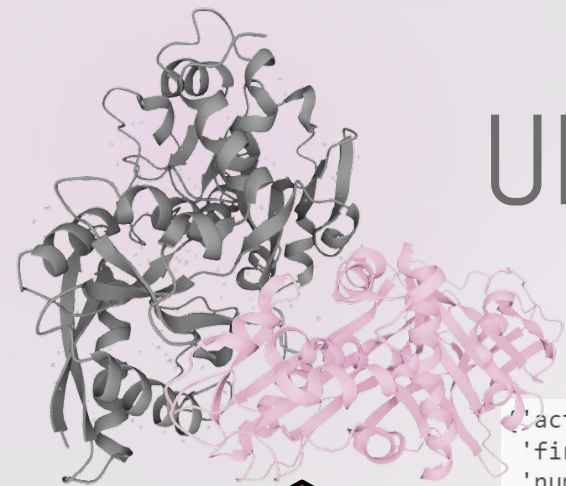
Protein clustering



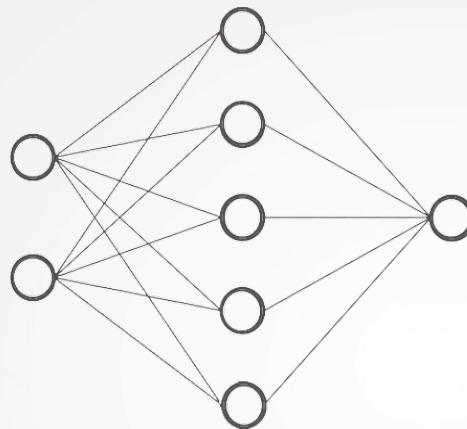
Fluctuating Proteins

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



```
{'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,  
'tuner/epochs': 7,  
'tuner/initial_epoch': 0,  
'tuner/bracket': 1,  
'tuner/round': 0}
```



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?