Centrality in Protein Networks from Neurodegenerative Diseases

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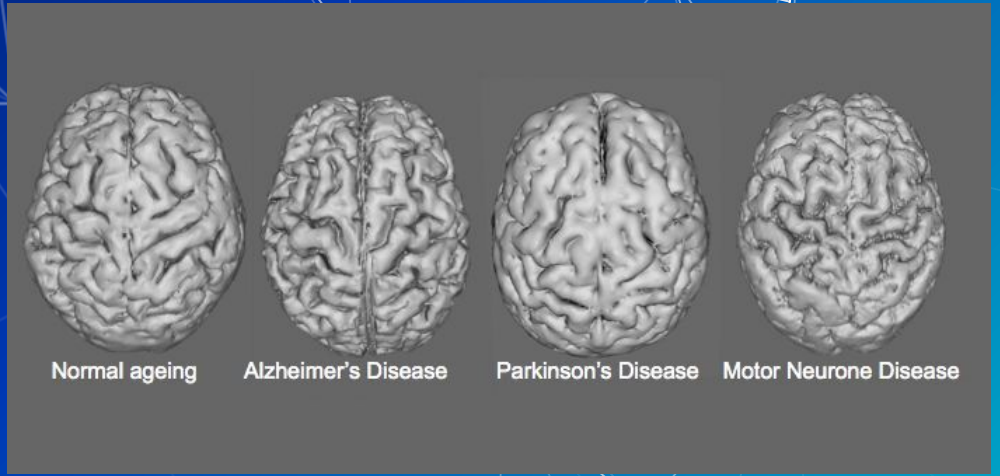
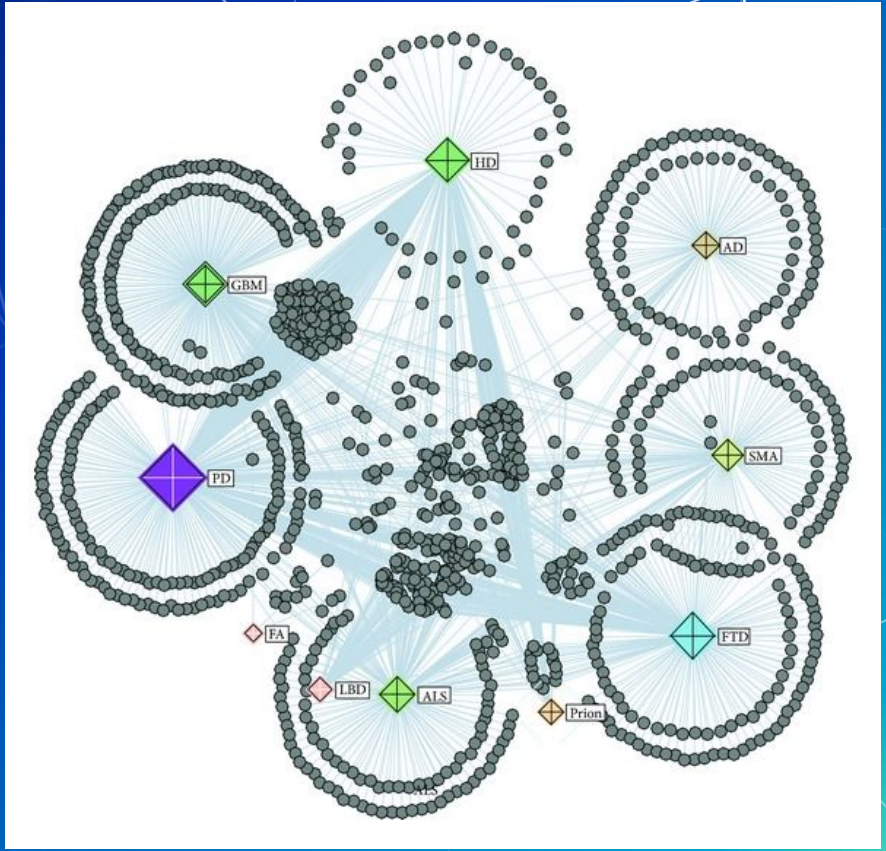
Background

- Protein-Protein Interaction Networks (**PPI**)
- Neurodegenerative diseases (**ND**)
- **Goal:** Find relatedness of NDs
- **Centrality** → Protein importance, generalizable system



Steps

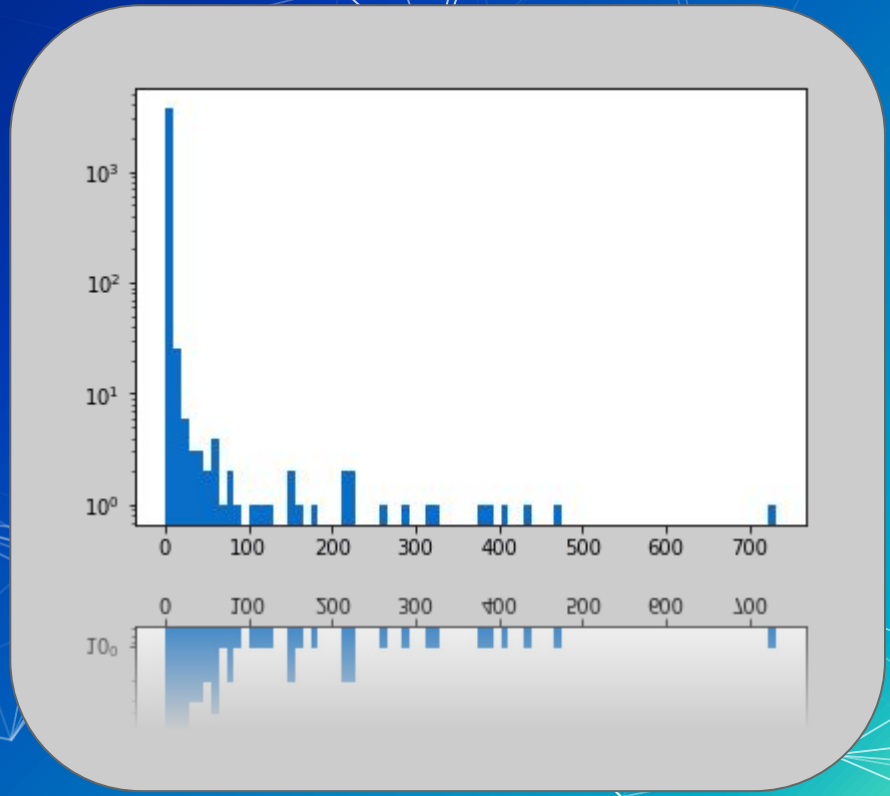
1. Build network from the list of disease proteins
2. Calculate centrality measures for every node
3. Analyze results



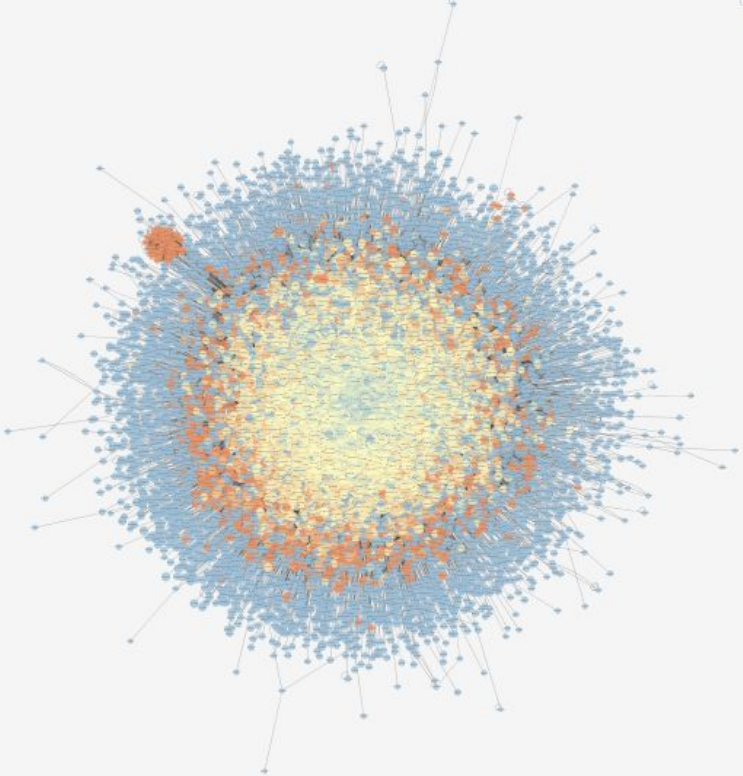
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3914352/

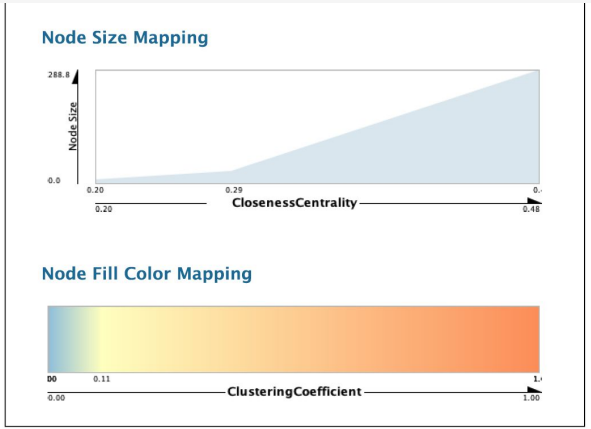
Network Properties

- Undirected
- First degree neighbors only
- Nodes, Edges = 3758, 6957
- Min degree: 1
- Max degree: 731
- Density: 0.0009854
- Avg. degree = 3-4

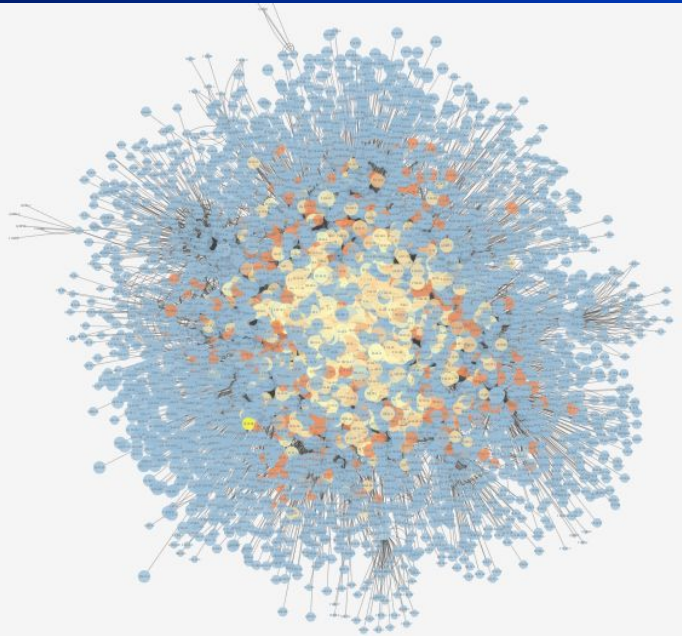


PPI Network




Node Size Mapping
288.8
Node Size
0.0
0.20
0.29
0.20
ClosenessCentrality
0.48
Node Fill Color Mapping
0.11
0.00
ClusteringCoefficient
1.00

Reduced network



Centrality results

Closeness

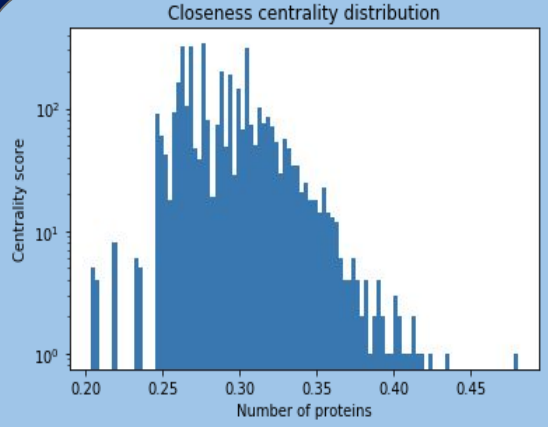
1. 'P0CG48': 0.480 | (None)
2. 'P55072': 0.435 | (FTD)
3. 'O60260': 0.423 | (PD)

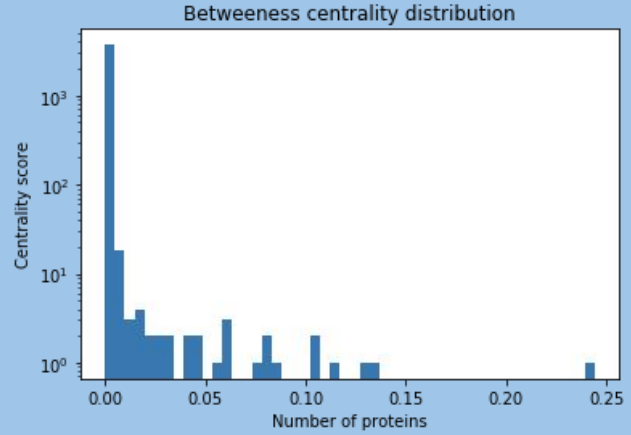
Betweeness

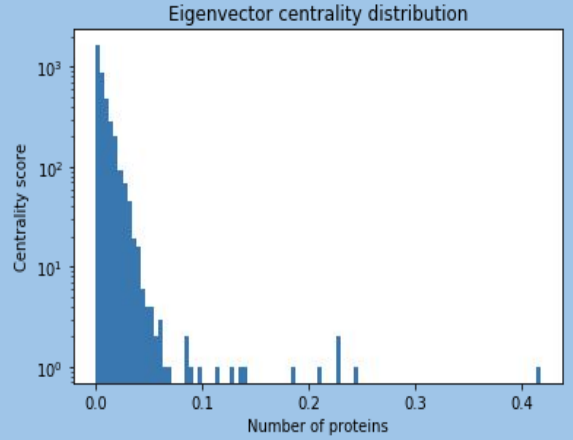
1. 'P55072': 0.243
2. 'Q5S007': 0.133 | (PD)
3. 'P42858': 0.130 | (HD)

Eigenvector

1. 'P55072': 0.417
2. 'O60260': 0.244
3. 'P35637': 0.227 | (ALS)

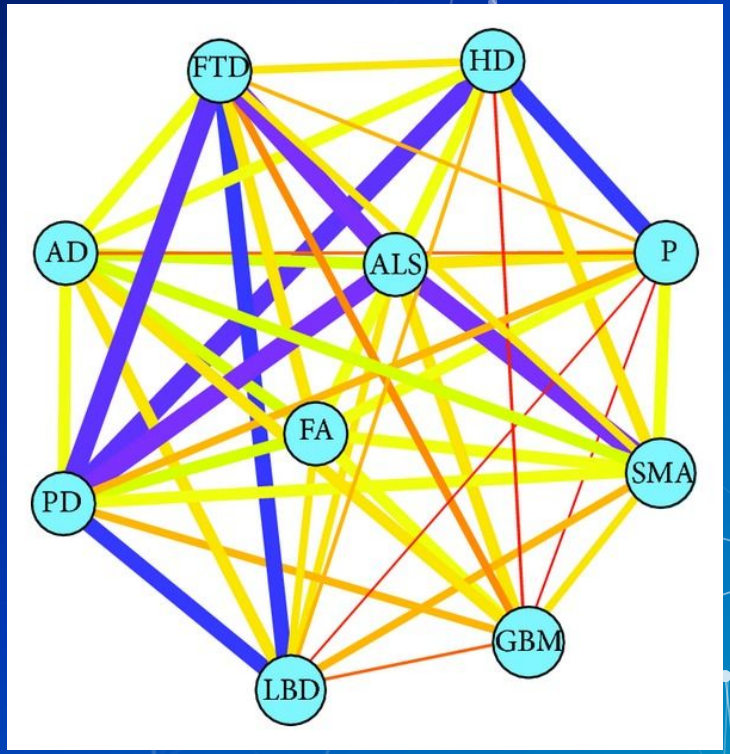






Disease relations

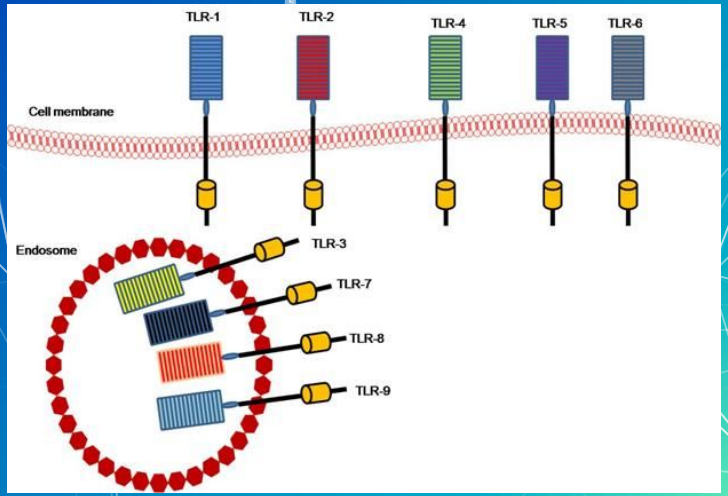
- PD → HD
- HD → P
- FTD → PD
- FTD → ALS
- PD → LBD
- FTD → LBD
- ALS → PD
- ALS → SMA



- ***Parkinson's disease (PD): 4***
- ***Frontotemporal dementia (FTD): 3***
- ***Amyotrophic lateral sclerosis (ALS): 3***
- ***Lewy body disease (LBD): 2***
- ***Huntington's disease (HD): 2***

Key point

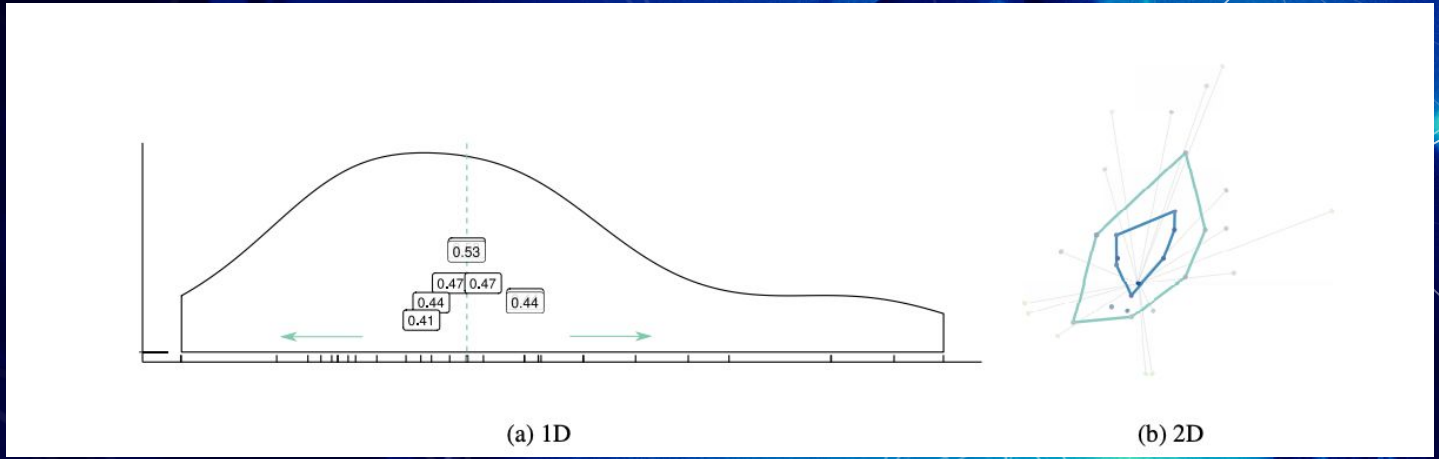
- What do all these proteins have in common?
  - ***Part of the toll-like receptor path***
- **...Toll-like receptor path?**
  - **CRITICAL in "pathogen-associated molecular patterns and play a critical role in innate immune responses"**
- Hyperactive immune system → NDs



New centrality: Network Depth

- *Network embedding using Multidimensional Scaling*
- *Median of the graph*

BERTAGNOLLI et al, 2019. arXiv:1904.05060v1



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