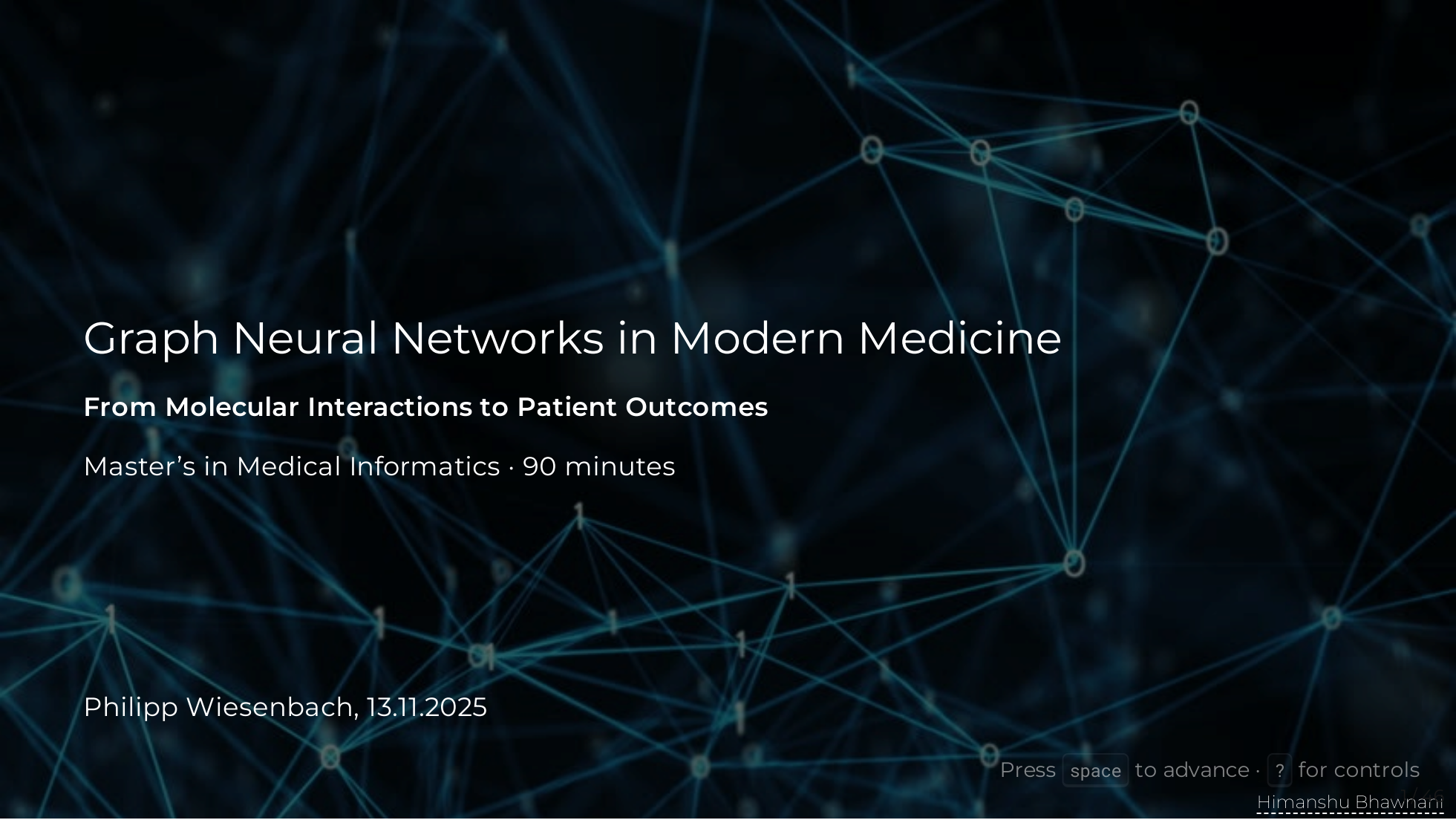


Graph Neural Networks in Modern Medicine

From Molecular Interactions to Patient Outcomes

Master’s in Medical Informatics · 90 minutes

Philipp Wiesenbach, 13.11.2025

Before We Begin

You know

- Neural networks
- Backpropagation
- Loss functions

Today you'll learn

- **Why** graphs matter
- **How** GNNs work
- **Where** they're deployed

Approach

- Light math
- Heavy intuition
- Clinical relevance

Learning Objectives

Agenda & Timing

Part 1 (10 min)

Why graphs in medicine?

Part 2 (30 min)

Core GNN mechanics

Part 3 (15 min)

Interactive calculation

Part 4 (10 min)

Building graphs from text

Part 5 (15 min)

Medical use cases

Part 6 (10 min)

Wrap-up and Q&A

Part 1

Why Graphs in Medicine?

Connect familiar neural network ideas to relational inductive bias
Ground the motivation in concrete biomedical structure before the math

The Central Question

Why can't we just use tables and CNNs?

From Tables to Relationships

Tabular Assumption

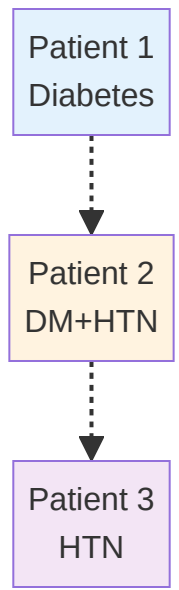
Each patient independent, features isolated, no shared context

Patient 1	Patient 2	Patient 3
Diabetes	DM + HTN	HTN
Age: 45	Age: 52	Age: 48
BMI: 28	BMI: 31	BMI: 26

Rows treated as isolated data points

Reality

Patients interact in cohorts, diseases co-occur, treatments cascade



Graphs encode structure that tabular models discard

Biomedical Graph Examples

Biology & Chemistry

- **Protein-protein** interaction networks
- **Gene regulatory** networks
- **Molecular graphs**: atoms = nodes, bonds = edges

Sources: STRING, ChEMBL, PubChem

Clinical Cohorts

- **Patient similarity** graphs from diagnoses
- **Care pathways** capturing temporal encounters
- **Treatment cascades** and drug combinations

Sources: MIMIC-III, UK Biobank, EHR systems

Knowledge Synthesis

- **Literature-derived** knowledge graphs
- **Disease-symptom-drug** relationships
- **Multi-modal fusion**: structured + NLP-extracted relations

Sources: PubMed, UMLS, DrugBank

Spatial Biology

- **Tissue microenvironment** graphs
- **Cell-cell interaction** networks
- **Histopathology scene** graphs

Sources: Spatial transcriptomics, multiplex imaging

What Do GNNs Predict?

Node Classification

Question: Is this entity associated with an outcome?

Example: "Is this protein linked to Alzheimer's?"

Metrics: AUROC, Average Precision

Link Prediction

Question: Will these entities interact?

Example: "Will this drug bind to this protein?"

Metrics: AUROC, Hits@K, MRR

Graph Classification

Question: What class is this entire structure?

Example: "Is this molecule toxic?"

Metrics: Accuracy, F1, AUC

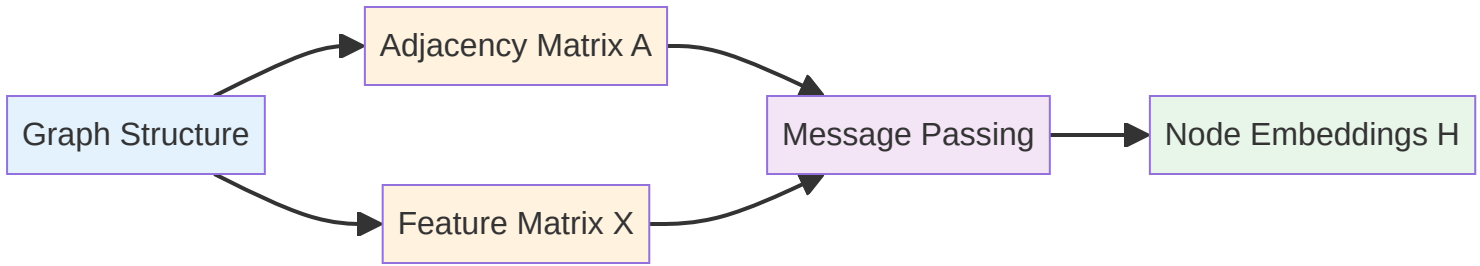
Real Examples

Part 2

Core GNN Mechanics

Translate graphs into matrices ready for deep learning
Build intuition for message passing before diving into equations

Core GNN Concepts



Representing a Graph

The Adjacency Matrix `A`

`A[i, j] = 1` if nodes `i` and `j` connect

- **Square** matrix: `N × N`
- **Symmetric** for undirected graphs
- **Diagonal** = self-loops

The Feature Matrix `X`

Each row = one node's attributes

- **Shape:** `N × F`
- **F** = feature dimension
- Examples: gene expression, lab values

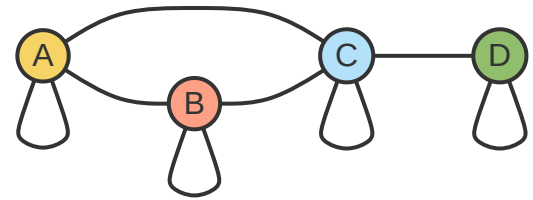
Example Adjacency Matrix

Matrix Structure

	A	B	C	D
A	1	1	1	0
B	1	1	1	0
C	1	1	1	1
D	0	0	1	1

Diagonal = self-loops
Symmetric (undirected)

Visual Representation

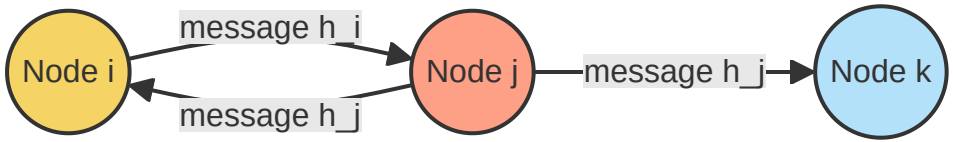


The Core Idea

"You are the average of your five closest colleagues"

Message Passing: Step by Step

Visual: Message Passing



Message passing injects **relational inductive bias**: nodes continually refine themselves using neighborhood evidence instead of treating samples as independent.

The Math: GNN Layer Update

The Formula

$$H^{(l+1)} = \sigma(\tilde{A}H^{(l)}W^{(l)})$$

Breaking it down

Normalization in Action

Degree Normalization: $D^{-1/2}$

Node	Degree	$D^{-1/2}$

$$\tilde{A} = D^{-1/2}(A + I)D^{-1/2}$$

	A	B	C	D

How Deep Should You Go?

1 Layer

Neighborhood: Direct neighbors only

Risk: Too local

Use when: Dense graphs, simple patterns

2-3 Layers

Neighborhood: 2-3 hops

Risk: Moderate smoothing

Sweet spot: Most applications

Mitigation: Residual connections, layer norm

4+ Layers

Neighborhood: Many hops

Risk: Over-smoothing / **Over-squashing**

Solutions: Jump knowledge, attention, adaptive depth

Narrow bottlenecks force many paths through single nodes. Consider **adaptive sampling** (GraphSAGE) or **edge rewiring** to relieve pressure.

Beyond Averaging: Attention

The Problem

Not all neighbors equally informative: some edges carry stronger signals, dense graphs have noise

Solution: GAT

1. Learn **edge weights**
2. **Attention** scores importance
3. **Explainable** weights

Example: Attention upweights matching comorbidities vs weak demographics

Attention: Not all neighbors are created equal

Part 3

Interactive Practice

Slow down for a pencil-and-paper message passing walkthrough
Surface common implementation gotchas before touching code

Let’s Calculate Together

Manual message passing on a 4-node graph

The Setup
Our Graph

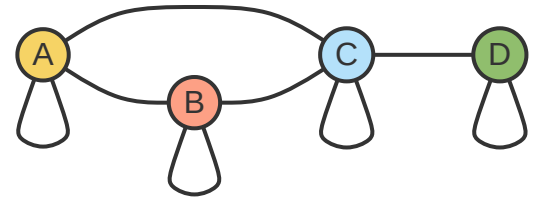
Node Features (2D vectors)

Step 1: Build the Adjacency Matrix

The Matrix A

	A	B	C	D
A	1	1	1	0
B	1	1	1	0
C	1	1	1	1
D	0	0	1	1

The Topology



Step 2: Aggregate Node A

Debrief: What Did We Learn?

GraphSAGE: Scalable Learning

The Problem

Standard GNN aggregates **ALL** neighbors → memory explosion

The Solution

Sample **fixed k** neighbors → constant memory usage

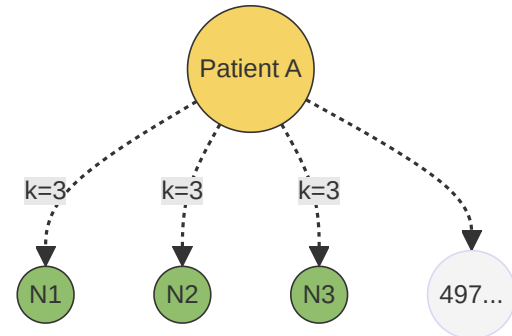
Key Innovation: Inductive Learning

Transductive (Traditional):

- Learns specific node embeddings
- New nodes require full retraining □

Inductive (GraphSAGE):

- Learns the aggregation function
- New nodes use existing function □



Sample 3 of 500 neighbors
Fixed k=25 in practice

Part 4

Building Graphs from Text

Extract structure from unstructured clinical narratives and literature

Surface the NLP tooling needed before a GNN ever trains

The Challenge

Most biomedical knowledge is trapped in unstructured text

Graph Construction Pipeline

Method 1: Co-occurrence & PMI

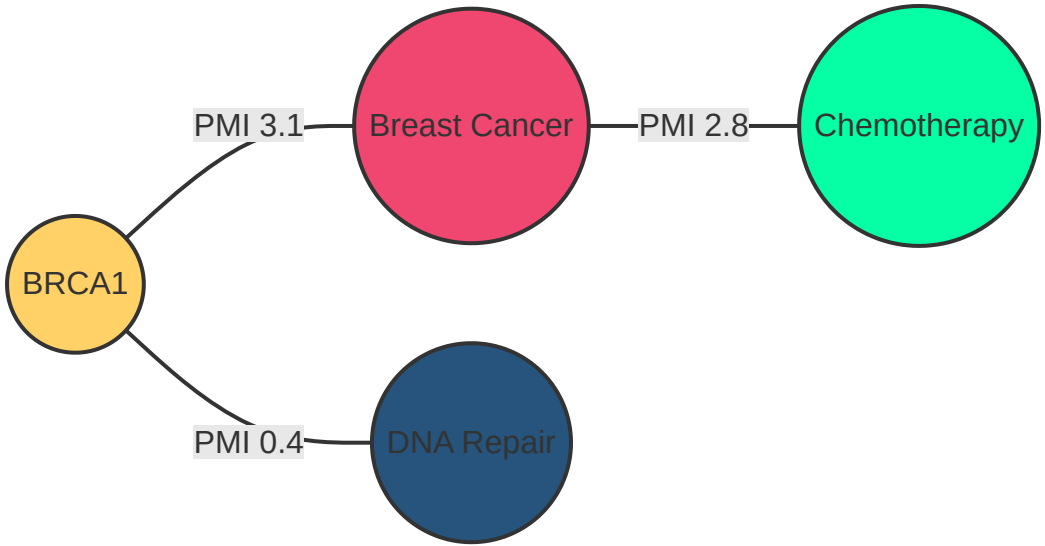
The Idea

- **Nodes:** Diseases, genes, drugs, symptoms
- **Edges:** Created when entities co-occur in text
- **Weight:** Pointwise Mutual Information (PMI)

PMI Formula

$$\text{PMI}(i, j) = \log \frac{p(i, j)}{p(i) \cdot p(j)}$$

PMI Visualization



Method 2: TF-IDF for Node Features

The Formulas

Term Frequency:

$$tf_{term,doc} = \frac{\text{count in doc}}{\text{total terms in doc}}$$

Inverse Document Frequency:

$$idf_{term} = \log \frac{N_{docs}}{1 + \text{docs containing term}}$$

Final Score:

$$\text{TF-IDF} = tf \times idf$$

What It Does

TF-IDF Example

Scenario: 3 medical abstracts

Term	Doc A (oncology)	Doc B (cardiology)	Doc C (oncology)	IDF
chemotherapy	$2/120$	$0/110$	$1/95$	$\log \frac{3}{1+2} = 0.00$
arrhythmia	$0/120$	$3/110$	$0/95$	$\log \frac{3}{1+1} = 0.41$
biomarkers	$1/120$	$1/110$	$2/95$	$\log \frac{3}{1+3} = -0.29$

Part 5

Medical Use Cases

Connect abstract mechanics to translational wins clinicians care about
Highlight evaluation patterns students can investigate post-lecture

Real-World Impact

Drug Discovery

Link prediction for repurposing

Patient Risk

Node classification for outcomes

Pathology

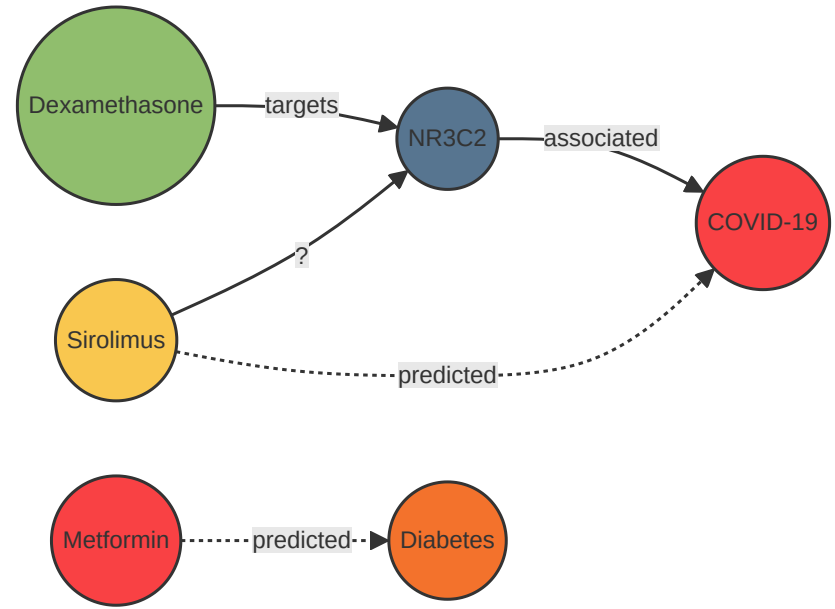
Graph classification for tissue

Use Case 1: Drug Repurposing

The Problem

- Drug discovery is **slow** and **expensive**
- Existing drugs may have **hidden uses**
- Need: prioritize hypotheses for validation

The GNN Solution



Use Case 2: Clinical Risk Prediction from EHRs

The Challenge

How to leverage **complex, heterogeneous**
EHR data for clinical predictions?

GNN Approaches

Use Case 3: Histopathology Scene Graphs

Beyond CNNs

Standard CNNs see **pixels**, not **spatial structure**

The GNN Approach

Part 6

Future Directions

Step back from case studies to map upcoming research frontiers
Frame actionable next steps for students' own projects

The Road Ahead: Emerging Directions

Explainable GNNs

Dynamic Graphs

Multi-Modal Fusion

Deployment Challenges

Discussion & Q&A

Question 1

What datasets in your projects have latent graph structure?

Question 2

Where do you foresee the biggest implementation friction?

Question 3

How could we evaluate fairness and bias in medical GNNs?

References

Use Cases & Applications

- **Doshi, P., & Chepuri, S.** (2022). A computational approach to drug repurposing using graph neural networks. *Computers in Biology and Medicine*, 150, 106152.
- **Oss Boll, L., et al.** (2024). Graph neural networks for clinical risk prediction based on electronic health records: A survey. *Journal of Biomedical Informatics*, 152, 104618.
- **Tepe, B., & Bilgin, G.** (2022). Graph Neural Networks for Colorectal Histopathological Image Classification. In *TIPTEKNO 2022: Proceedings of the 2022 Medical Technologies Congress* (pp. 1-4).

Graph Neural Network Foundations (not referenced)

- **Hamilton, W. L.** (2020). Graph representation learning. In *Synthesis Lectures on Artificial Intelligence and Machine Learning* (Vol. 14, No. 3, pp. 1-159). Morgan & Claypool Publishers.
- **Wu, Z., et al.** (2020). A comprehensive survey on graph neural networks. *IEEE Transactions on Neural Networks and Learning Systems*, 32(1), 4-24.
- **Zhou, J., et al.** (2020). Graph neural networks: A review of methods and applications. *AI Open*, 1, 57-81.

Key Papers (not referenced)

- **Kipf, T. N., & Welling, M.** (2017). Semi-supervised classification with graph convolutional networks. In *International Conference on Learning Representations (ICLR)*.
- **Hamilton, W., Ying, Z., & Leskovec, J.** (2017). Inductive representation learning on large graphs. In *Advances in Neural Information Processing Systems (NeurIPS)*, 30.

Thank You

Keep Exploring

Slides

```
git clone https://github.com/phiwi/graphnn_lecture
npx slidev slides.md
```

Contact

philipp.wiesenbach@uni-heidelberg.de