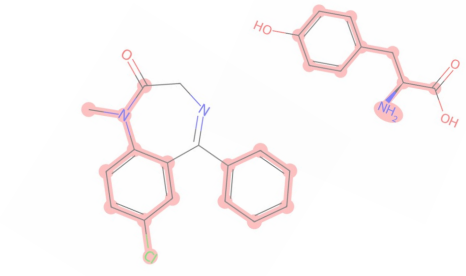
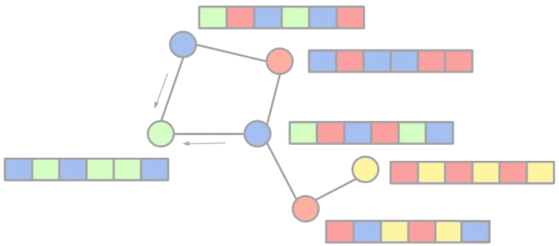
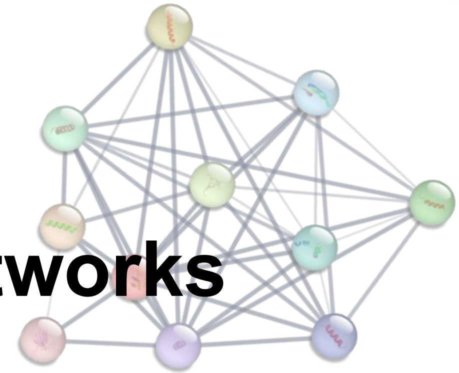
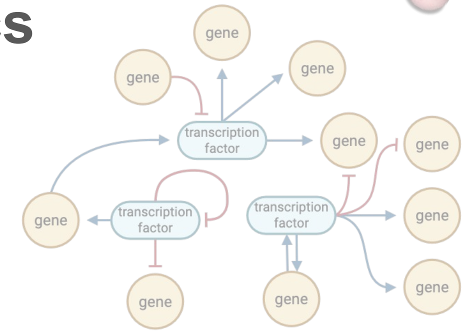






Introduction to Graph Neural Networks

Applications in Bioinformatics

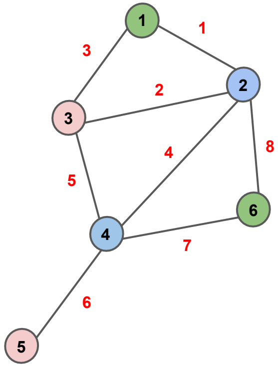


Sumit Kumar
Senior Research Fellow
Translational Bioinformatics Group
ICGEB, New Delhi

Supervisor: Dr. Dinesh Gupta

What are Graphs?

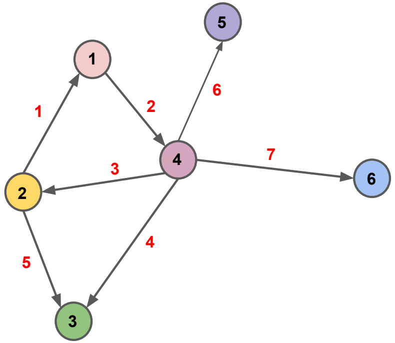
Undirected Graph



Vertices (Nodes): 6
Edges: 8

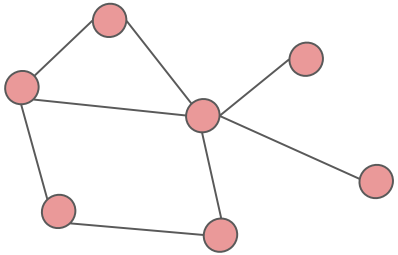
$G = (V, E)$

Directed Graph

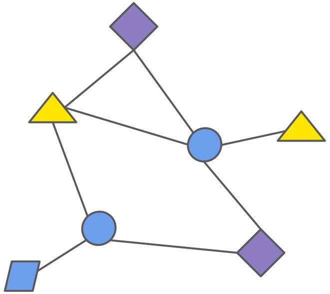


Vertices (Nodes): 6
Edges: 7

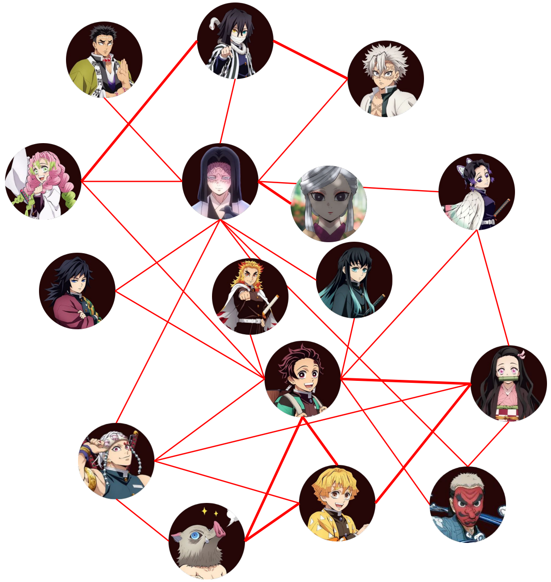
Homogenous Graph

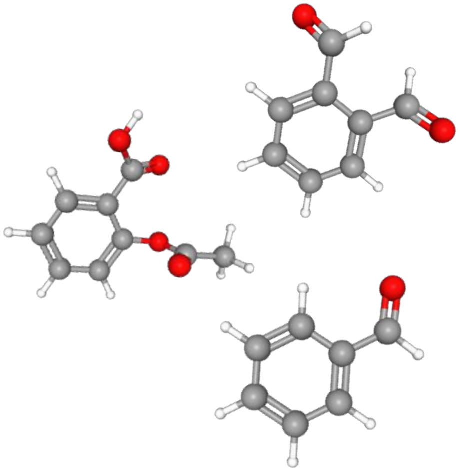


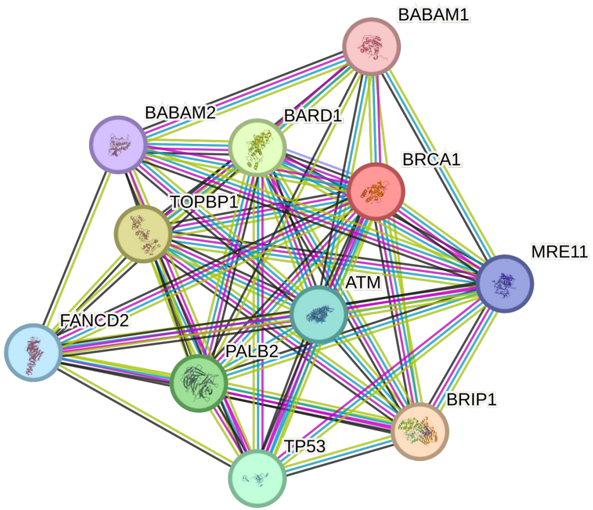
Heterogenous Graph



Graphs are all around us 🌍





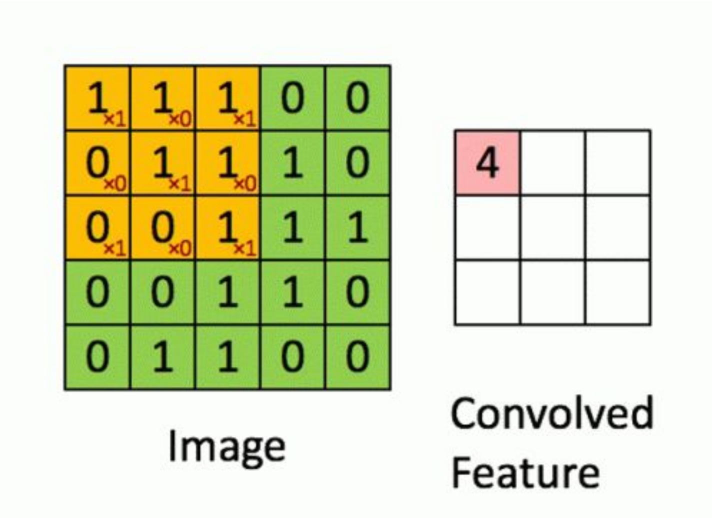


SOCIAL NETWORKS

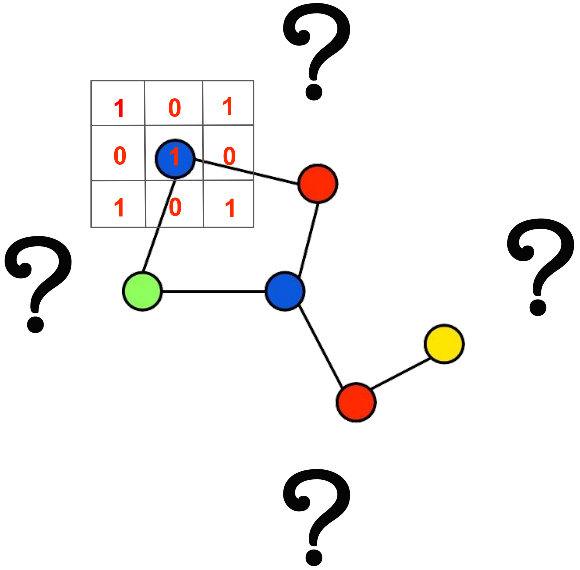
MOLECULES

PROTEIN-PROTEIN INTERACTION

Motivation behind Graph Neural Networks



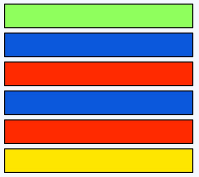
Images are euclidean as 2D/3D pixel grid



Graphs are non-euclidean (now how to operate convolutions?)

Message Passing (The Core Concept) 📩

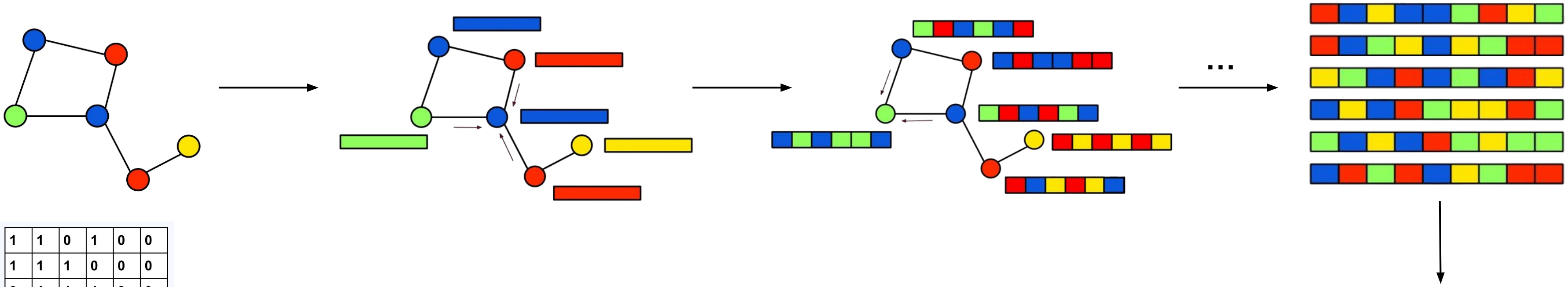
Updated Node A = **Update**(Node A, **Aggregate**(Neighbors of Node A))



Node Feature Matrix

$$\mathbf{x}'_i = \mathbf{\Theta}^\top \sum_{j \in \mathcal{N}(i) \cup \{i\}} \frac{e_{j,i}}{\sqrt{\hat{d}_j \hat{d}_i}} \mathbf{x}_j$$

Kipf, T. N., & Welling, M. (2016)



1	1	0	1	0	0
1	1	1	0	0	0
0	1	1	1	0	0
1	0	1	1	1	0
0	0	0	1	1	1
0	0	0	0	1	1

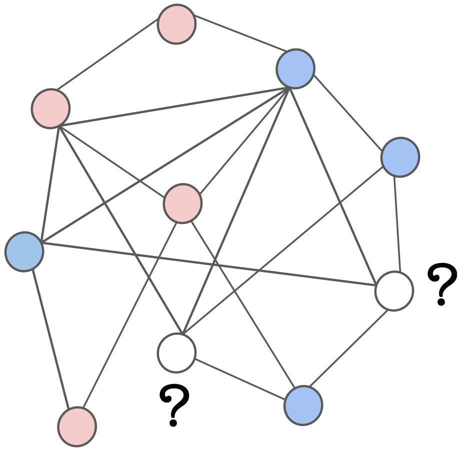
Adjacency Matrix

Feed-Forward MLP Layer

Source: *Kumar et al.* graphB3 - An Interpretable Graph Learning Approach for Predicting Blood-Brain Barrier Permeability (Under Revision in BIB)

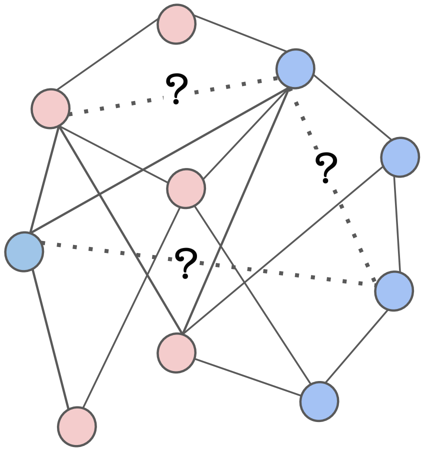
Types of prediction tasks with GNNs

Node-Level



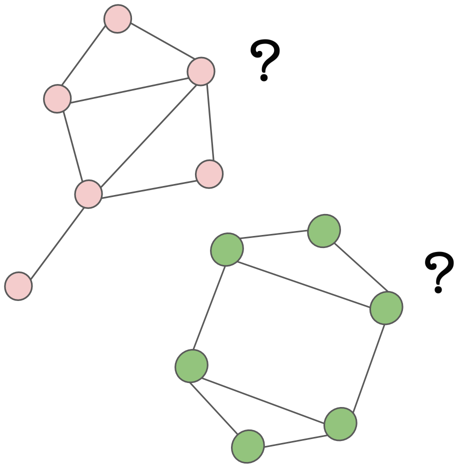
- Protein function in a PPI Network
- Gene expression state in a GRN
- Cell-cell interaction in multi omics data

Edge-Level



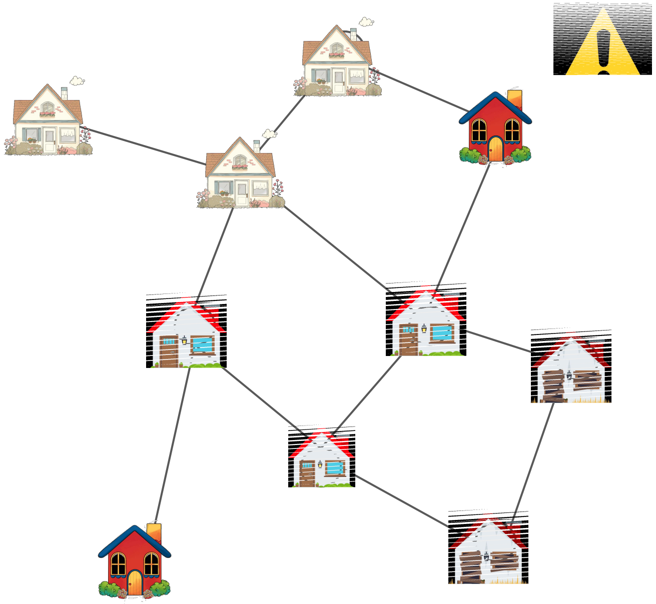
- Relation between a gene and a disease in a gene-disease network
- Whether two proteins are interacting in a PPI network
- Predict if two drugs work synergistically

Graph-Level

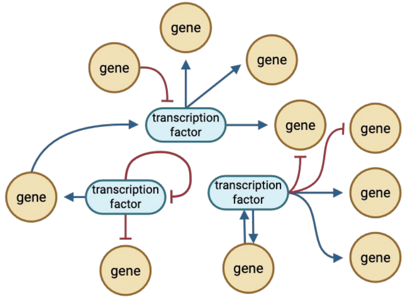


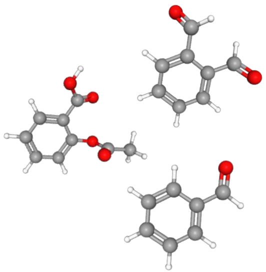
- Drug Discovery
- Protein function prediction

When to use Graph Neural Networks?



Predicting housing prices using GNNs?

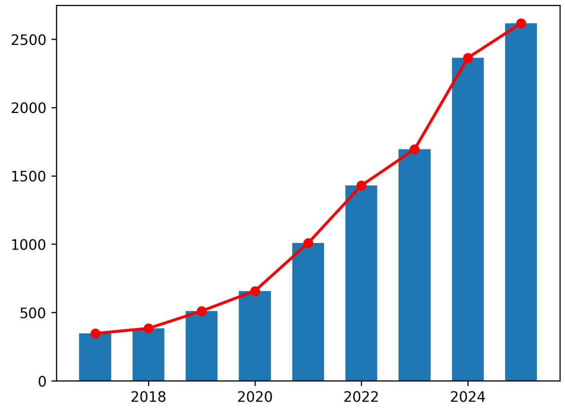




Predicting a gene activity in a Gene Regulatory Network or Predicting a molecules activity?

KEYWORDS: Dependency, diversity, size, etc.

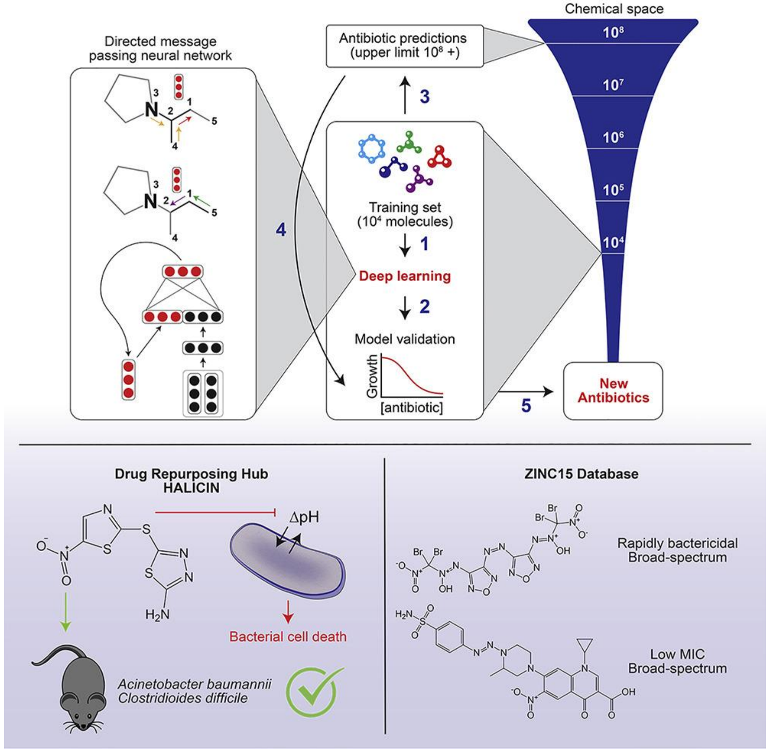
Why Graph Neural Networks?



Number of publications in PubMed mentioning Graph Neural Networks/GNN

Examples

Stokes et al.



Cell

CellPress

Volume 180, Issue 4, 20 February 2020, Pages 688-702.e13

Article

A Deep Learning Approach to Antibiotic Discovery

Jonathan M. Stokes [1 2 3], Kevin Yang [3 4 10], Kyle Swanson [3 4 10], Wengong Jin [3 4], Andres Cubillos-Ruiz [1 2 5], Nina M. Donghia [1 5], Craig R. MacNair [6], Shawn French [6], Lindsey A. Carfrae [6], Zohar Bloom-Ackermann [2 7], Victoria M. Tran [2], Anush Chiappino-Pepe [5 7], Ahmed H. Badran [2], Ian W. Andrews [1 2 5], Emma J. Chory [1 2], George M. Church [5 7 8], Eric D. Brown [6], Tommi S. Jaakkola [3 4], Regina Barzilay [3 4 9], James J. Collins [1 2 5 8 9 11]

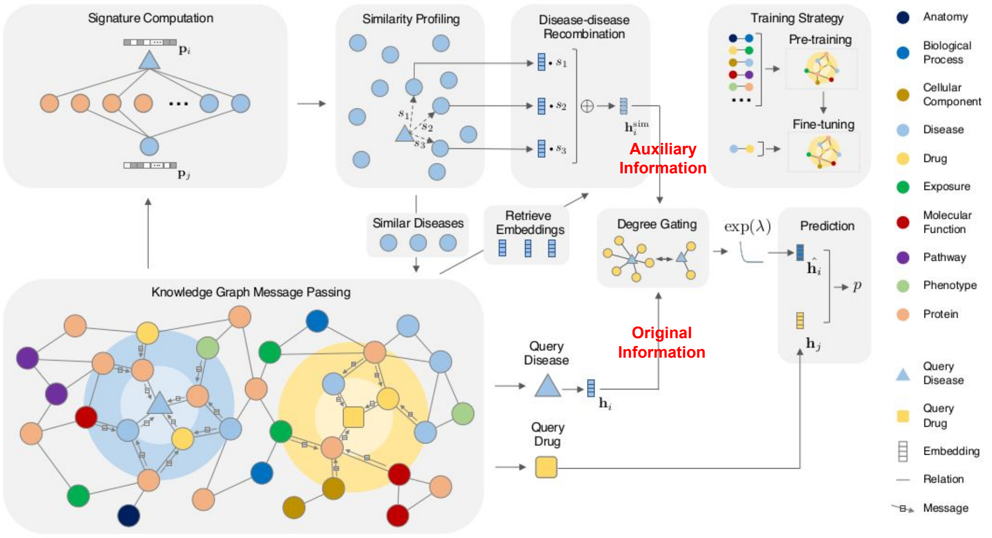
Model	Feature	Rank of Halicin
Graph neural network	**Learned**	**61**
Feed-forward neural network	RDKit features (fixed)	273
Feed-forward neural network	Morgan fingerprint (fixed)	1217
Random forest	Morgan fingerprint (fixed)	2640
Support vector machine	Morgan fingerprint (fixed)	771

Top 99 compounds were experimentally validated out of which 51 were indeed antibiotics

***Source:** Wengong Jin, CSAIL, MIT*

Examples

Huang et al.

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Article | Open access | Published: 25 September 2024

A foundation model for clinician-centered drug repurposing

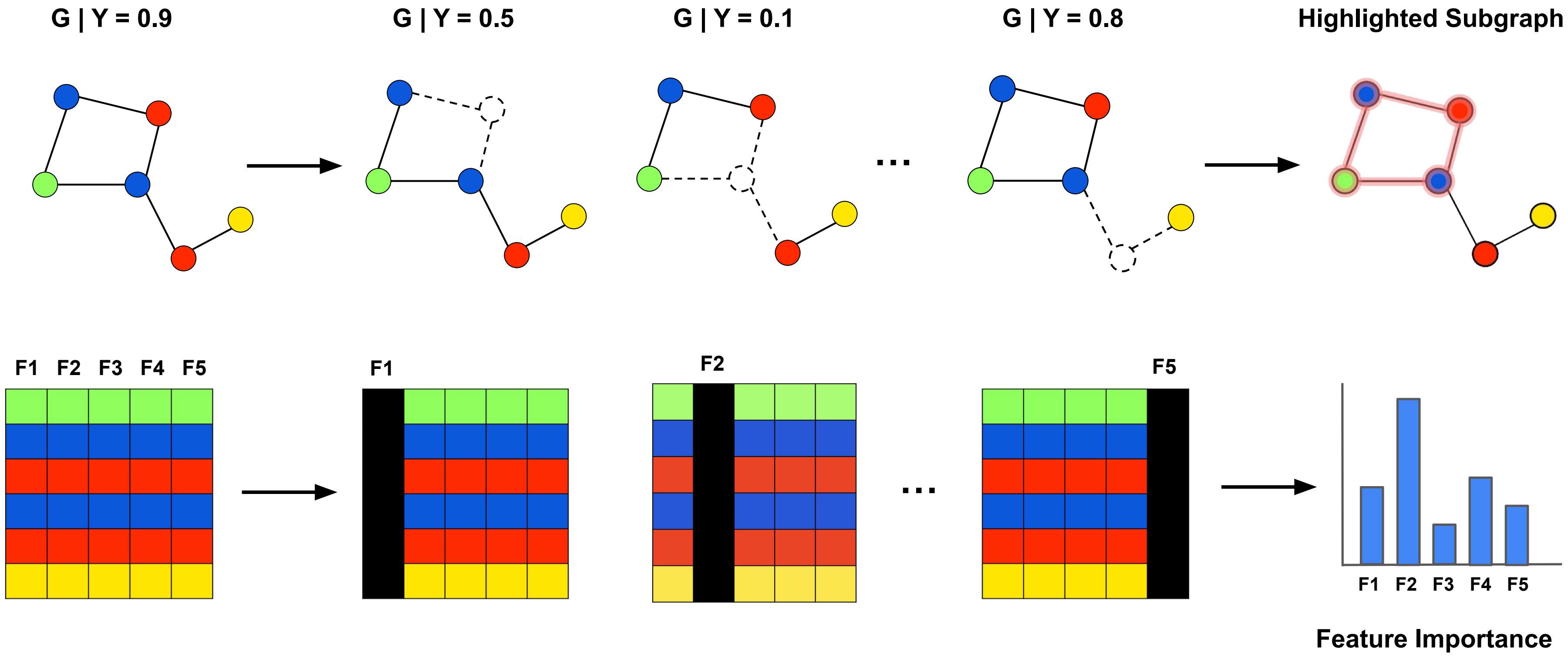
Kexin Huang, Payal Chandak, Qianwen Wang, Shreyas Havaldar, Akhil Vaid, Jure Leskovec, Girish N. Nadkarni, Benjamin S. Glicksberg, Nils Gehlenborg & Marinka Zitnik

Nature Medicine 30, 3601–3613 (2024) | Cite this article

60k Accesses | 16 Citations | 223 Altmetric | Metrics

TxGNN predicted 478 diseases and 1290 drugs found in electronic medical records.

Graph-Based Explainable AI (graphXAI)



Example: Perturbation-Based Method (GNNExplainer, PGExplainer, SubgraphX, etc.)

Source: *Kumar et al.* graphB3

Limitations & Future Directions

- **Over-Smoothing**: Repeated aggregation can make node embeddings too similar.
- **Scalability**: GNNs struggle with large graphs, long-range connections are challenging to handle.
- **Computation-Cost**: Message passing can be memory-intensive and slow for deep architectures.
- Lack of standardized frameworks to build your own graphs.
- **Graph Transformers** is an active area of research that deals with a problem of over-smoothing and scalability; however it increases computational cost further.
- **Graph coarsening** or **hierarchical pooling** can alleviate scalability issues by reducing graph size while preserving key structural information.

Resources

References:

- Kipf, T. N., & Welling, M. (2016). Semi-supervised classification with graph convolutional networks. In arXiv [cs.LG]. http://arxiv.org/abs/1609.02907, ICLR 2017
- Morris, C., Ritzert, M., Fey, M., Hamilton, W. L., Lenssen, J. E., Rattan, G., & Grohe, M. (2019). Weisfeiler and Leman go neural: Higher-order graph neural networks. Proceedings of the ... AAAI Conference on Artificial Intelligence. AAAI Conference on Artificial Intelligence, 33(01), 4602–4609. https://doi.org/10.1609/aaai.v33i01.33014602
- Ying, R., Bourgeois, D., You, J., Zitnik, M., & Leskovec, J. (2019). GNNExplainer: Generating explanations for graph Neural Networks. Neural Information Processing Systems, 32, 9240–9251.

Get started with Pytorch basics: https://docs.pytorch.org/tutorials/index.html

Get started with Pytorch-Geometric: https://pytorch-geometric.readthedocs.io/en/2.6.1/get_started/colabs.html

Helpful video-series:

- https://youtube.com/playlist?list=PLV8yxwGOxvvoNkzPfCx2i8an--Tkt7O8Z&si=VTnpJtlq_r4B3Gkj
- https://youtube.com/playlist?list=PLoROMvodv4rPLKxIpqhjhPgdQy7imNkDn&si=NYW9fLugoMyndkm1

GNN for Drug Discovery:

- https://deepchem.readthedocs.io/en/latest/api_reference/featurizers.html#graph-convolution-featurizers
- https://deepchem.io/tutorials/introduction-to-graph-convolutions/


Thank You


Thank you!