2026. 01. 20. UNIST 슈퍼컴퓨팅 청소년캠프

화학 분자를 그래프로 이해하기: 그래프 신경망 실습

우제헌

KISTI 슈퍼컴퓨팅가속화연구단

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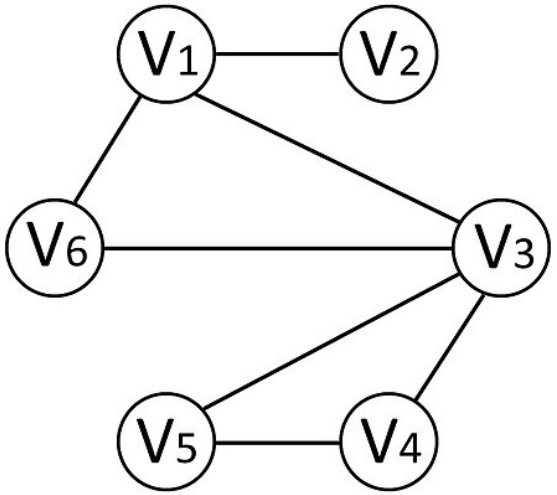
목차

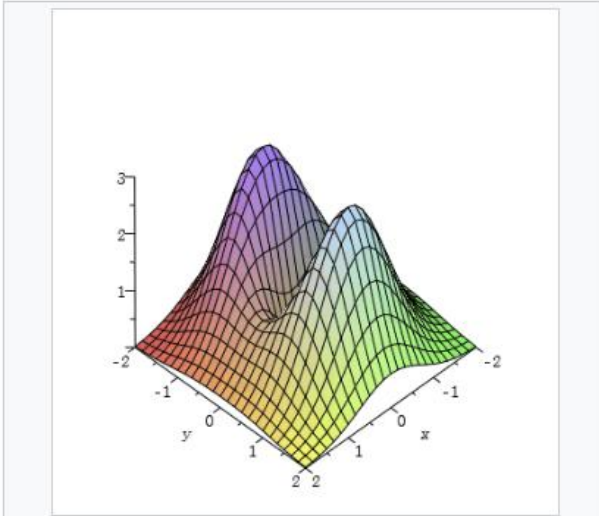
What is the graph?

What is the graph?

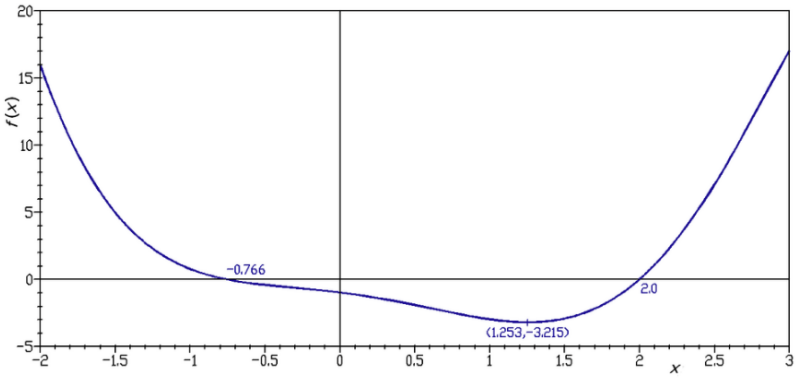


6 nodes + 7 edges로 구성된 graph

- Graph: 일련의 꼭짓점(vertex or node)들과 그 사이를 잇는 변(edge)들로 구성된 구조
- “Graph”의 어원:
  - γράφειν (graphein) = 긁다, 새기다, 쓰다, 그리다
  - 함수의 그래프, 그래픽(graphic), etc.
- “Graph”라는 용어는 1878년 수학자 J. J. 실베스터에 의해 처음 사용



함수 $f(x,y) = (x^2 + 3y^2)\exp(1 - x^2 - y^2)$ 의 그래프



함수 $f(x) = x^4 - 4^x$의 그래프

Why Graphs?

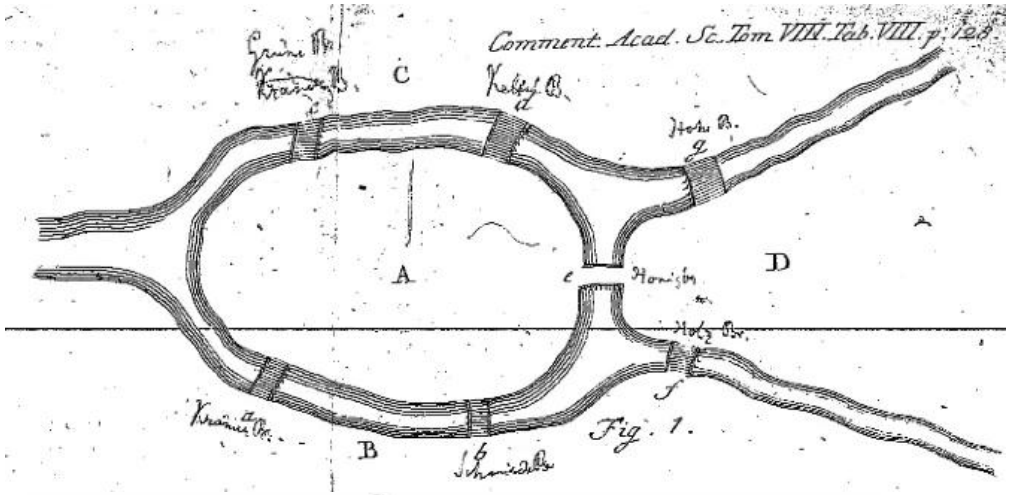
Graphs are a general language for describing and analyzing entities with relations/interactions.

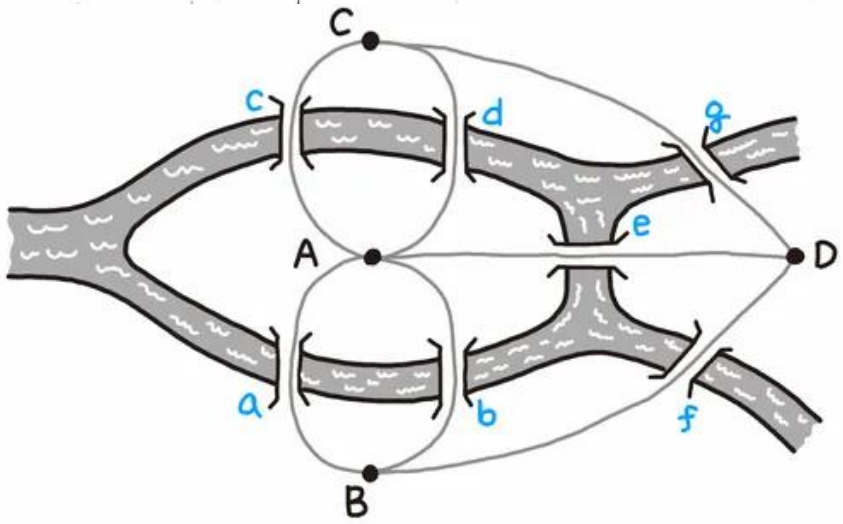
What is the graph?

레온하르트 오일러
Leonhard Euler

쾨니히스베르크 다리 건너기 문제 (한붓그리기)

쾨니히스베르크시의 한 가운데는 프레겔 강이 흐르고 있고 여기에는 가운데 섬들과 연결되어있는 일곱 개의 다리가 있다. 그 다리들을 한 번씩만 차례로 모두 건널 수 있겠는가?





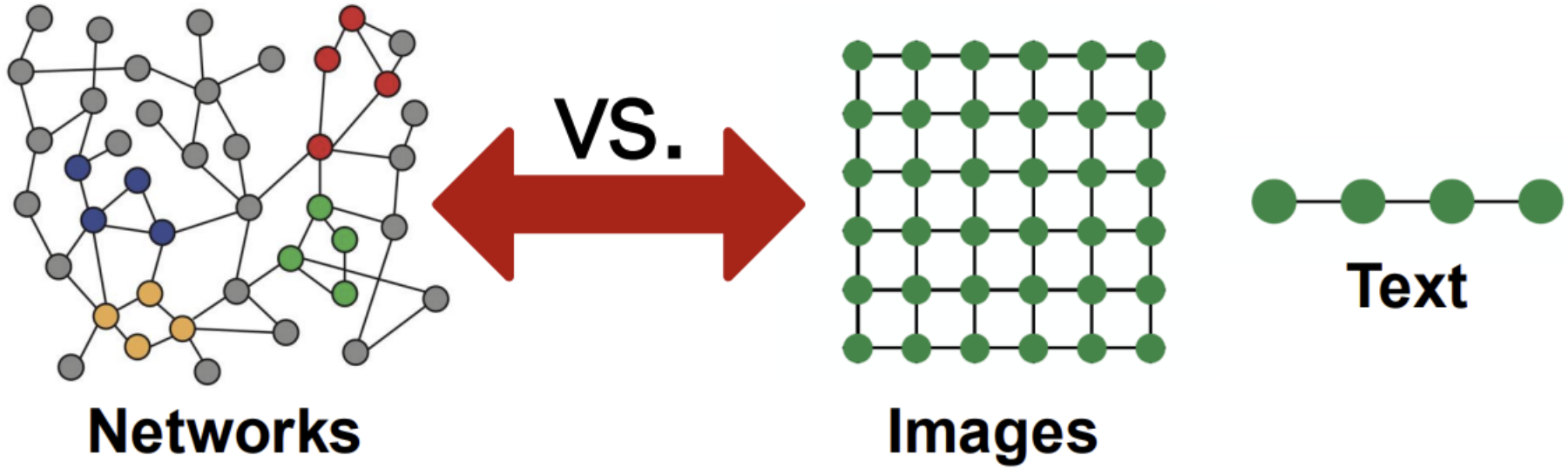
- **오일러 경로**: 그래프 에서 모든 간선을 정확히 한 번씩 방문하는 경로
  - G는 오일러 경로를 가진다.
  - G의 모든 꼭짓점의 차수는 짝수이다.

- **오일러 회로**: 시작점과 끝 점이 같은 오일러 경로
  - G는 오일러 회로를 가진다.
  - G의 홀수 차수 꼭짓점의 수는 0 또는 2이다.

당시 오일러는 이 문제를 다음 그림과 형태로 각각의 다리에 a부터 g까지 이름을 부여하고 도식화해 1735년에 논문을 발표, 해답이 없음을 수학적으로 증명.
(새로운 학문 “그래프 이론”의 시작)

What is the graph?

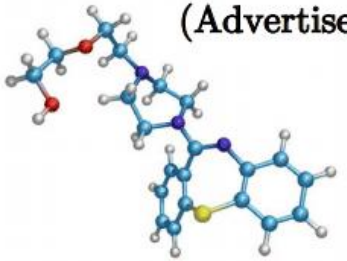
- Arbitrary size and complex topological structure (*i.e.*, no spatial locality like grids)



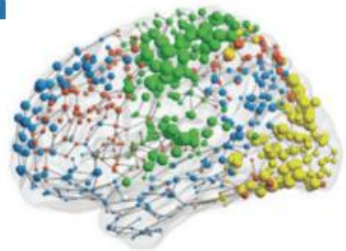
- No fixed node ordering or reference point
- Often dynamic and have multimodal features

What is the graph?

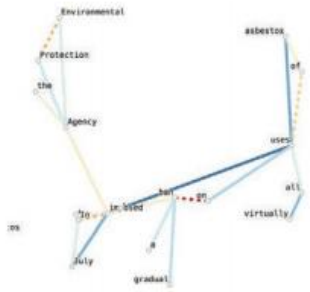
Social networks (Advertisement)



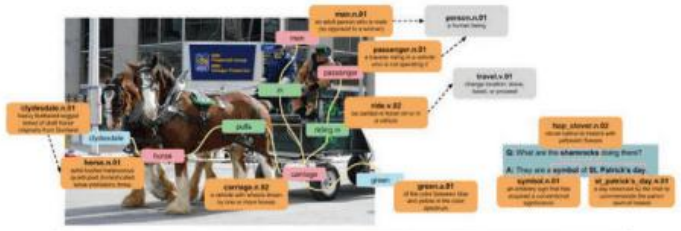
Drug/Material molecules (Chemistry)



Brain connectivity (Neuroscience)

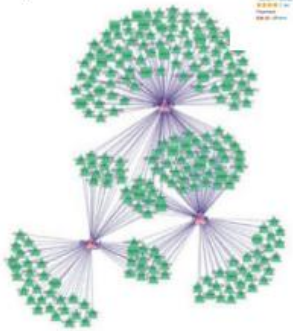


Words relationships (NLP)

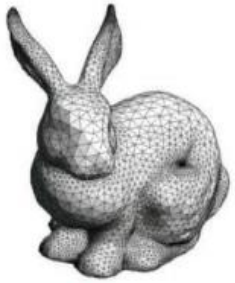


Scene understanding

Recommender systems (Amazon, Netflix)

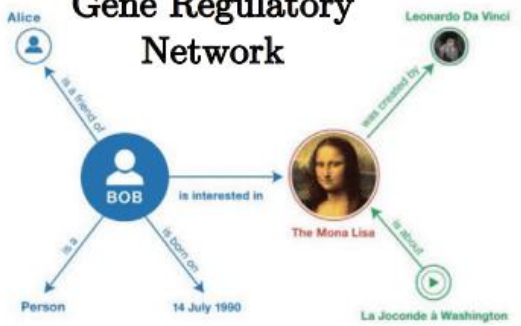


Gene Regulatory Network

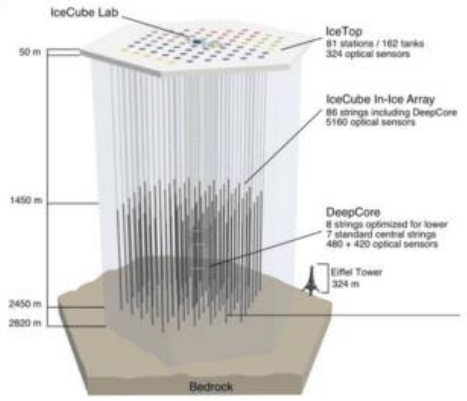


3D Meshes (Computer Graphics)

Transportation networks

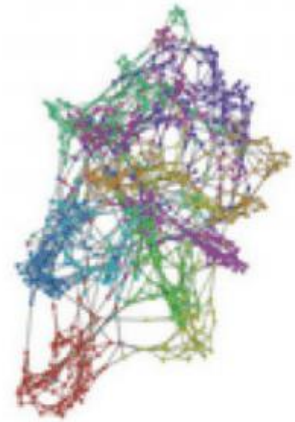


Knowledge graphs



Neutrino detection (High-energy Physics)

=

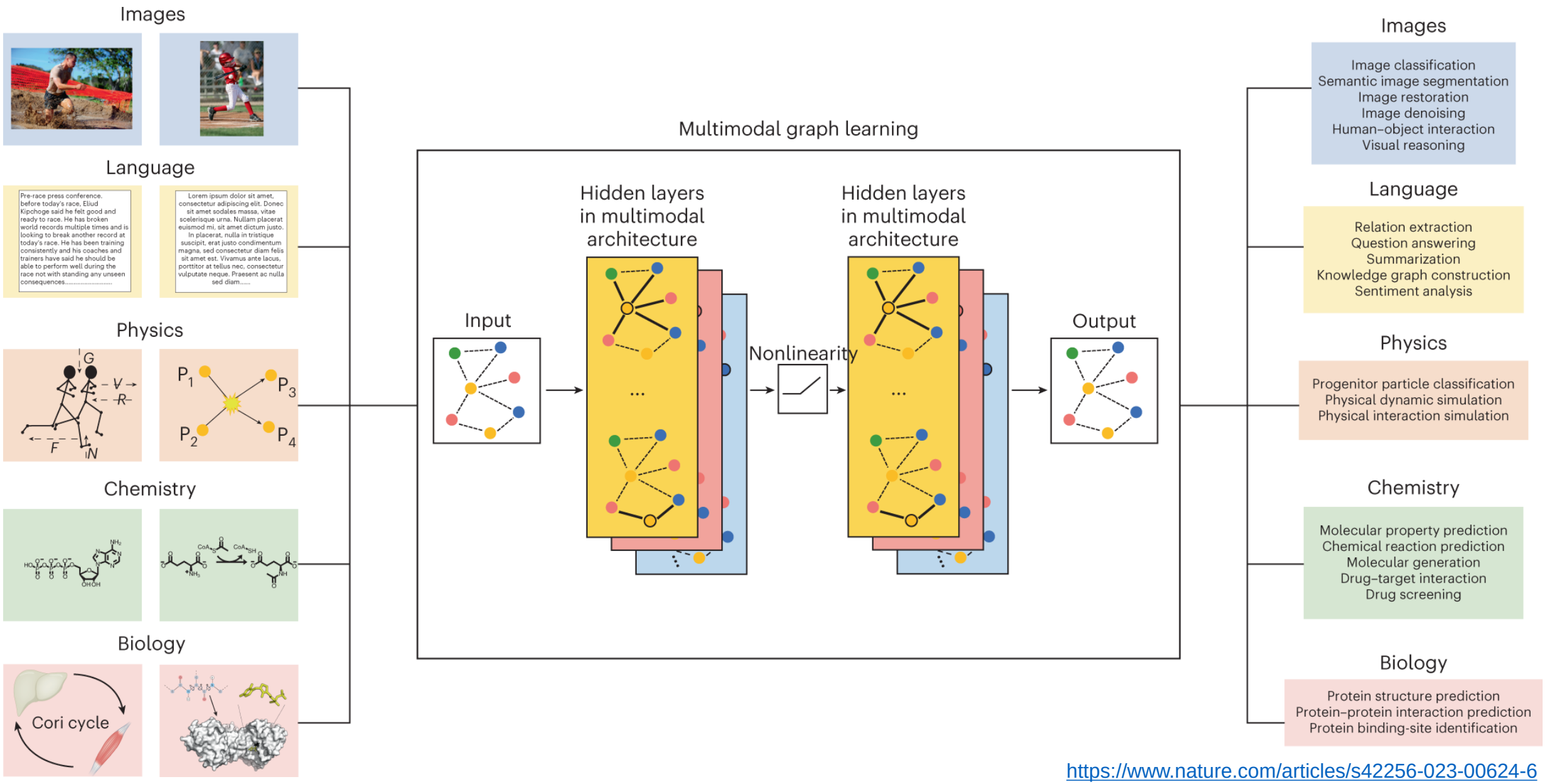


Graph

Graph Neural Network

- Graph Neural Network
- Graph Convoultion Network (GCN)
- Graph Isomorphism Network (GIN)
- Graph Attention Network (GAT)

Graph Neural Network



https://www.nature.com/articles/s42256-023-00624-6

Graph Neural Network

GNN에서의 예측 종류 (Prediction Levels)
GNN은 그래프의 어느 단위를 예측 대상으로 삼느냐에 따라 세 가지 문제로 나뉩니다.

1. Node-level prediction

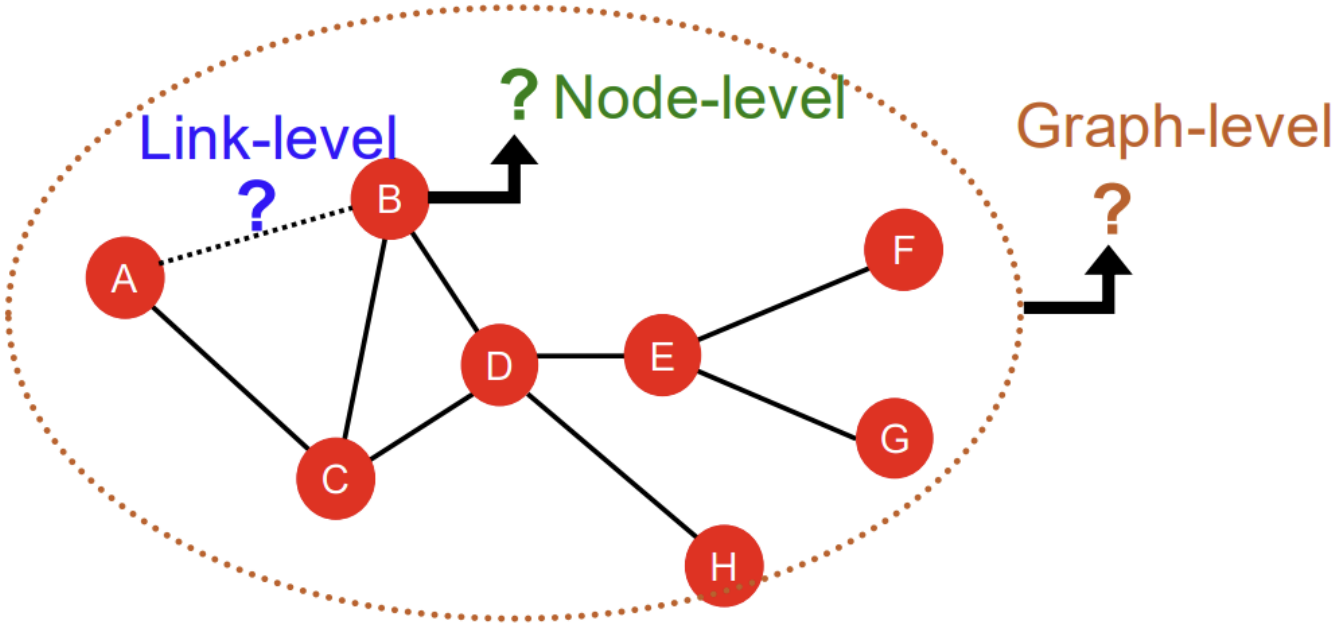
(노드 하나하나에 대한 예측)
- 각 노드의 속성 / 상태 / 라벨
- “이 노드는 어떤 클래스에 속하는가?”
- “이 노드의 값은 얼마인가?”

2. Link-level (Edge-level) prediction

(노드 쌍 사이 관계에 대한 예측)
- 두 노드 사이에 edge가 존재하는지 혹은 edge의 타입 / 강도
- “이 두 노드는 연결될까?”
- “이 연결은 어떤 의미인가?”

3. Graph-level prediction

(그래프 전체에 대한 예측)
- 그래프 하나당 하나의 값/라벨
- “이 그래프의 전체 성질은?”
- “이 시스템의 결과는?”



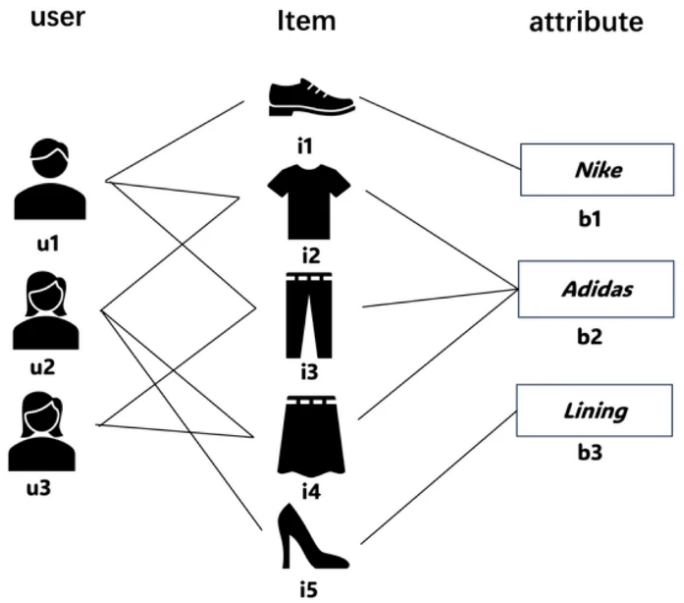
Graph Neural Network

Example: Social network

- Nodes: 사용자 계정 (Facebook, Instagram 등)
  - 나이, 지역, 관심사, 활동 이력 등
- Edges: 사용자 간의 관계
  - follow, message 등
- Predictions:
  - People You May Know
  - 추천 친구 (link prediction)

https://medium.com/analytics-vidhya/social-network-analytics-f082f4e21b16

Example: Recommender system



- Nodes: 사용자, 아이템 (상품, 영화, 음악 등)
  - 나이, 성별, 지역, 관심사, 구매/클릭 이력
  - 카테고리, 브랜드, 가격, 설명, 메타데이터
- Edges: 사용자–아이템 간 상호작용
  - 빈도, 평점, 시간 정보
- Predictions:
  - 추천 상품 / 콘텐츠
  - 평점 예측, 클릭 확률

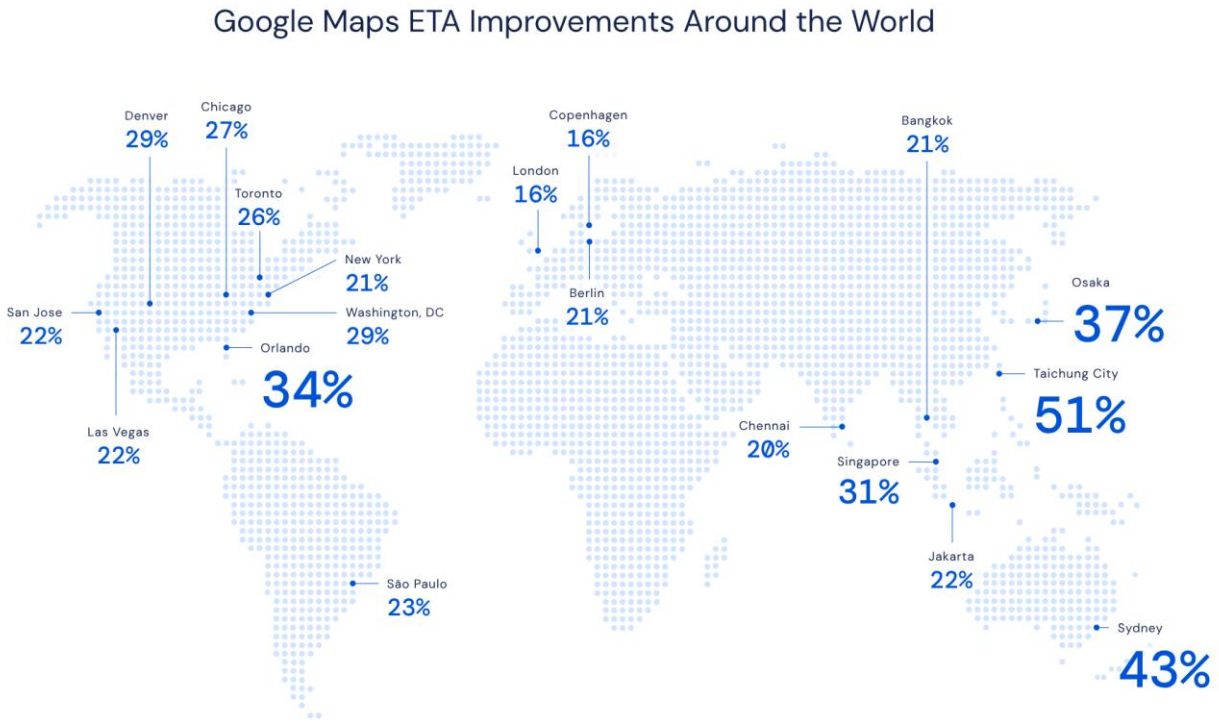
https://www.nature.com/articles/s41598-024-54376-3

Graph Neural Network

Example: Estimated Time of Arrival (ETA, 도착 시간) 예측

교통 지도(Transportation map)는 **그래프(Graph)** 로 자연스럽게 표현할 수 있습니다.

- **Nodes**: 교차로
- **Edges**: 도로
- **Features**: 도로 길이, 현재 차량 속도, 과거 평균 속도



이렇게 만든 **도로 그래프**에 **GNN**을 적용하여
도착 시간(ETA)을 예측하는 문제로 만들 수 있습니다.
(= graph regression 문제)

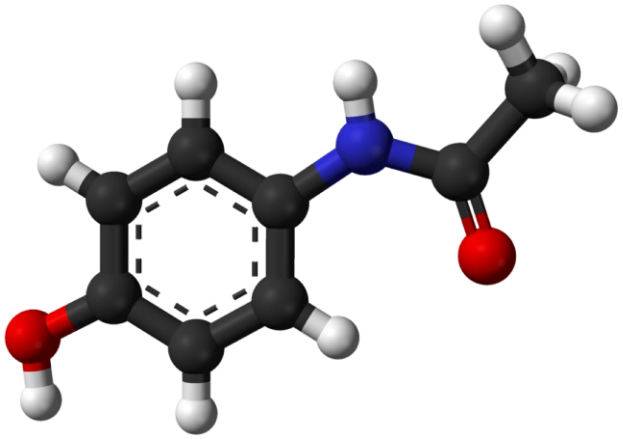
https://deepmind.google/blog/traffic-prediction-with-advanced-graph-neural-networks/

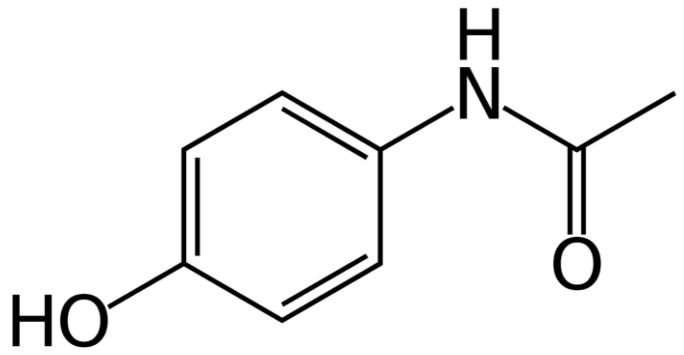
Graph Neural Network

Example: Molecules

분자(Molecule) 역시 **그래프 구조**로 표현할 수 있습니다.
Molecules can be represented by a graph

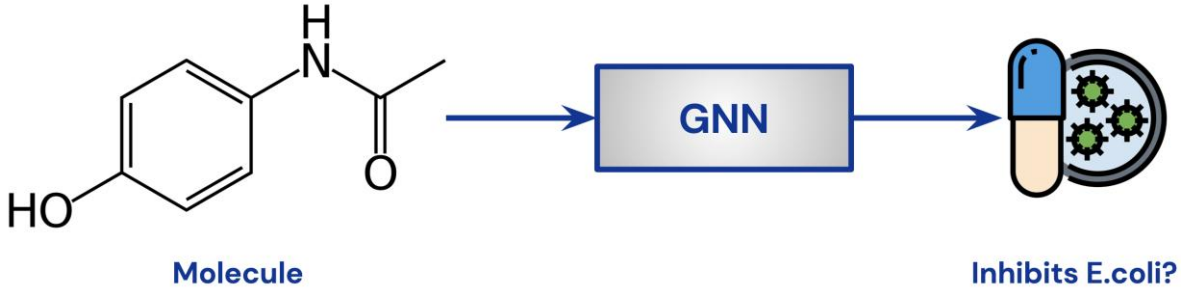
- **Nodes**: 원자 (atoms)
- **Edges**: 화학 결합 (bonds)
- **Features**:
  - 원자 종류 (C, O, N, etc.)
  - 결합 종류 (single, double, aromatic, etc.)
  - 전하 (charge)

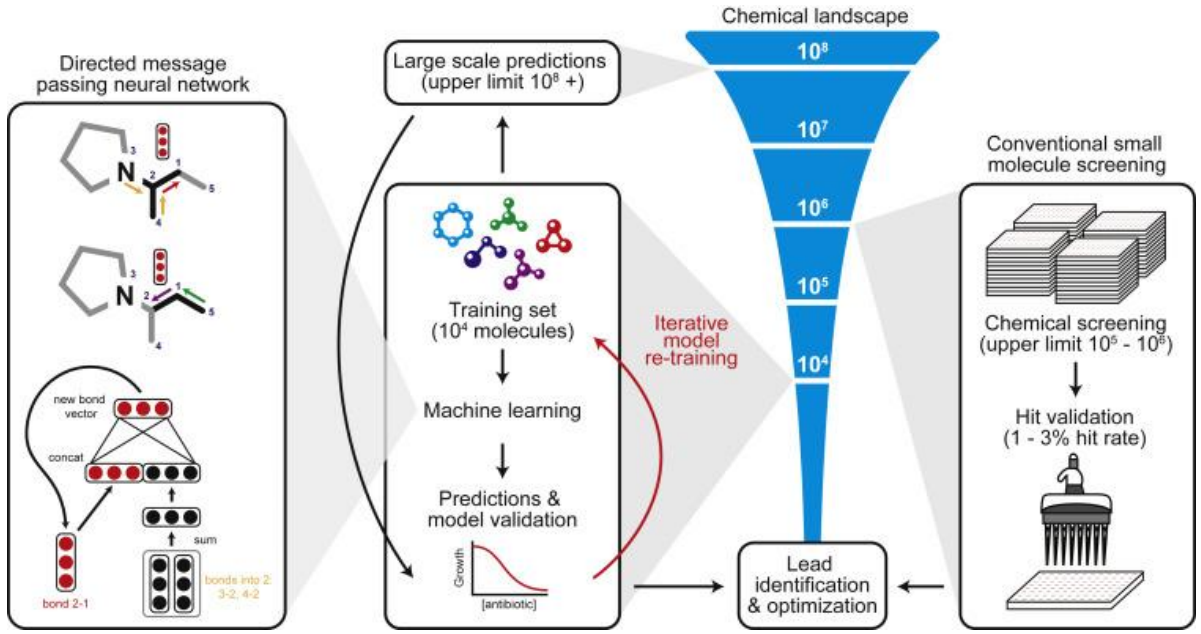




해당 분자가 **대장균(E. coli)을 억제하는 효과가 있는지** 예측.
결과는 **Yes / No (→ Binary Classification 문제)**

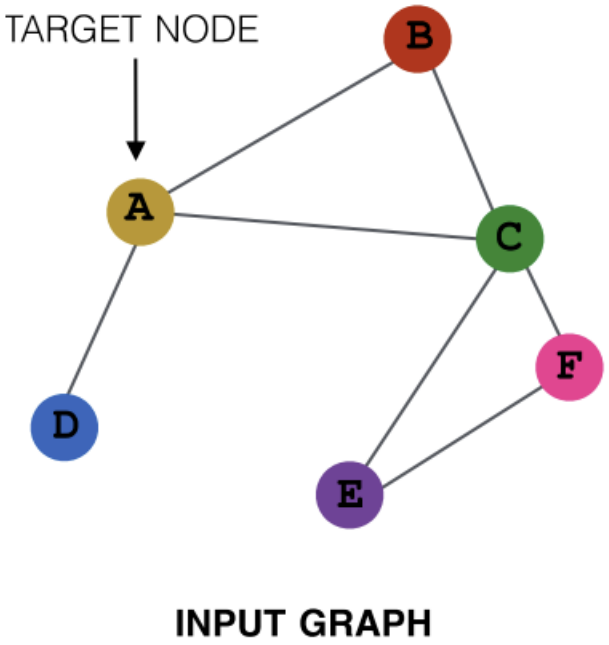
이미 실험 결과가 알려진 분자들로 구성된 **데이터셋**을 사용.
GNN을 학습시켜 새로운 분자의 효과를 예측.



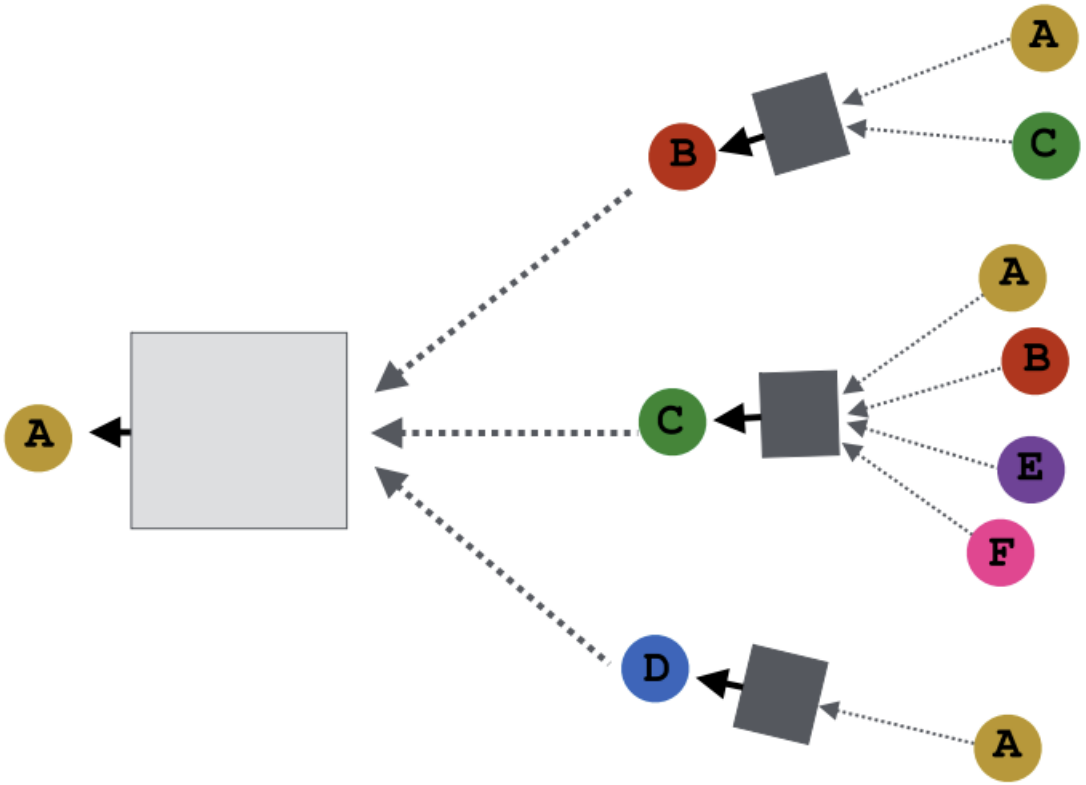


https://www.sciencedirect.com/science/article/pii/S0092867420301021

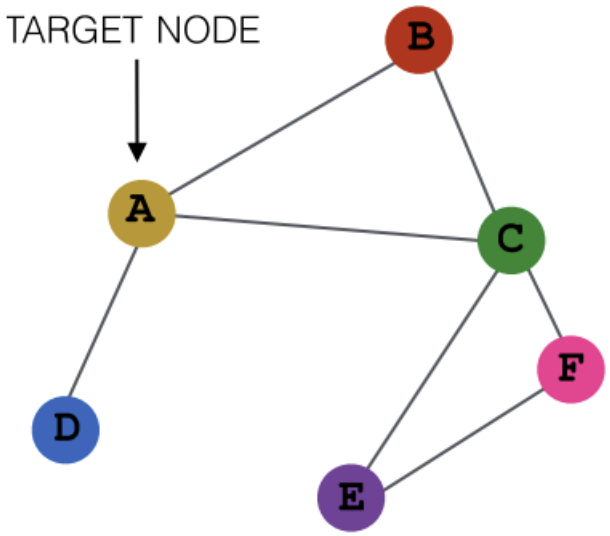
Graph Neural Network



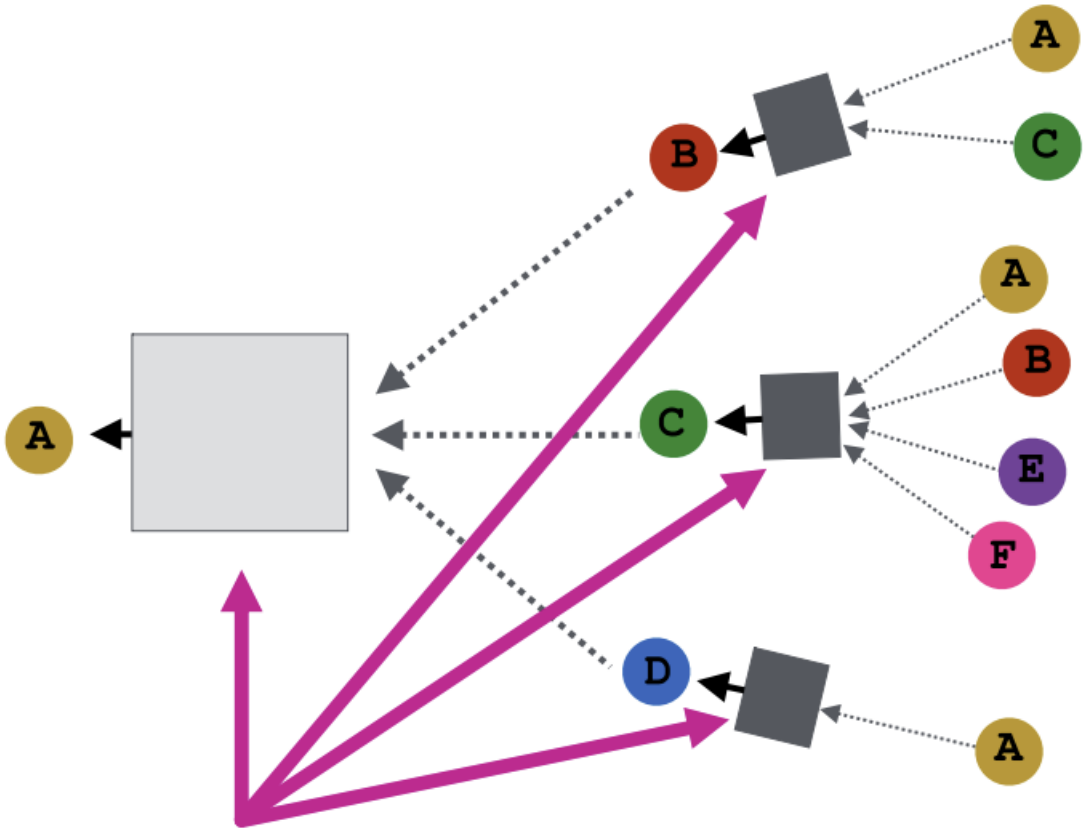
INPUT GRAPH



Graph Neural Network



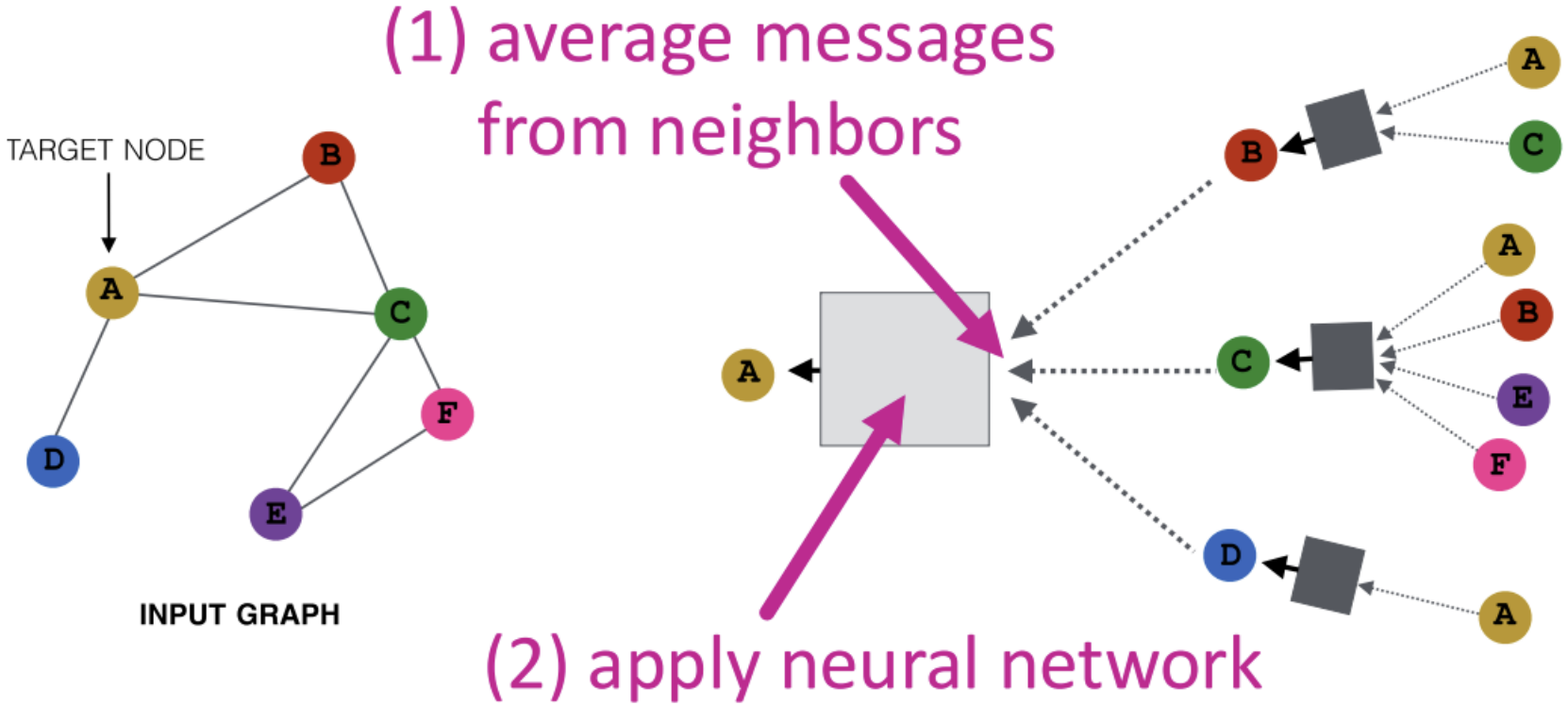
INPUT GRAPH



Graph Neural Network

Graph Convolution Network (GCN); ICLR 2017

- **Basic approach:** Average information from neighbors and apply a neural network

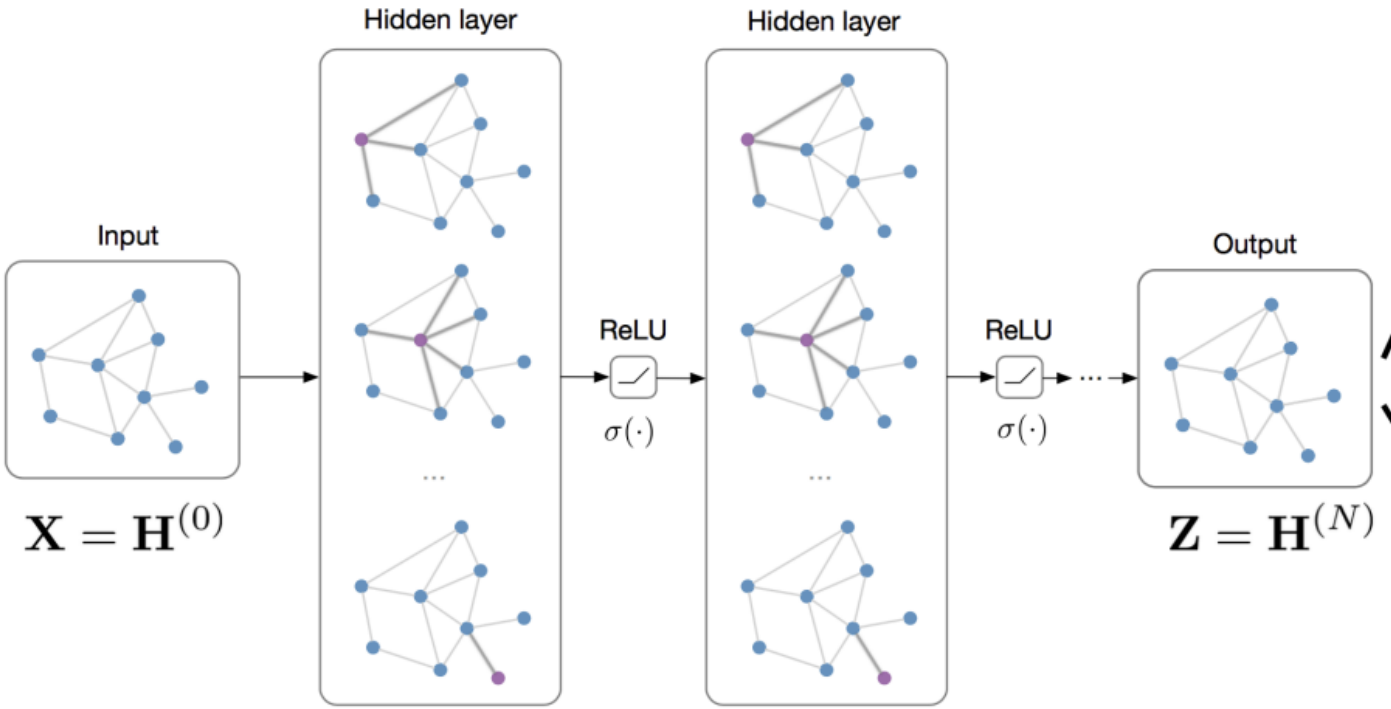


https://arxiv.org/abs/1609.02907

Graph Neural Network

Classification and **Link Prediction** with GNNs / GCNs

Input: Feature matrix $\mathbf{X} \in \mathbb{R}^{N \times E}$, preprocessed adjacency matrix $\hat{\mathbf{A}}$



$$\mathbf{H}^{(l+1)} = \sigma\left(\hat{\mathbf{A}}\mathbf{H}^{(l)}\mathbf{W}^{(l)}\right)$$

Node classification:

$\mathrm{softmax}(\mathbf{z_n})$

e.g. Kipf & Welling (ICLR 2017)

Graph classification:

$\mathrm{softmax}(\sum_n \mathbf{z_n})$

e.g. Duvenaud et al. (NIPS 2015)

Link prediction:

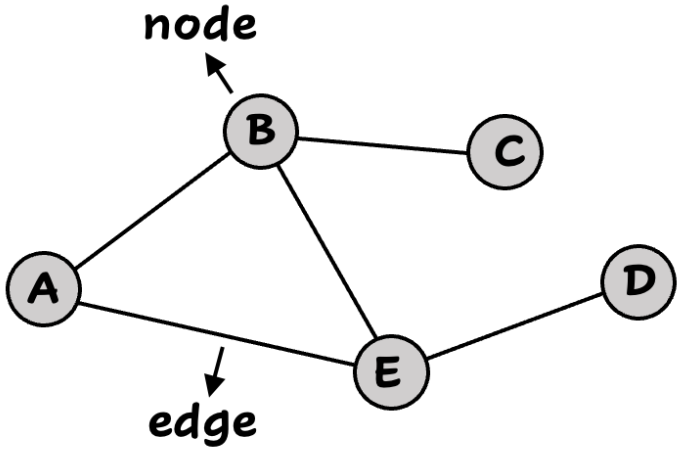
$p(A_{ij}) = \sigma(\mathbf{z_i^T z_j})$

Kipf & Welling (NIPS BDL 2016)

"Graph Auto-Encoders"

* slide from Thomas Kipf, **University of Amsterdam**

Graph Neural Network



adjacency matrix

$$\begin{pmatrix} 0 & 1 & 0 & 0 & 1 \\ 1 & 0 & 1 & 0 & 1 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 1 & 1 & 0 & 1 & 0 \end{pmatrix}$$

A — Adjacency Matrix (인접 행렬)

- 그래프의 **연결 구조(topology)** 를 행렬로 표현한 것
- 노드 개수 N일 때,

$$A = \begin{pmatrix} a_{11} & a_{12} & \cdots & a_{1N} \\ a_{21} & a_{22} & \cdots & a_{2N} \\ \vdots & \vdots & \ddots & \vdots \\ a_{N1} & a_{N2} & \cdots & a_{NN} \end{pmatrix}$$

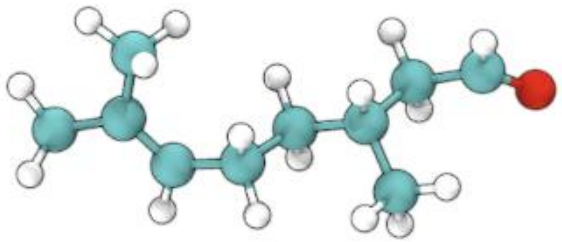
$$a_{ij} = \begin{cases} 1 & \text{노드 } i\text{와 } j\text{가 연결되어 있으면} \\ 0 & \text{그렇지 않으면} \end{cases}$$

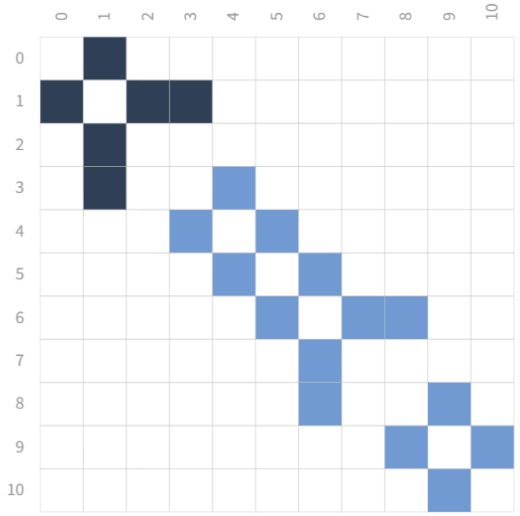
- x_i
  - **i번째 노드의 입력 feature 벡터**
  - 예:
    - 분자 그래프: 원자 번호, 전하, hybridization 등
  - 차원: $x_i \in \mathbb{R}^F$

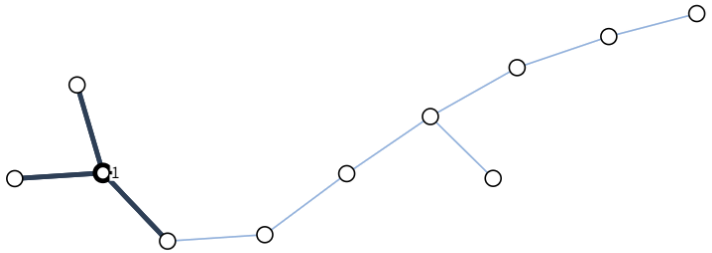
- X
  - **전체 노드의 입력 feature 행렬**
  - 각 행이 하나의 노드

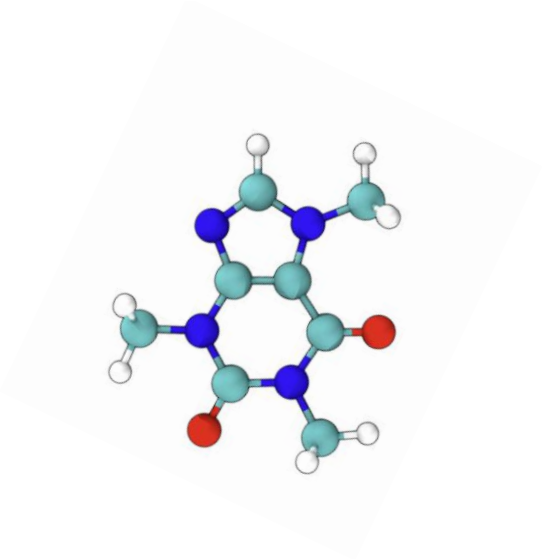
$$X = \begin{bmatrix} x_1^\top \\ x_2^\top \\ \vdots \\ x_N^\top \end{bmatrix} \in \mathbb{R}^{N \times F}$$

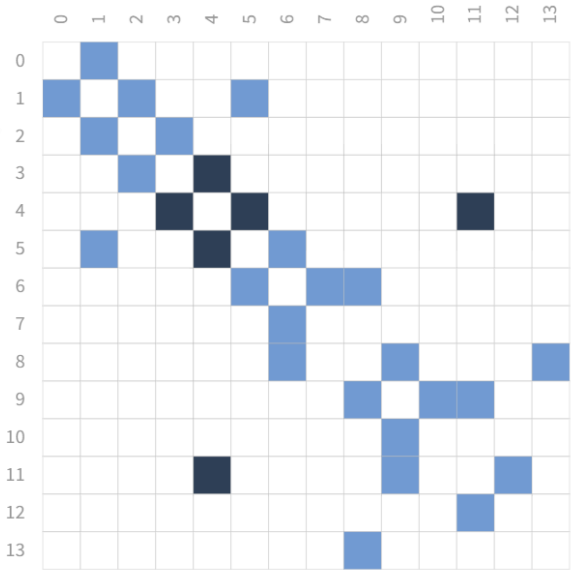
Graph Neural Network: Adjacency Matrix

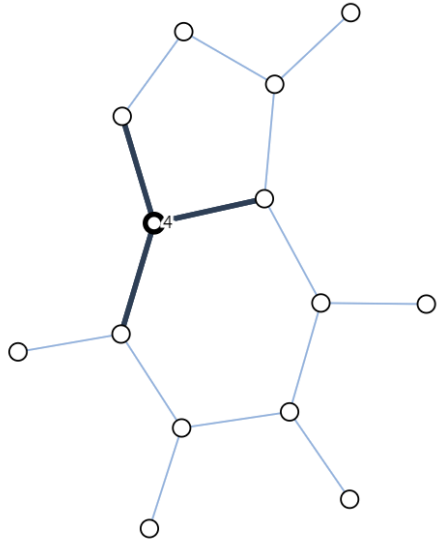












https://hal.cse.msu.edu/teaching/2024-spring-deep-learning/15-graph-neural-networks/#/3/17

Graph Neural Network: Adjacency Matrix

Images as graphs

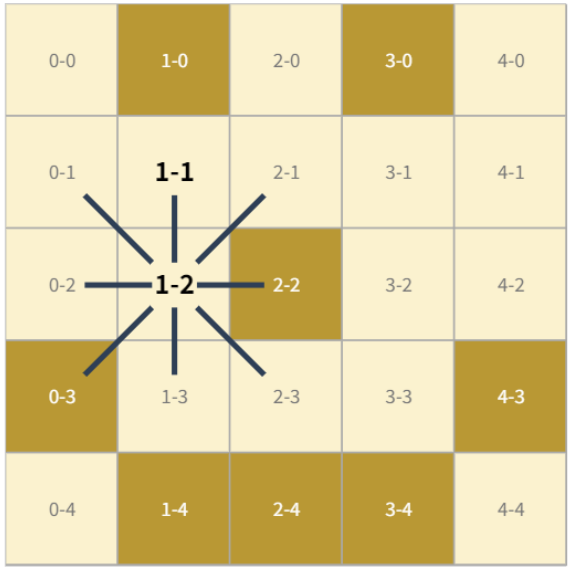
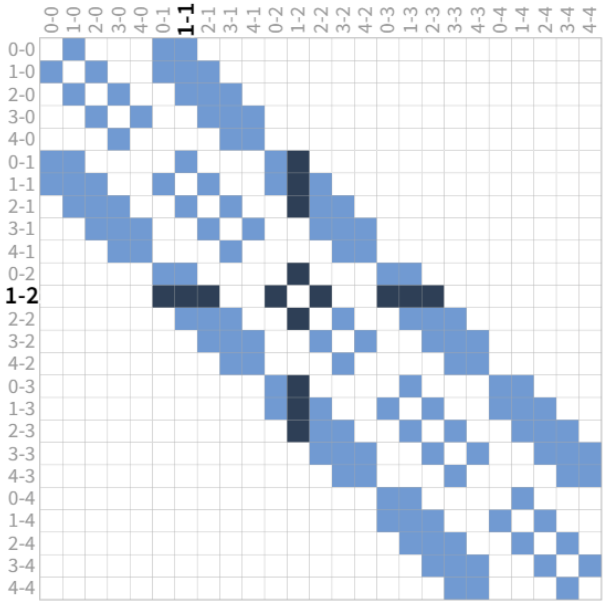
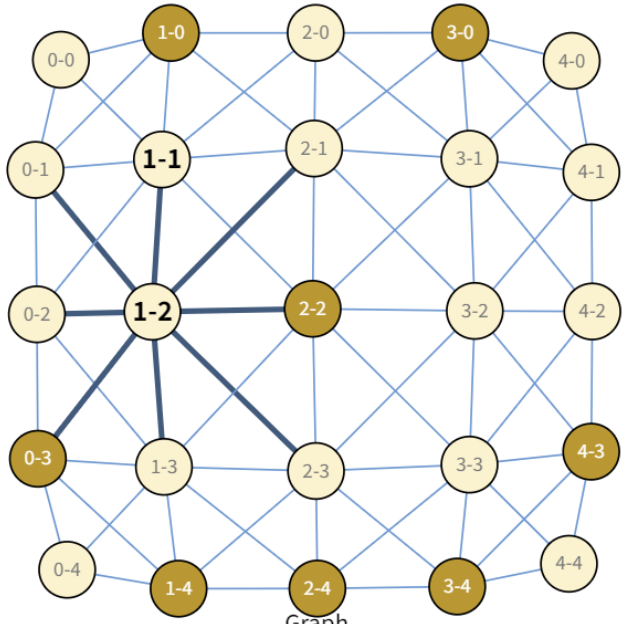


Image Pixels

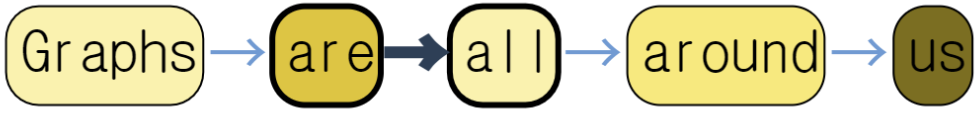


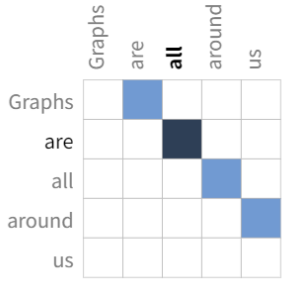
Adjacency Matrix



Graph

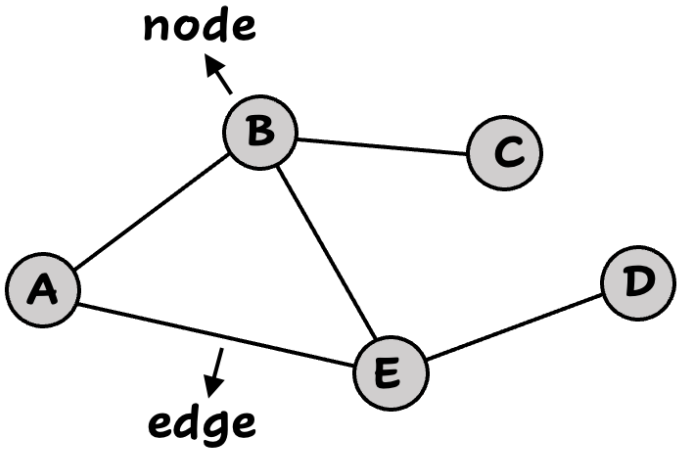
Text as graphs





https://hal.cse.msu.edu/teaching/2024-spring-deep-learning/15-graph-neural-networks/#/3/17

Graph Neural Network



- $h_i^{(l)} \in \mathbb{R}^{F_l}$
  - **l번째 GCN layer에서 i번째 노드의 hidden representation**
  - 즉, 노드 임베딩

- $H^{(l)}$
  - **l번째 layer에서의 전체 노드 표현 행렬**

$$H^{(l)} = \begin{bmatrix} h_1^{(l)\top} \\ h_2^{(l)\top} \\ \vdots \\ h_N^{(l)\top} \end{bmatrix} \in \mathbb{R}^{N \times F_l}$$

  - $H^{(0)} = X$

l — 레이어 인덱스 (Layer index)

- GCN의 **layer 번호**
- $l = 0, 1, 2, \ldots$
- 의미:
  - $l = 0$: 입력 feature
  - $l = 1$: 1-hop 이웃 정보 반영
  - $l = 2$: 2-hop 이웃 정보 반영

W — 학습 파라미터 (Weights)

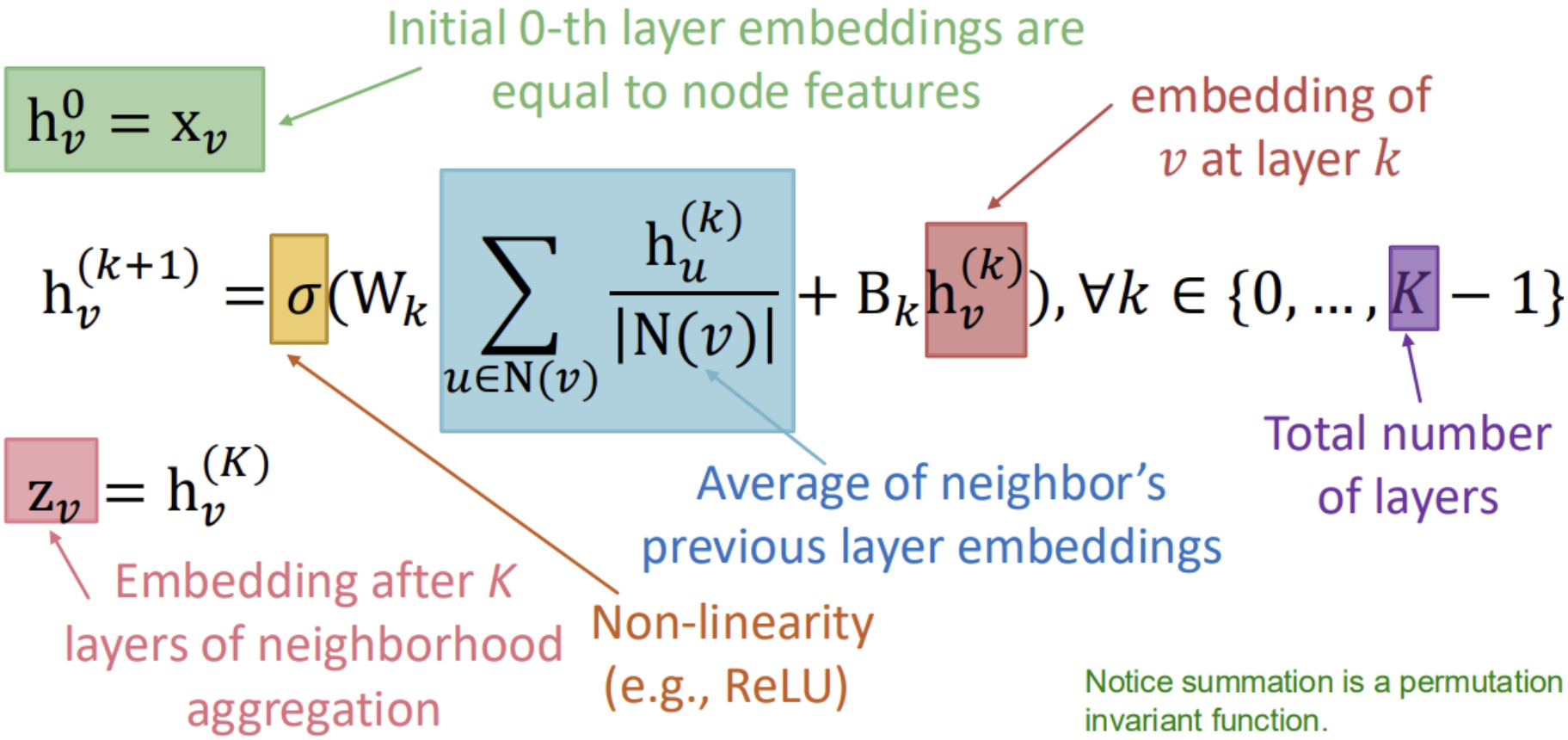
- $W^{(l)} \in \mathbb{R}^{F_l \times F_{l+1}}$
  - **l번째 GCN layer의 weight matrix**
  - feature 변환 역할

$$\mathbf{H}^{(l+1)} = \sigma\left(\hat{\mathbf{A}}\mathbf{H}^{(l)}\mathbf{W}^{(l)}\right)$$

- $\hat{A}$: normalized A
- σ: non-linear function

Graph Convolution Network (GCN)

Graph Convolution Network (GCN); ICLR 2017



https://arxiv.org/abs/1609.02907

Graph Convolution Network (GCN)

Graph Convolution Network (GCN); ICLR 2017

Trainable weight matrices
(i.e., what we learn)

$$h_v^{(0)} = x_v$$

$$h_v^{(k+1)} = \sigma\left(W_k \sum_{u \in N(v)} \frac{h_u^{(k)}}{|N(v)|} + B_k h_v^{(k)}\right), \forall k \in \{0..K-1\}$$

$$z_v = h_v^{(K)}$$

Final node embedding

We can feed these **embeddings into any loss function** and run SGD to **train the weight parameters**

h_v^k: the hidden representation of node v at layer k

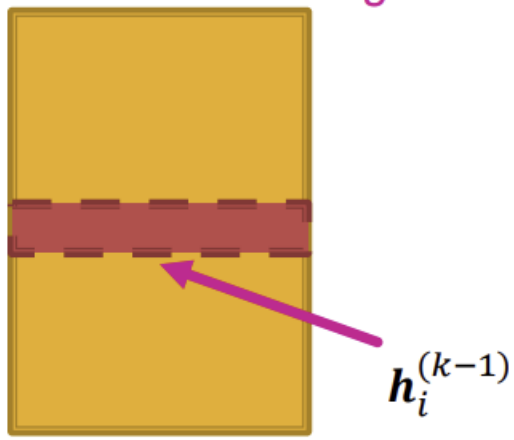
- W_k: weight matrix for neighborhood aggregation
- B_k: weight matrix for transforming hidden vector of self

Graph Convolution Network (GCN)

Graph Convolution Network (GCN); ICLR 2017

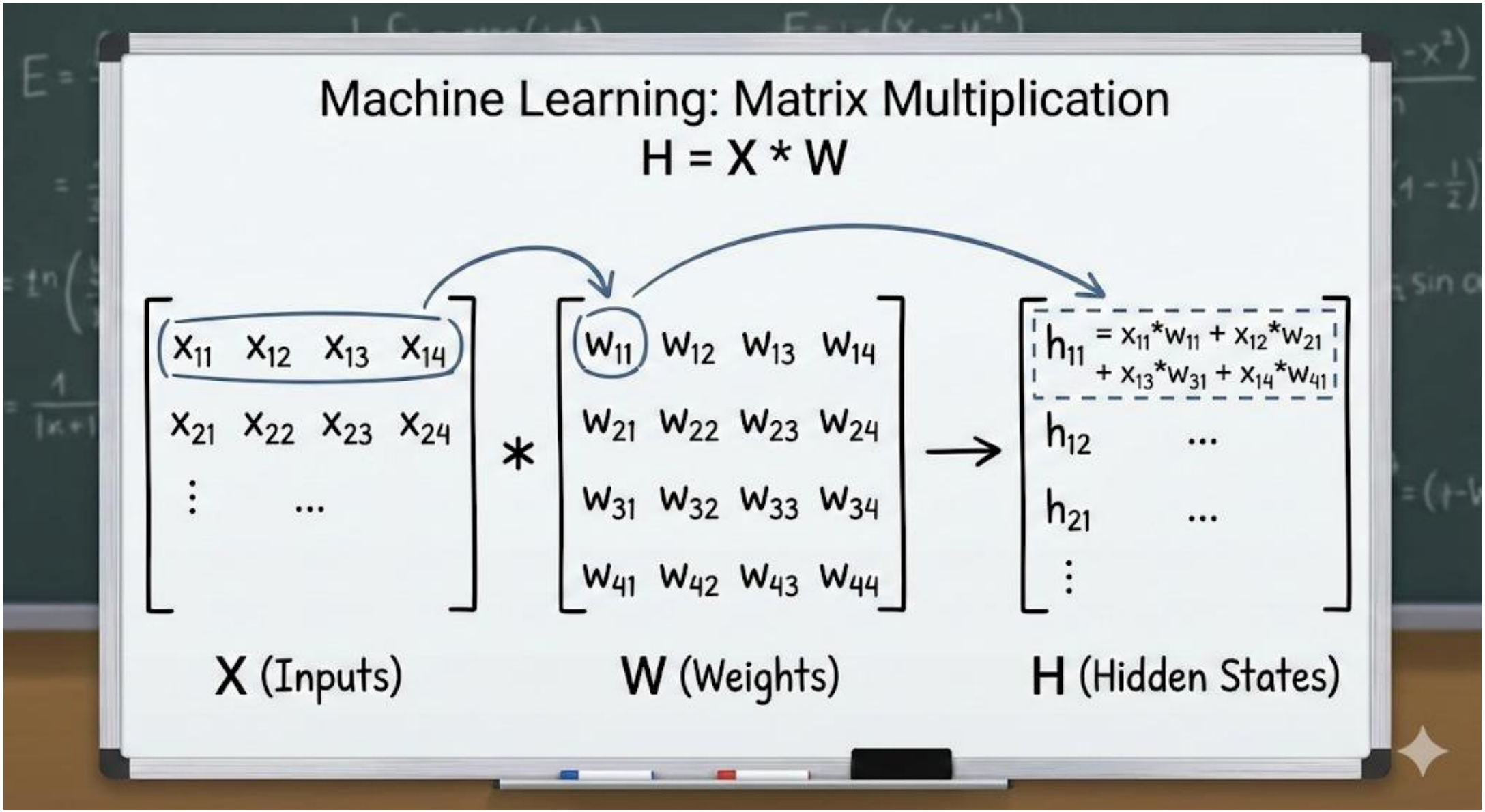
- **Many aggregations can be performed efficiently by (sparse) matrix operations**
- Let $H^{(k)} = [h_1^{(k)} \dots h_{|V|}^{(k)}]^{\mathrm{T}}$
- Then: $\sum_{u \in N_v} h_u^{(k)} = \mathrm{A}_{v,:}\mathrm{H}^{(k)}$
- Let D be diagonal matrix where $D_{v,v} = \mathrm{Deg}(v) = |N(v)|$
  - The inverse of D: D^{-1} is also diagonal: $D_{v,v}^{-1} = 1/|N(v)|$
- **Therefore,**

Matrix of hidden embeddings $H^{(k-1)}$



$$\sum_{u \in N(v)} \frac{h_u^{(k-1)}}{|N(v)|} \Rightarrow H^{(k+1)} = D^{-1}AH^{(k)}$$

Matrix Multiplication



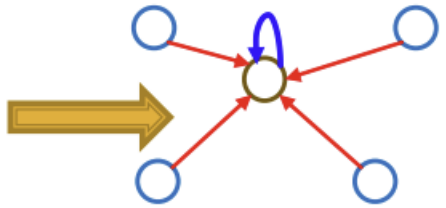
Graph Convolution Network (GCN)

Graph Convolution Network (GCN); ICLR 2017

- Re-writing update function in matrix form:

$$H^{(k+1)} = \sigma(\tilde{A}H^{(k)}W_k^{\mathrm{T}} + H^{(k)}B_k^{\mathrm{T}})$$

where $\tilde{A} = D^{-1}A$



$H^{(k)} = [h_1^{(k)} \dots h_{|V|}^{(k)}]^T$

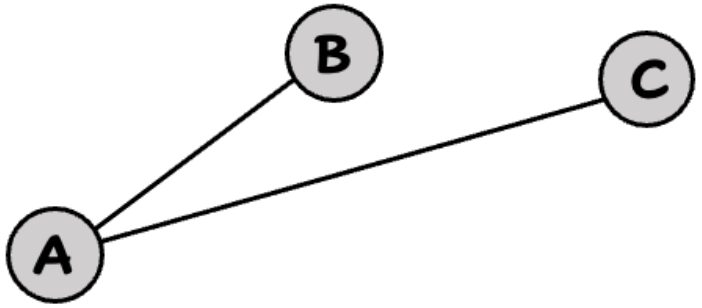
  - Red: neighborhood aggregation
  - Blue: self transformation

- In practice, this implies that efficient sparse matrix multiplication can be used ($\tilde{A}$ is sparse)

- **Note**: not all GNNs can be expressed in a simple matrix form, when aggregation function is complex

Graph Convolution Network (GCN)

Graph Convolution Network (GCN); ICLR 2017



$$\begin{pmatrix} 0 & 1 & 1 \\ 1 & 0 & 0 \\ 1 & 0 & 0 \end{pmatrix}$$

$$A + I = \begin{pmatrix} 0 & 1 & 1 \\ 1 & 0 & 0 \\ 1 & 0 & 0 \end{pmatrix} + \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix} = \begin{pmatrix} 1 & 1 & 1 \\ 1 & 1 & 0 \\ 1 & 0 & 1 \end{pmatrix} = \hat{A}$$

$$H = \hat{A}^T X W^T$$

$$D + I = \begin{pmatrix} 2 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix} + \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix} = \begin{pmatrix} 3 & 0 & 0 \\ 0 & 2 & 0 \\ 0 & 0 & 2 \end{pmatrix} = \hat{D}$$

$$normalized\ \hat{A} = \hat{D}^{-\frac{1}{2}} \hat{A}^T \hat{D}^{-\frac{1}{2}}$$

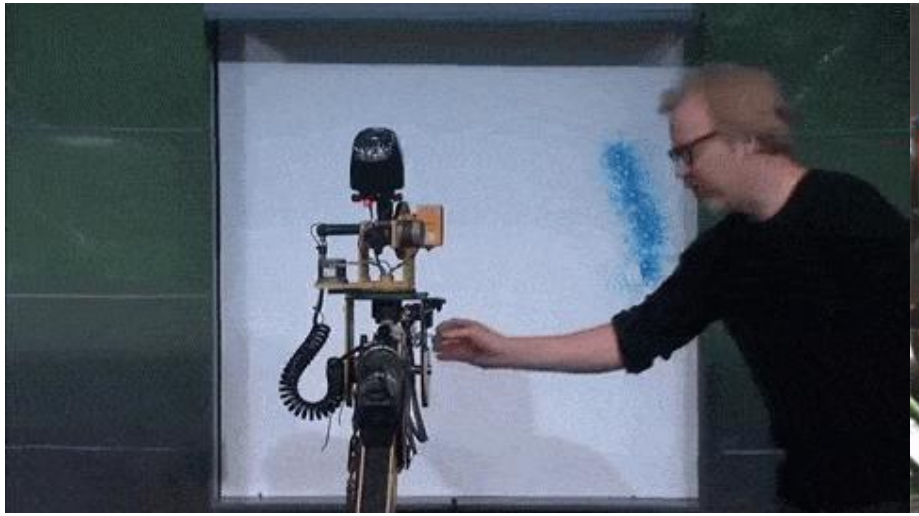
$$\hat{D}^{-1} = \begin{pmatrix} \frac{1}{3} & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & \frac{1}{2} \end{pmatrix}$$

$$H = \hat{D}^{-\frac{1}{2}} \hat{A}^T \hat{D}^{-\frac{1}{2}} X W^T$$

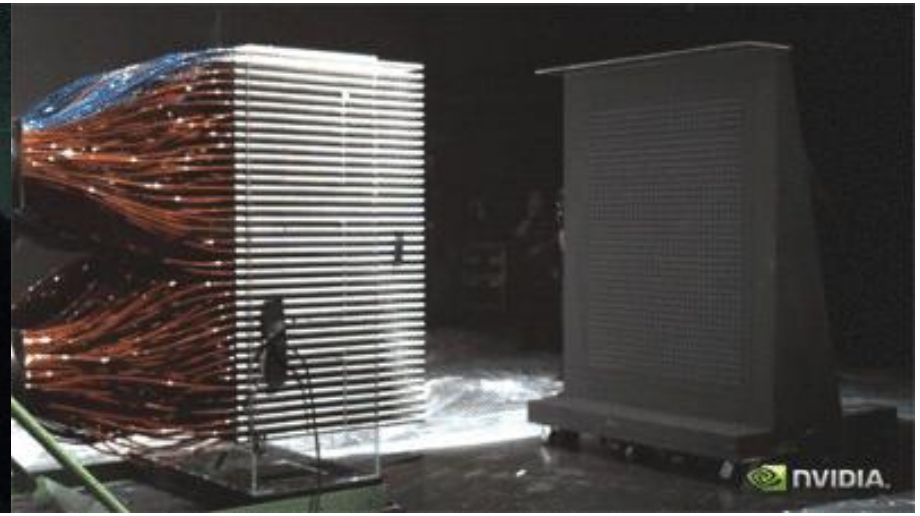
https://towardsdatascience.com/graph-neural-networks-part-1-graph-convolutional-networks-explained-9c6aaa8a406e/

Graph Convolution Network (GCN)

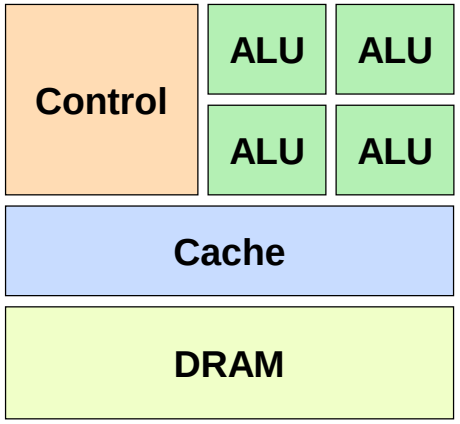
Matrix Multiplication & GPU



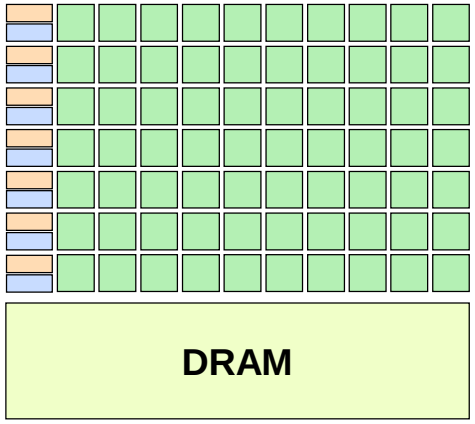
CPU



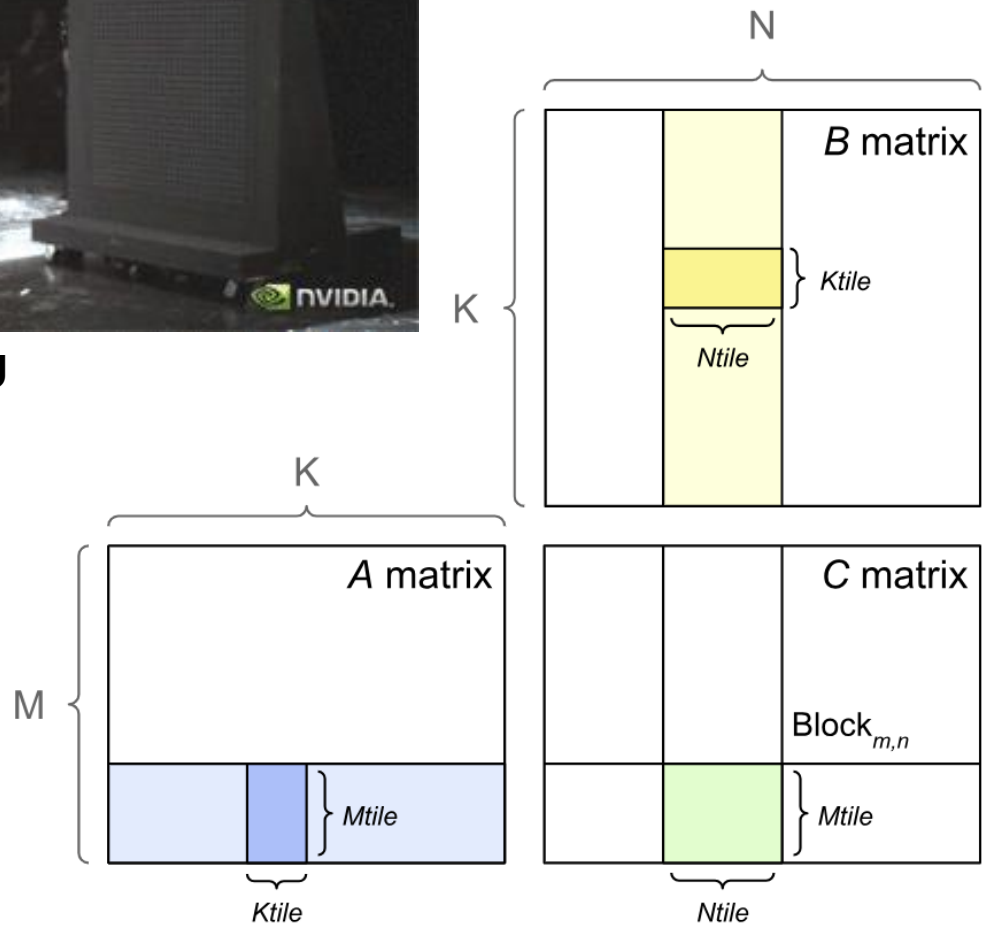
GPU



CPU

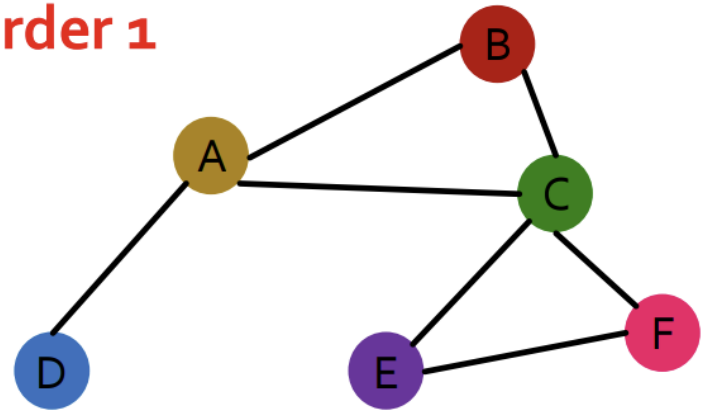


GPU

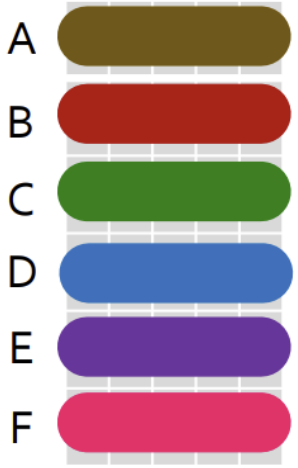


Graph Neural Network: Permutation

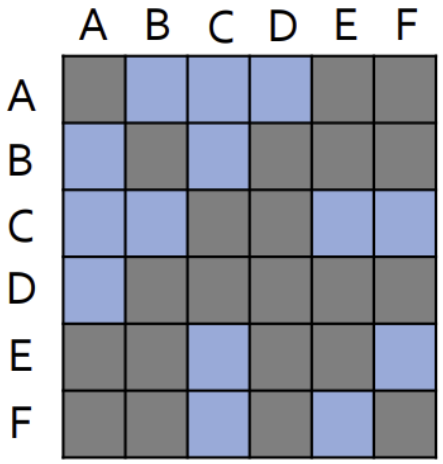
Order 1



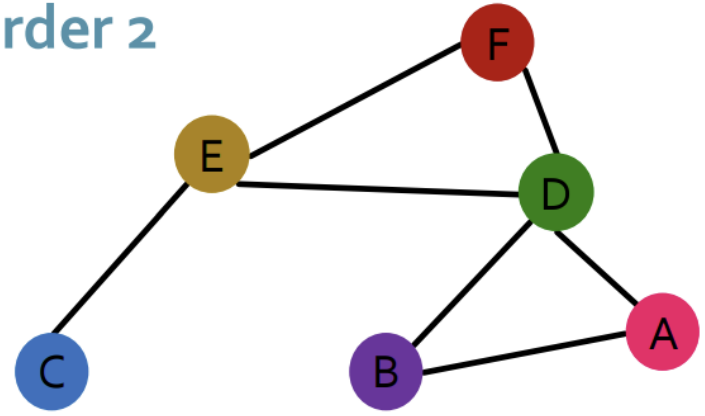
Node features X_1



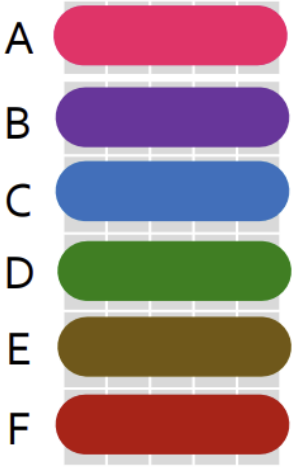
Adjacency matrix A_1



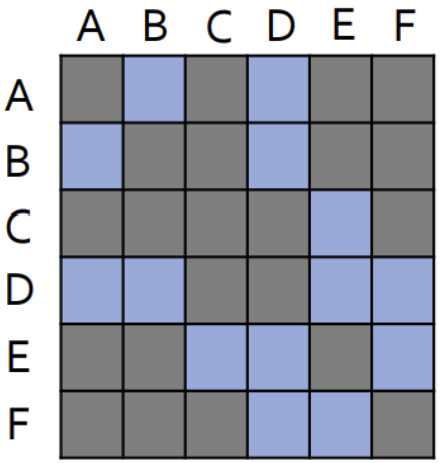
Order 2



Node features X_2

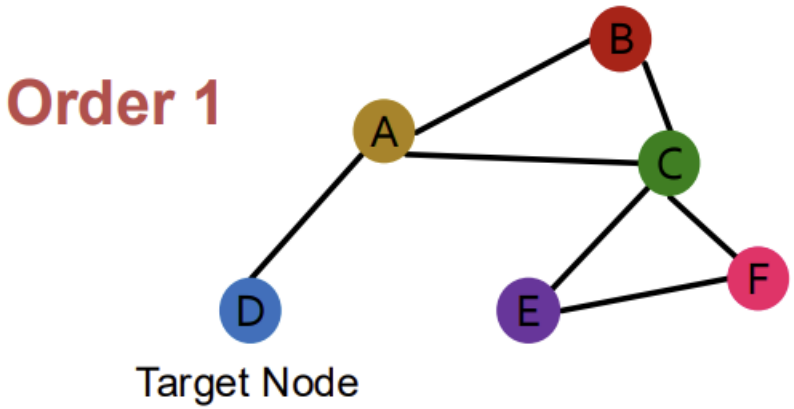


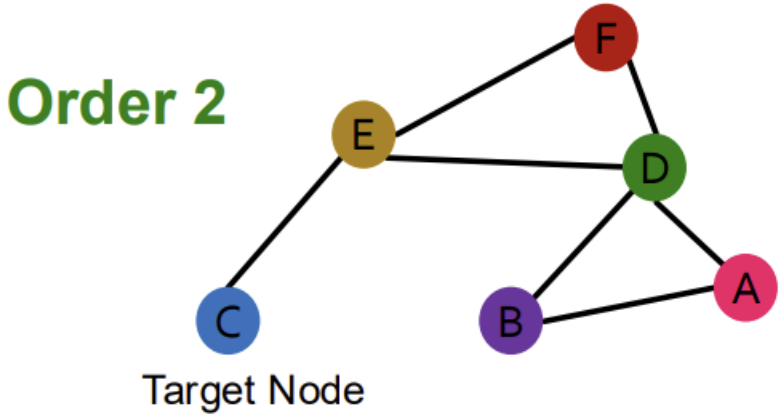
Adjacency matrix A_2

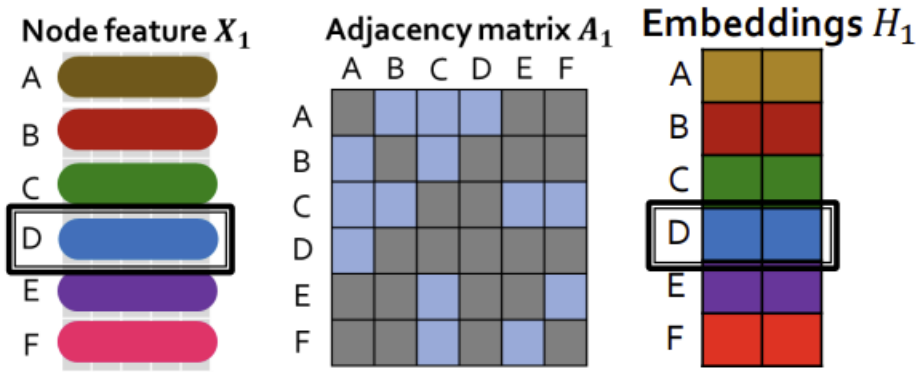


Graph Neural Network: Permutation

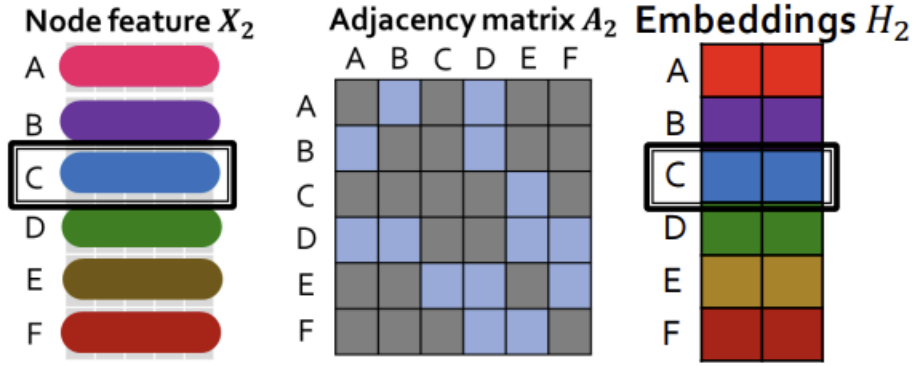
- **Considering all nodes in a graph**, GCN computation is **permutation equivariant**







Permute the input, the output also permutes accordingly - permutation equivariant



https://arxiv.org/abs/1609.02907

Graph Convolution Network (GCN)

Graph Convolution Network (GCN); ICLR 2017

- Node embedding $\boldsymbol{z}_v$ is a function of input graph
- **Supervised setting**: We want to minimize loss $\mathcal{L}$:

$$\min_{\Theta} \mathcal{L}(\boldsymbol{y}, f_{\Theta}(\boldsymbol{z}_v))$$

  - $\boldsymbol{y}$: node label
  - $\mathcal{L}$ could be L2 if $\boldsymbol{y}$ is real number, or cross entropy if $\boldsymbol{y}$ is categorical
- **Unsupervised setting:**
  - No node label available
  - **Use the graph structure as the supervision!**

Graph Neural Network

Standard GNN Pipeline:

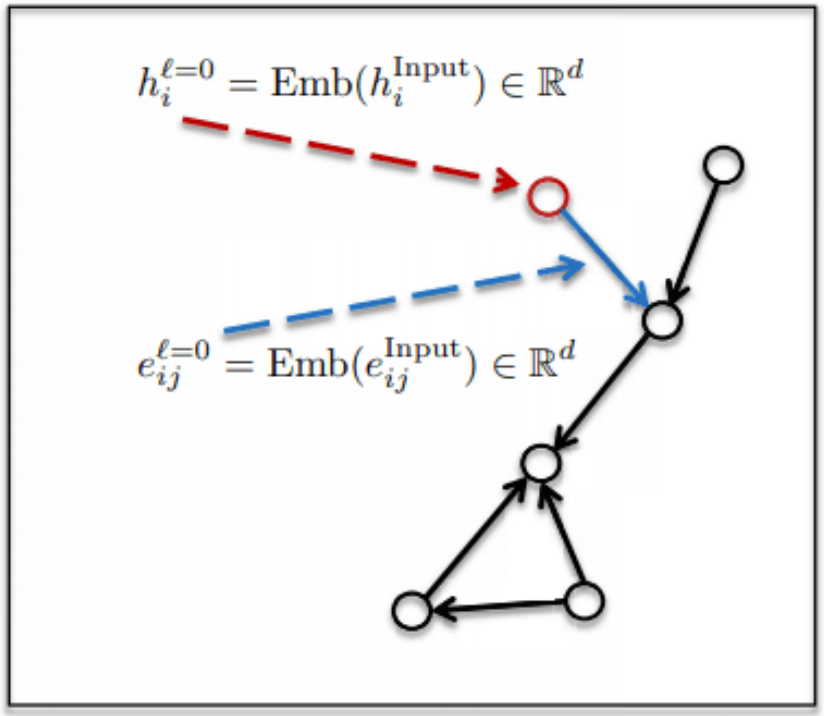
- Input Layer: Linear embedding of input node/edge features.
- GNN Layers: Apply favorite GNN layer L times.
- Task-based layer : Graph/node/edge prediction layer.

Graph Neural Network

- Input layer :

$$h^{\text{Input}}$$
$$e^{\text{Input}}$$

$\Rightarrow$



$\Rightarrow$

$$h^{\ell=0} \in \mathbb{R}^{n \times d}$$
$$e^{\ell=0} \in \mathbb{R}^{E \times d}$$

Input node/edge features

Embedding layer of input features

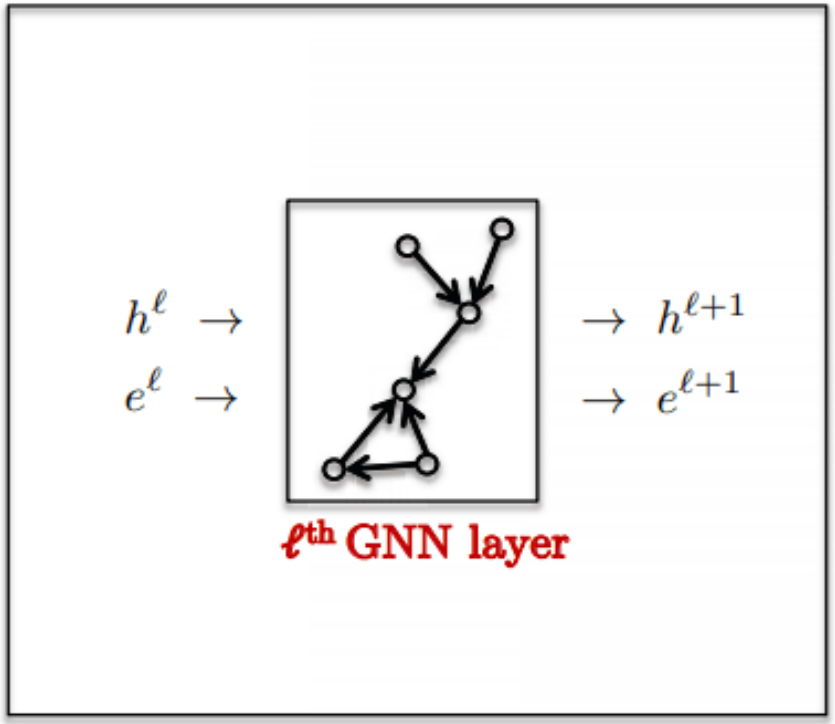
Input features embedded into d-dim spaces, and passes to the GNN layers.

Graph Neural Network

- GNN layers :

$$h^{\ell=0} \in \mathbb{R}^{n \times d}$$
$$e^{\ell=0} \in \mathbb{R}^{E \times d}$$

$\Rightarrow$



$\Rightarrow$

$$h^{\ell=L} \in \mathbb{R}^{n \times d}$$
$$e^{\ell=L} \in \mathbb{R}^{E \times d}$$

Input of GNNs indexed by $\ell=0$.

GNN layers applied L times

Output of GNNs indexed by $\ell=L$.

Graph Neural Network

- Task-based layer
  - Graph-level prediction :

$$h^{\mathcal{G}} = \frac{1}{n}\sum_{i=0}^{n} h_i^{\ell=L} \in \mathbb{R}^d \quad \Rightarrow \quad \boxed{\text{MLP}} \quad \Rightarrow \quad \text{score} \in \begin{cases} \mathbb{R} & \text{regression} \\ \mathbb{R}^K, \ K > 1 & \text{classification} \end{cases}$$

  - Node-level prediction :

$$h_i^{\ell=L} \in \mathbb{R}^d \quad \Rightarrow \quad \boxed{\text{MLP}} \quad \Rightarrow \quad \text{score}_i \in \begin{cases} \mathbb{R} & \text{regression} \\ \mathbb{R}^K, \ K > 1 & \text{classification} \end{cases}$$

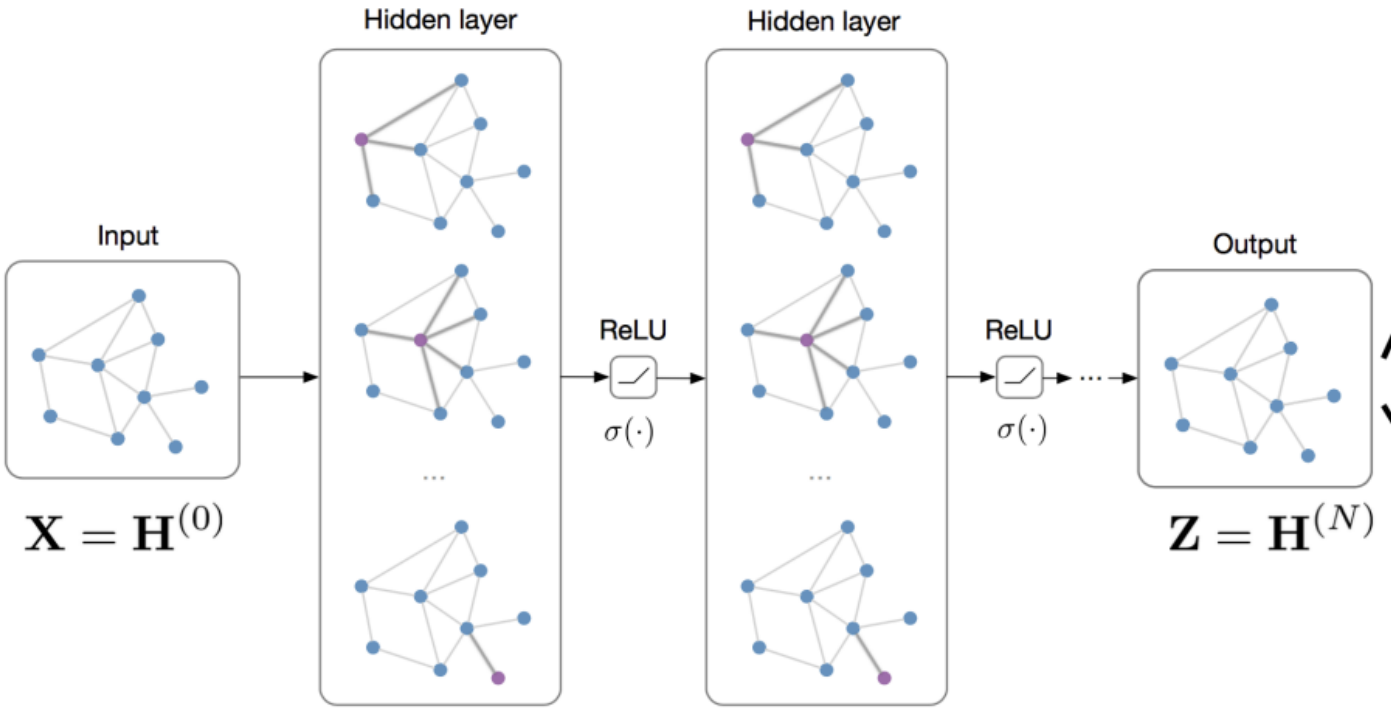
  - Edge-level prediction :

$$e_{ij}^{\text{link}} = \text{Concat}(h_i^{\ell=L}, h_j^{\ell=L}) \in \mathbb{R}^d \quad \Rightarrow \quad \boxed{\text{MLP}} \quad \Rightarrow \quad \text{score}_{ij} \in \begin{cases} \mathbb{R} & \text{regression} \\ \mathbb{R}^K, \ K > 1 & \text{classification} \end{cases}$$

Graph Neural Network

Classification and **Link Prediction** with GNNs / GCNs

Input: Feature matrix $\mathbf{X} \in \mathbb{R}^{N \times E}$, preprocessed adjacency matrix $\hat{\mathbf{A}}$



$$\mathbf{H}^{(l+1)} = \sigma\left(\hat{\mathbf{A}}\mathbf{H}^{(l)}\mathbf{W}^{(l)}\right)$$

Node classification:

$\mathrm{softmax}(\mathbf{z_n})$

e.g. Kipf & Welling (ICLR 2017)

Graph classification:

$\mathrm{softmax}(\sum_n \mathbf{z_n})$

e.g. Duvenaud et al. (NIPS 2015)

Link prediction:

$p(A_{ij}) = \sigma(\mathbf{z_i^T z_j})$

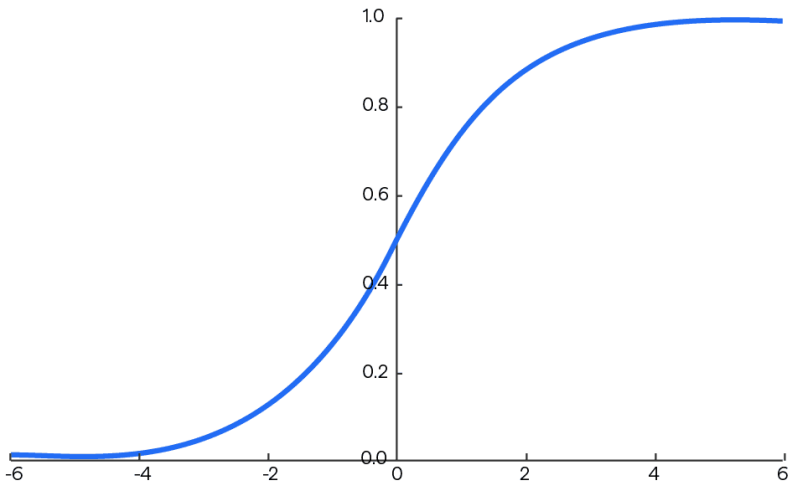
Kipf & Welling (NIPS BDL 2016)

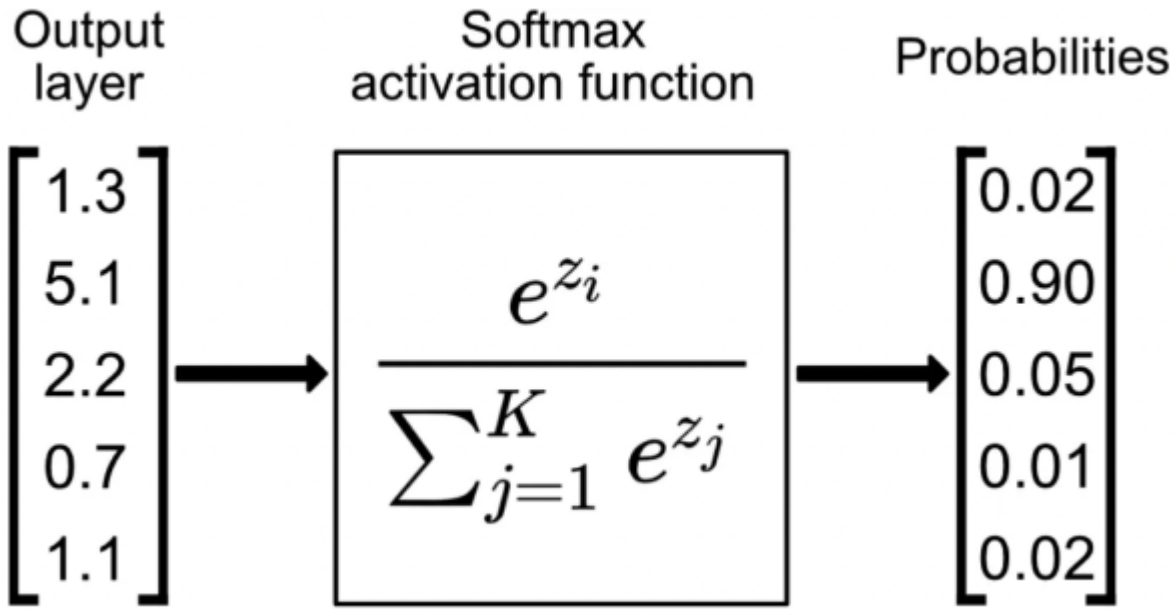
"Graph Auto-Encoders"

* slide from Thomas Kipf, **University of Amsterdam**

Graph Neural Network

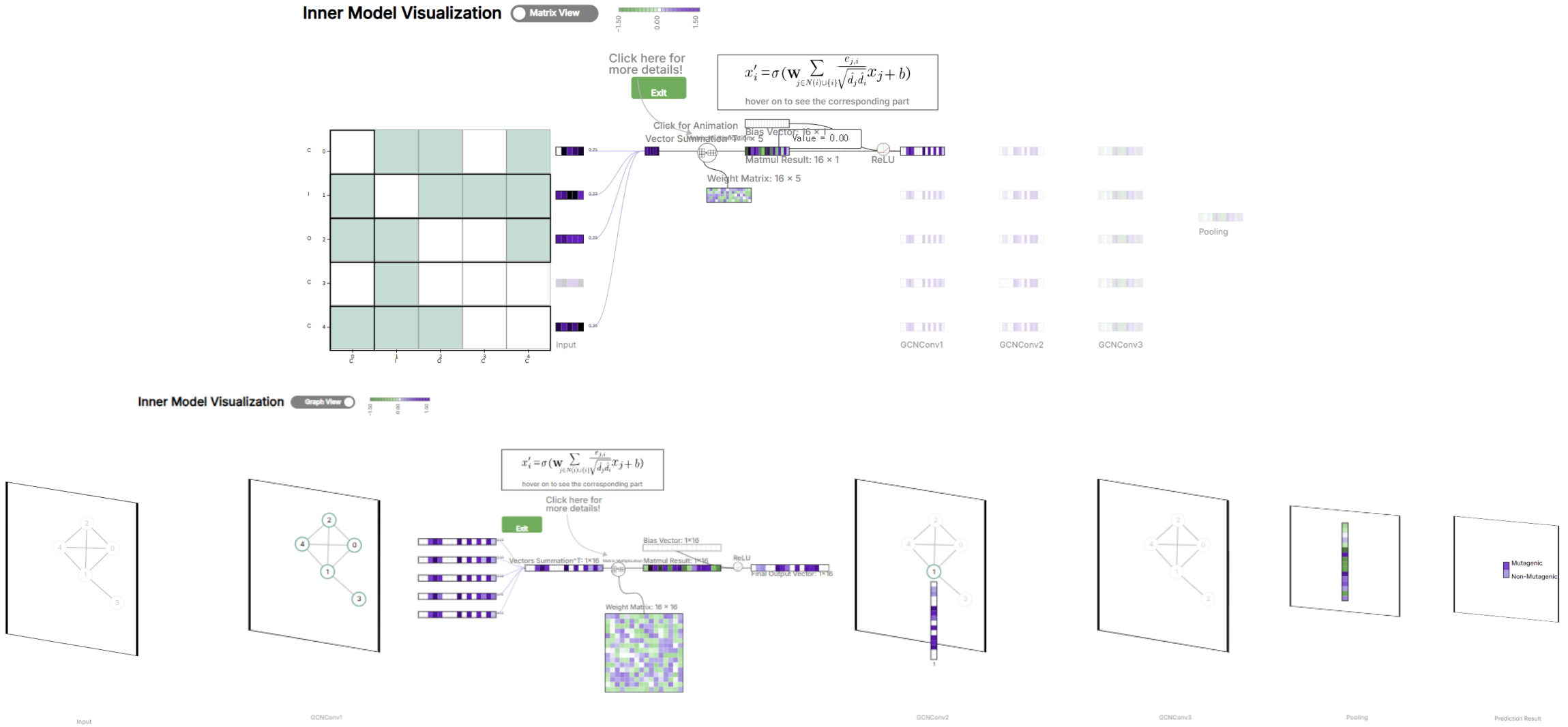
Softmax Function





Graph Neural Network

Visual Learning of Graph Neural Networks in Your Web Browser:
https://visual-intelligence-umn.github.io/GNN-101/ (Model-Task: GCN – graph classification(Sandbox))



Graph Attention Network (GAT)

Graph Attention Network (GAT); ICLR 2018

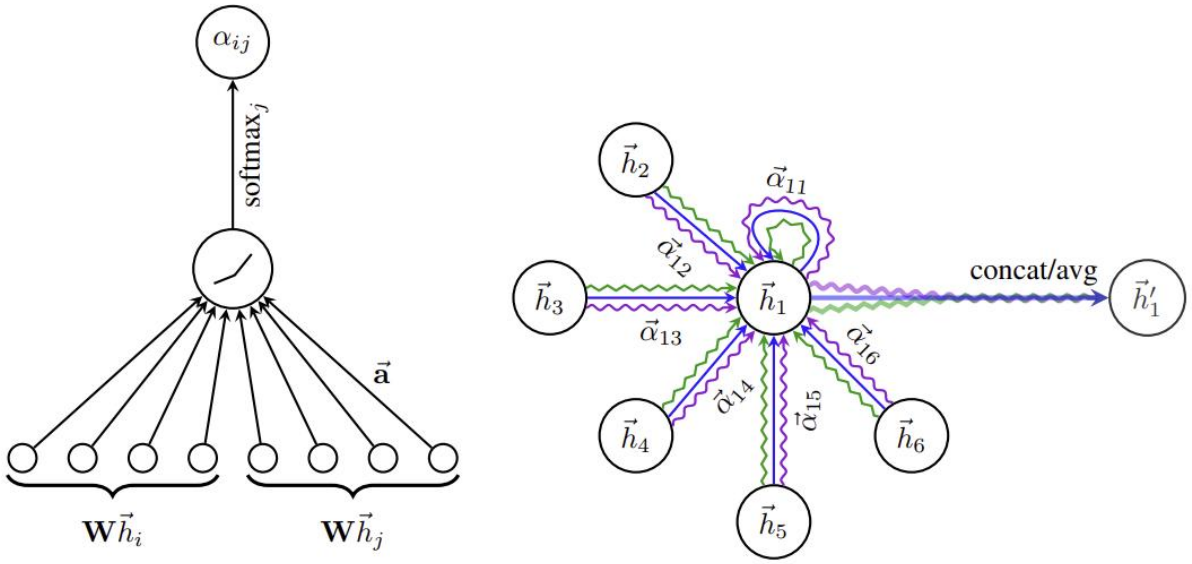


Table 2: Summary of results in terms of classification accuracies, for Cora, Citeseer and Pubmed. GCN-64* corresponds to the best GCN result computing 64 hidden features (using ReLU or ELU).

	Transductive		
Method	**Cora**	**Citeseer**	**Pubmed**
MLP	55.1%	46.5%	71.4%
ManiReg (Belkin et al., 2006)	59.5%	60.1%	70.7%
SemiEmb (Weston et al., 2012)	59.0%	59.6%	71.7%
LP (Zhu et al., 2003)	68.0%	45.3%	63.0%
DeepWalk (Perozzi et al., 2014)	67.2%	43.2%	65.3%
ICA (Lu & Getoor, 2003)	75.1%	69.1%	73.9%
Planetoid (Yang et al., 2016)	75.7%	64.7%	77.2%
Chebyshev (Defferrard et al., 2016)	81.2%	69.8%	74.4%
GCN (Kipf & Welling, 2017)	81.5%	70.3%	**79.0%**
MoNet (Monti et al., 2016)	81.7 ± 0.5%	—	78.8 ± 0.3%
GCN-64*	81.4 ± 0.5%	70.9 ± 0.5%	**79.0** ± 0.3%
GAT (ours)	**83.0** ± 0.7%	**72.5** ± 0.7%	**79.0** ± 0.3%

$$\vec{h}'_i = \sigma\left(\frac{1}{K}\sum_{k=1}^{K}\sum_{j\in\mathcal{N}_i}\alpha_{ij}^k\mathbf{W}^k\vec{h}_j\right)$$

$$e_{ij} = a(\mathbf{W}\vec{h}_i, \mathbf{W}\vec{h}_j)$$

$$\alpha_{ij} = \text{softmax}_j(e_{ij}) = \frac{\exp(e_{ij})}{\sum_{k\in\mathcal{N}_i}\exp(e_{ik})}$$

$$\alpha_{ij} = \frac{\exp\left(\text{LeakyReLU}\left(\vec{\mathbf{a}}^T[\mathbf{W}\vec{h}_i\|\mathbf{W}\vec{h}_j]\right)\right)}{\sum_{k\in\mathcal{N}_i}\exp\left(\text{LeakyReLU}\left(\vec{\mathbf{a}}^T[\mathbf{W}\vec{h}_i\|\mathbf{W}\vec{h}_k]\right)\right)}$$

- **In GCN / GraphSAGE**
  - $\alpha_{vu} = \frac{1}{|N(v)|}$ is the **weighting factor (importance)** of node u's message to node v
  - $\Longrightarrow \alpha_{vu}$ is defined **explicitly** based on the structural properties of the graph (node degree)
  - $\Longrightarrow$ All neighbors $u \in N(v)$ are equally important to node v

https://arxiv.org/abs/1710.10903

Graph Isomorphism Networks (GIN)

Graph Isomorphism Networks (GIN); ICLR 2019

$$h_i^{(l+1)} = \mathrm{MLP}^{(l)}\left((1+\epsilon^{(l)})\,h_i^{(l)} + \sum_{j\in\mathcal{N}(i)} h_j^{(l)}\right)$$

$$h_i^{(l+1)} = \phi^{(l)}\left(h_i^{(l)},\ \square_{j\in\mathcal{N}(i)}\psi^{(l)}(h_i^{(l)}, h_j^{(l)})\right)$$

모델	$\square$	ψ	ϕ
GCN	sum	고정 계수 × Wh_j	σ
GIN	sum	h_j	MLP
GAT	weighted sum	attention × Wh_j	σ

https://arxiv.org/abs/1810.00826

Graph Representation of Molecules

- SMILES Representation
- RDKit

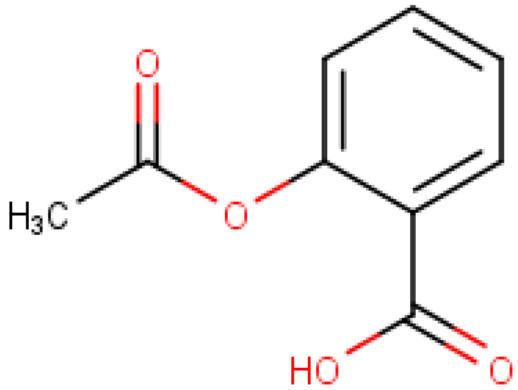
SMILES Representation

SMILES (Simplified Molecular Input Line Entry System)

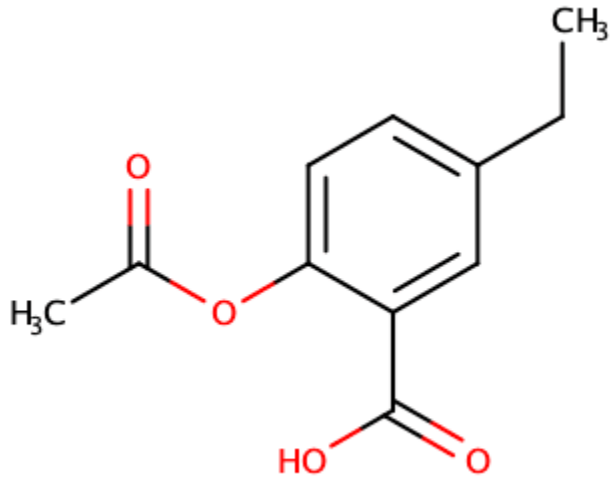
분자 구조를 '문자열 형태'로 표현하는 표기법.

Example)

Aspirin (or O-Acetylsalicylic acid)



CC(=O)OC1=CC=CC=C1C(O)=O



CCC1=CC=C(OC(C)=O)C(=C1)C(O)=O

https://hyperlab.hits.ai/blog/SMILES-Part-1

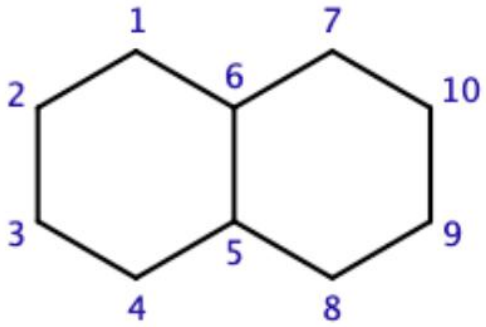
SMILES Representation

SMILES를 구성하는 5가지 요소

1) 원자 (atom)
각 원소는 고유 기호로 표기되니다.
단, 표기를 간단하게 하기 위해 수소는 생략됩니다.

3) 고리 (ring)
고리 구조는 고리가 시작되는 원자를 기준으로 반시계 방향으로 돌아가며 표기합니다.
이때, 고리의 시작 원자와 마지막 원자에는 동일한 숫자를 표시하여 고리의 연결을 나타냅니다.

ex) C1CCCC2C1CCCC2



2) 결합 (bond)

.	결합되지 않음	$	사중결합
-	단일결합	:	방향족결합
=	이중결합	/	입체화학 표시
#	삼중결합	\	입체화학 표시

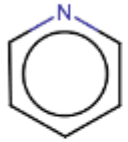
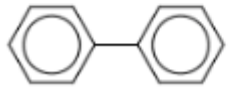
분자	SMILES
$H_2C{=}CH_2$	C=C
$H_3C{-}Br$	CBr
$HC{\equiv}N$	C#N
	F/C=C\F

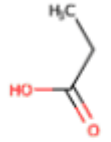
https://hyperlab.hits.ai/blog/SMILES-Part-1

SMILES Representation

4) 방향족 (aromaticity)
벤젠과 같은 방향족 고리들을 아래와 같이 표현할 수 있습니다.

i) C1=CC=CC=C1 → 단일결합과 이중결합이 교대로 일어나는 Kekule form
ii) C:1:C:C:C:C:C1 → 방향족결합 기호(:)를 사용
iii) c1ccccc1 → 방향족 고리에 포함된 B, C, N, O, P, S 원자를 소문자로 표시합니다.

분자	SMILES
	n1cccc1 (pyridine)
	o1cccc1 (furan)
	c1ccccc1-c2ccccc2 (biphenyl)

분자	SMILES
	CCC(=O)O (propionic acid)
	FC(F)F (fluoroform)
	FC(Br)(Cl)F, BrC(F)(F)Cl, C(F)(Cl)(F)Br, ...

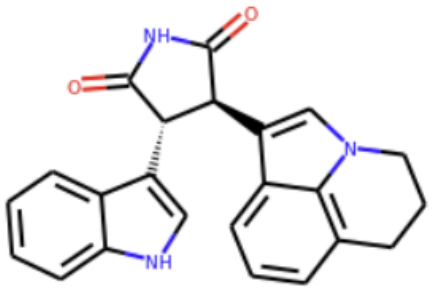
5) 가지 (branch)
분자의 가지는 괄호()로 표현합니다.
가지는 다양한 순서로 나타낼 수 있으며,
결합 역시 괄호 안에 포함되어야 합니다.

RDKit

RDKit: 파이썬 라이브러리를 활용하는 분자식 표현 오픈소스 프로그램

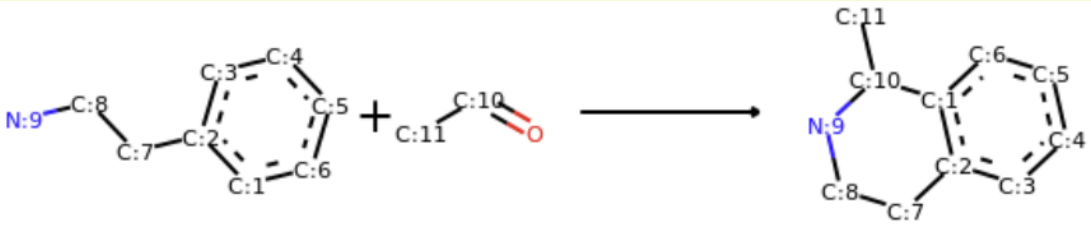
```
from rdkit import Chem
from rdkit.Chem.Draw import IPythonConsole
from rdkit.Chem import Draw
IPythonConsole.ipython_useSVG=True  #< set this to False if you want PNGs instead of SVGs
```

```
# Test in a kinase inhibitor
mol = Chem.MolFromSmiles("C1CC2=C3C(=CC=C2)C(=CN3C1)[C@H]4[C@@H](C(=O)NC4=O)C5=CNC6=CC=CC=C65")
# Default
mol
```



Open-Source Cheminformatics and Machine Learning

```
# Pictet-Spengler rxn
rxn = AllChem.ReactionFromSmarts('[cH1:1]1:[c:2](-[CH2:7]-[CH2:8]-[NH2:9]):[c:3]:[c:4]:[c:5]:[c:6]:1.[#6:11]-
[CH1;R0:10]=[OD1]>>[c:1]12:[c:2](-[CH2:7]-[CH2:8]-[NH1:9]-[C:10]-2(-[#6:11])):[c:3]:[c:4]:[c:5]:[c:6]:1')
rxn
```



- https://www.rdkit.org/
- https://www.rdkit.org/docs/Cookbook.html

Training GNN models

- Implementation of GCN model
- Paper Review: MolCLR
- Pre-Training / Fine-Tuning (Transfer Learning)
- Self-Supervised Learning

Implementation of GCN

Train your own GNN model

In the first glimpse of PyG, we implement the training of a GNN for classifying papers in a citation graph. For this, we load the Cora dataset, and create a simple 2-layer GCN model using the pre-defined `GCNConv`:

```python
import torch
from torch import Tensor
from torch_geometric.nn import GCNConv
from torch_geometric.datasets import Planetoid

dataset = Planetoid(root='.', name='Cora')

class GCN(torch.nn.Module):
    def __init__(self, in_channels, hidden_channels, out_channels):
        super().__init__()
        self.conv1 = GCNConv(in_channels, hidden_channels)
        self.conv2 = GCNConv(hidden_channels, out_channels)

    def forward(self, x: Tensor, edge_index: Tensor) -> Tensor:
        # x: Node feature matrix of shape [num_nodes, in_channels]
        # edge_index: Graph connectivity matrix of shape [2, num_edges]
        x = self.conv1(x, edge_index).relu()
        x = self.conv2(x, edge_index)
        return x

model = GCN(dataset.num_features, 16, dataset.num_classes)
```

- https://github.com/pyg-team/pytorch_geometric/tree/master?tab=readme-ov-file

Implementation of GCN

▼ We can now optimize the model in a training loop, similar to the standard PyTorch training procedure.

```python
import torch.nn.functional as F

data = dataset[0]
optimizer = torch.optim.Adam(model.parameters(), lr=0.01)

for epoch in range(200):
    pred = model(data.x, data.edge_index)
    loss = F.cross_entropy(pred[data.train_mask], data.y[data.train_mask])

    # Backpropagation
    optimizer.zero_grad()
    loss.backward()
    optimizer.step()
```

More information about evaluating final model performance can be found in the corresponding example.

- https://github.com/pyg-team/pytorch_geometric/tree/master?tab=readme-ov-file

Implementation of GCN

https://pytorch-geometric.readthedocs.io/en/2.5.2/_modules/torch_geometric/nn/conv/gcn_conv.html#GCNConv

Paper Review: MolCLR

MolCLR; NMI 2022

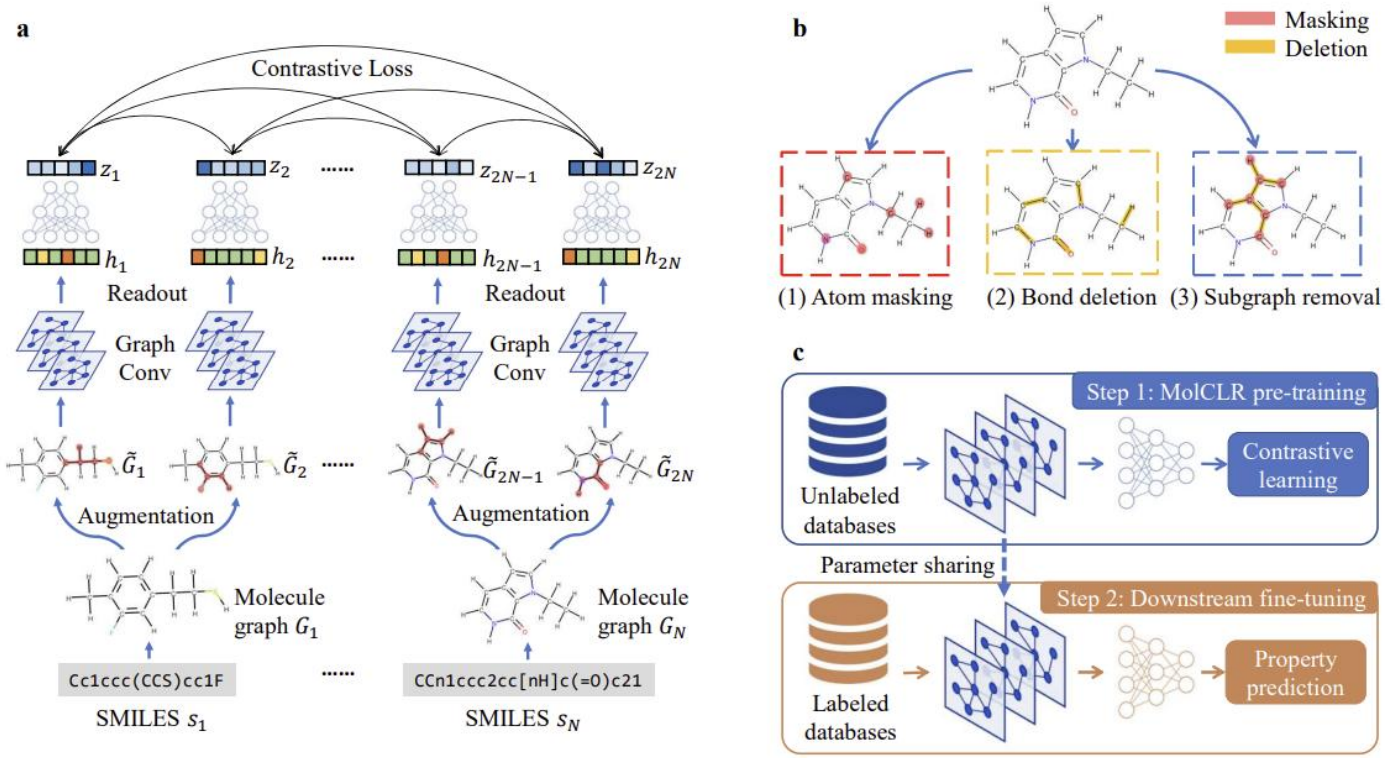


Figure 1. Overview of MolCLR. (a) MolCLR pre-training: A SMILES s_n from a mini-batch of N molecule data is converted to a molecule graph G_n. Two stochastic molecule graph data augmentation operators are applied to each graph, resulting two correlated masked graphs: $\tilde{G}_{2n-1}$ and $\tilde{G}_{2n}$. A base feature encoder built upon graph convolutions and the readout operation extracts the representation h_{2n-1}, h_{2n}. Contrastive loss is utilized to maximize agreement between the latent vectors z_{2n-1}, z_{2n} from the MLP projection head. (b) Molecule graph augmentation strategies: atom masking, bond deletion, and subgraph removal. (c) The whole MolCLR framework: GNNs are first pre-trained via MolCLR to learn representative features. Fine-tuning for downstream molecular property predictions shares the pre-trained parameters of the GNN encoder and randomly initializes an MLP head. It then follows the supervised learning to train the model.

`Cc1ccc(CCS)cc1F` ..... `CCn1ccc2cc[nH]c(=O)c21`

SMILES s_1 SMILES s_N

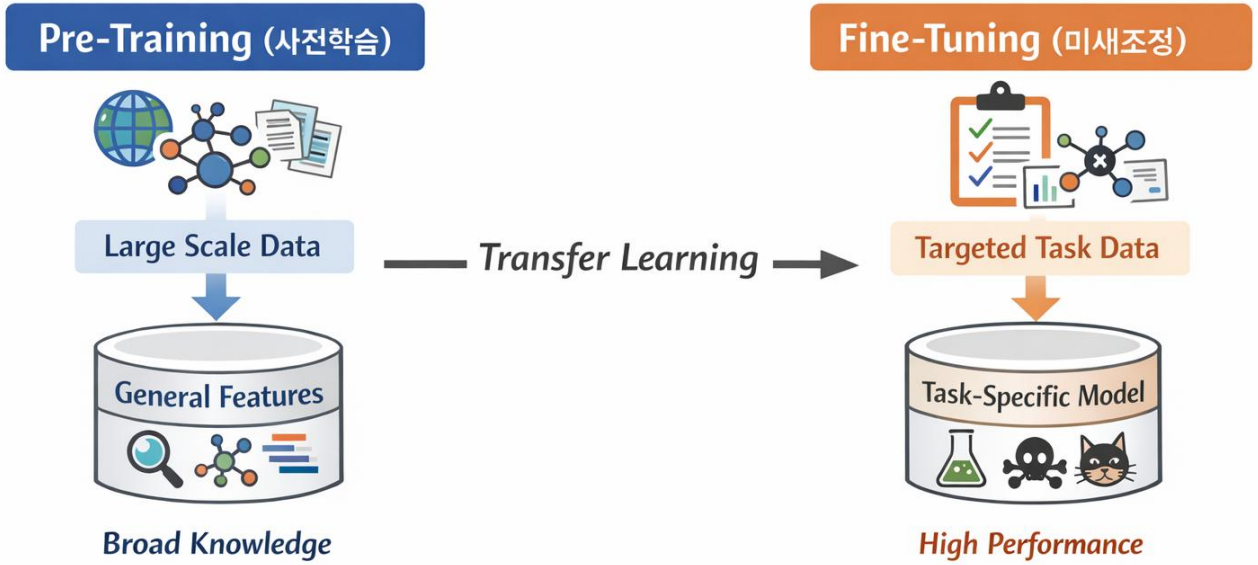
https://github.com/yuyangw/MolCLR

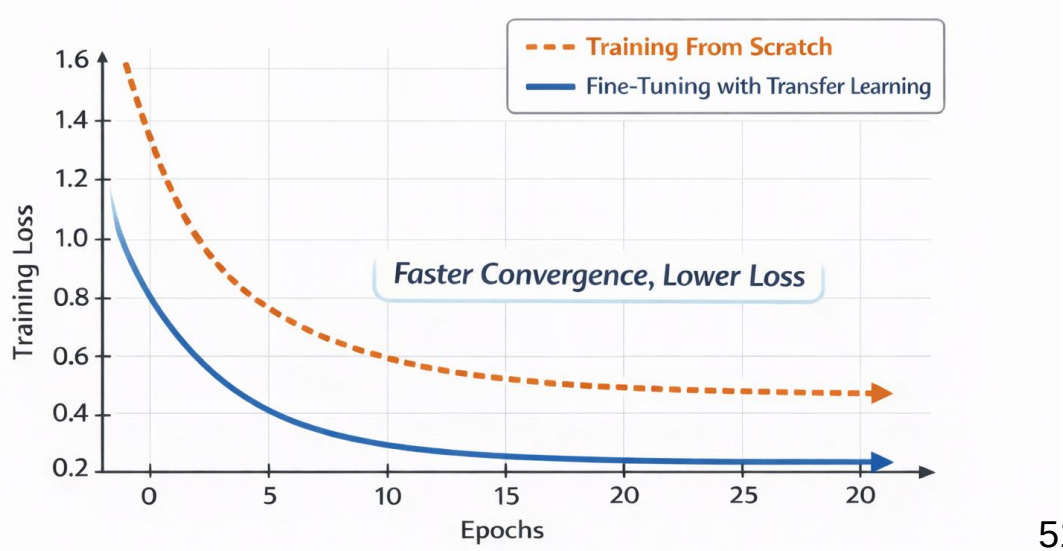
Pre-Training / Fine-Tuning (Transfer Learning)

Pre-Training (사전학습)
- 대규모 데이터에서 모델이 일반적인 표현 (Representation) 을 학습
- 레이블이 없거나 약한 경우가 많음 (Self-Supervised / Contrastive Learning 등)
- 목적: 문제 일반에 유용한 feature extractor 학습
- 예시:
  - 분자 ML: 대량의 SMILES/그래프로 분자 표현 학습
  - NLP: 대규모 텍스트로 언어 구조 학습

Fine-Tuning (미세조정)
- 작은 규모의 타깃 데이터에 대해 모델을 문제 특화로 조정
- Pre-trained 모델의 파라미터를 초기값으로 사용
- 목적: 특정 태스크 성능 극대화
- 예시:
  - 분자 ML: 독성 예측, HOMO–LUMO gap 예측 등
  - 이미지: 특정 클래스 분류

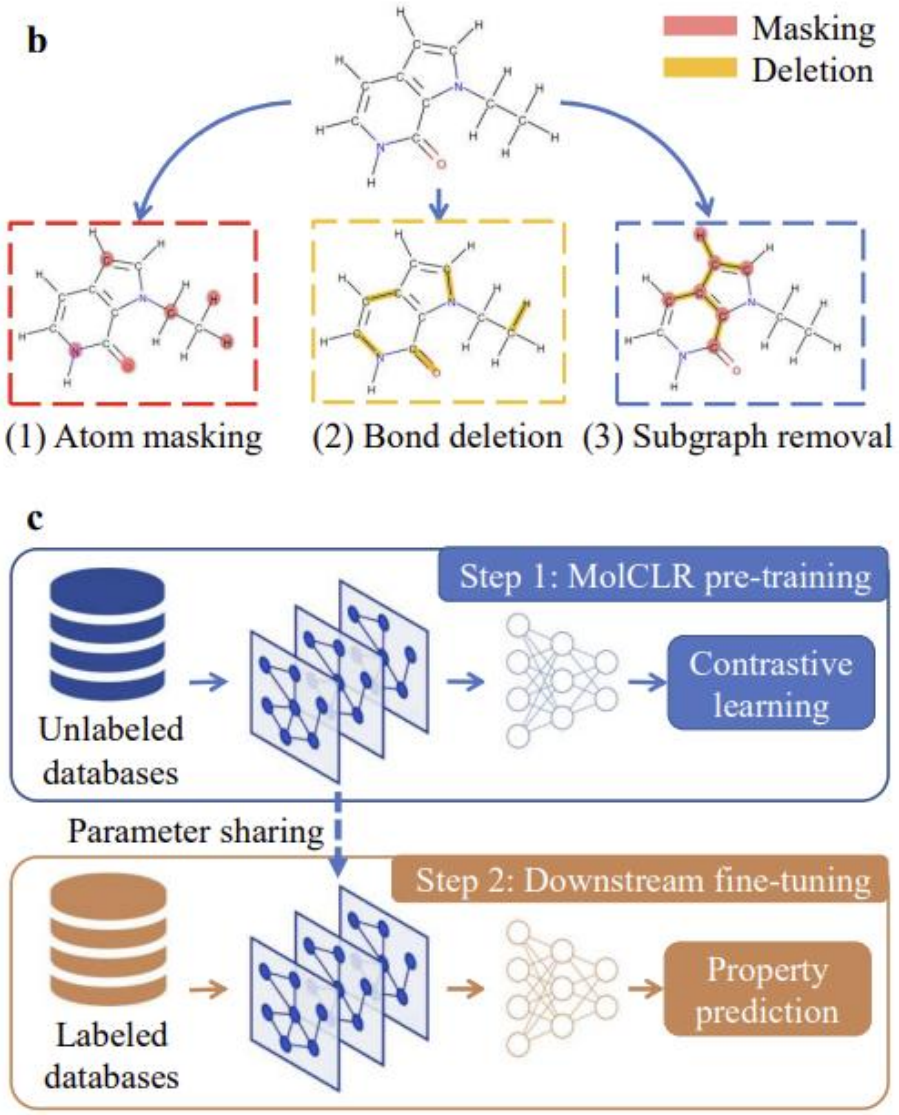
왜 Transfer Learning을 쓰는가?
- 적은 데이터에서도 높은 성능
- 학습 시간 단축
- 일반화 성능 향상

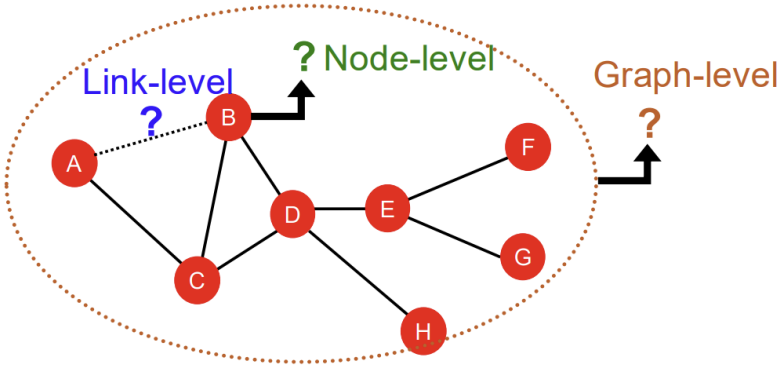




Self-Supervised Learning

MolCLR; NMI 2022





Self-Supervised Learning이란?

- 레이블이 없는 데이터(x only) 로부터 학습 목표(pseudo-label) 를 만들어 학습하는 방법
- 목적: 일반적이고 재사용 가능한 표현(Representation) 학습

☞ *"Label 없이 supervised learning처럼 학습한다"*

Contrastive Learning

- 같은 데이터의 다른 view는 **가깝게**
- 다른 데이터는 **멀게**

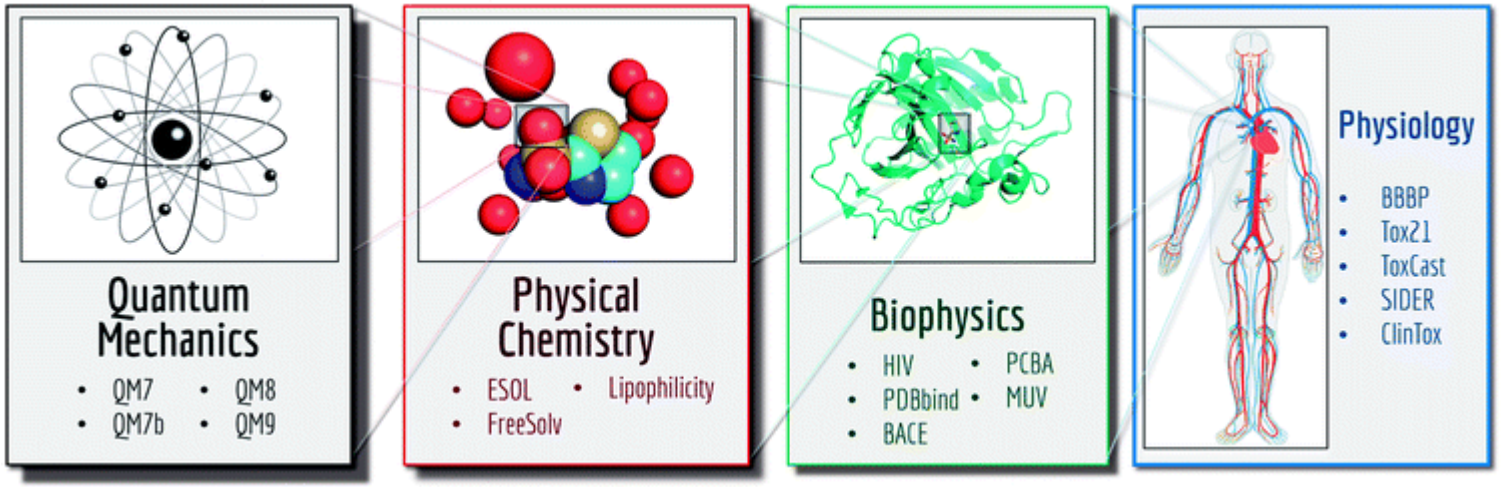
$$\mathcal{L}_{\text{contrastive}} = -\log \frac{\exp(\text{sim}(z_i, z_i^+)/\tau)}{\sum_j \exp(\text{sim}(z_i, z_j)/\tau)}$$

https://github.com/yuyangw/MolCLR

MoleculeNet

MoleculeNet: *"분자 머신러닝 모델을 공정하게 비교하기 위한 표준 벤치마크 모음"*
(*Wu et al., MoleculeNet, Chem. Sci. 2018*)

- 입력: **SMILES**
- 출력: **물성(property)**
- Task: regression 또는 classification



1) Classification Datasets (Metric: ROC-AUC)

Dataset	# Molecules	Prediction Target	Chemical / Practical Meaning
BBBP	~2,039	Blood–Brain Barrier permeability	약물이 혈뇌장벽(BBB)을 투과할 수 있는지 예측 (CNS 약물 설계
BACE	~1,513	β-secretase 1 inhibitio	
ClinTox	~1,478	Clinical toxicity / FDA approval	
SIDER	~1,427	Drug side effects (mul	
HIV	~41,127	Anti-HIV activity	

2) Regression Datasets

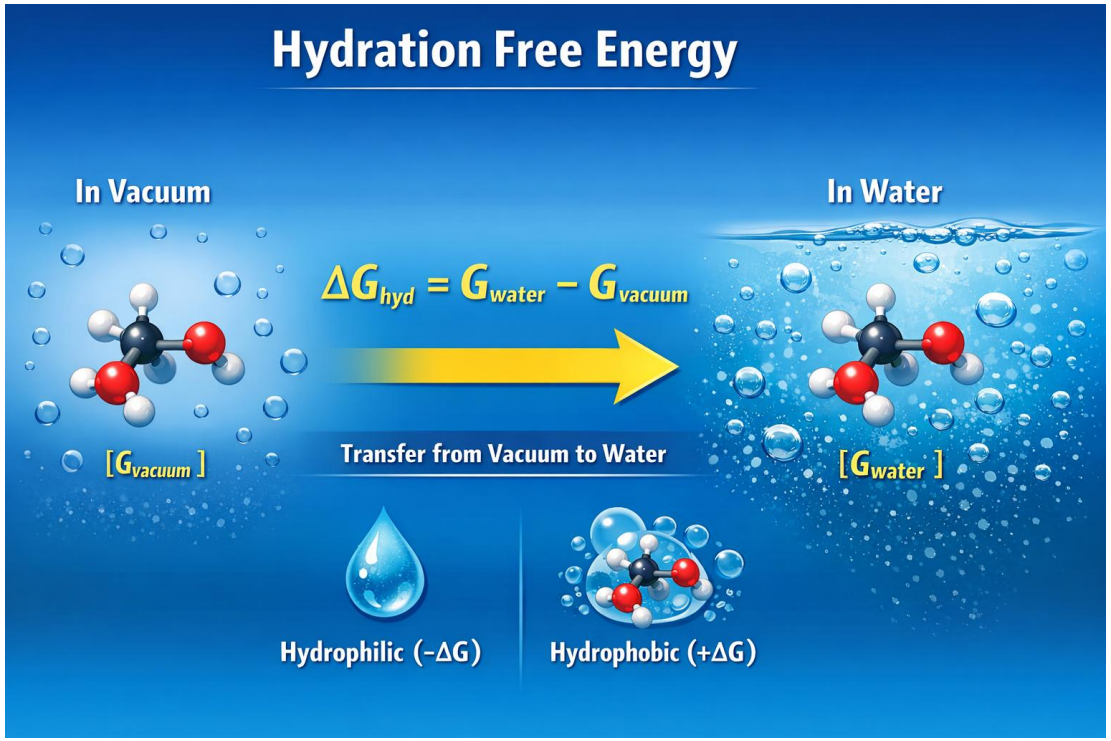
Dataset	# Molecules	Prediction Target	Chemical / Physical Meaning
ESOL	~1,128	Aqueous solubility (logS)	분자의 물에 대한 용해도 (약물 흡수/분포에 중요)
FreeSolv	~642	Hydration free energy	물 속에서의 자유에너지 변화 (용매화 특성)
Lipophilicity	~4,200	Octanol/water logD	분자의 소수성/친수성 균형 (막 투과성, ADMET 관련)
QM9	~133,000	Quantum mechanical properties	HOMO/LUMO 에너지, dipole moment 등 양자화학적 성질

https://pubs.rsc.org/en/content/articlelanding/2018/sc/c7sc02664a

MoleculeNet – FreeSolv

What is Hydration Free Energy (수화 자유에너지)?
분자를 **진공** → **물**로 옮길 때의 자유에너지 변화 (단위: **kcal/mol**).
물과의 친화도를 정량적으로 나타내는 물리량.

- 더 음수 → 더 친수성 (물에 잘 용해)
- 덜 음수 / 양수 → 소수성 (물에 잘 용해되지 않음)



Why is it important?
대부분의 **화학·생체 과정은 물 속**에서 일어남.
다음 물성들의 **기준(reference)** 역할:

- 용해도 (Solubility)
- 분배계수 (logP / logD)
- 생체 이용성 (Bioavailability)

Why FreeSolv?

- **실험 기반** hydration free energy 데이터
- 소규모 데이터셋 (~640 molecules)
- 단순한 입력 (SMILES) vs **복합적인 물리 효과**
  - 극성, 수소결합, 분자 크기

분자 representation의 중요성을 잘 드러내는 benchmark

	iupac	smiles	expt	calc
0	4-methoxy-N,N-dimethyl-benzamide	CN(C)C(=O)c1ccc(cc1)OC	-11.01	-9.625
1	methanesulfonyl chloride	CS(=O)(=O)Cl	-4.87	-6.219
2	3-methylbut-1-ene	CC(C)C=C	1.83	2.452
3	2-ethylpyrazine	CCc1cnccn1	-5.45	-5.809
4	heptan-1-ol	CCCCCCCO	-4.21	-2.917

코드 실습

Github link: https://github.com/jeheon1905/gnn-molecular-ml-tutorial

◆ 가상 환경 (Virtual Environment)

프로젝트마다 **독립된 파이썬 실행 공간**을 만드는 것

왜 필요할까?

- 프로젝트마다 필요한 **라이브러리 버전이 다름**
- 하나의 컴퓨터에서 여러 프로젝트를 **충돌 없이 관리**하기 위해

예시

- 프로젝트 A: numpy 1.26
- 프로젝트 B: numpy 2.0

→ 가상 환경이 없으면 충돌 발생

◆ 라이브러리 (Library)

이미 만들어진 **기능 모음 코드**

왜 사용할까?

- 복잡한 기능을 **직접 만들 필요 없음**
- 더 빠르고, 더 정확하게 개발 가능

예시

- numpy : 수치 계산
- torch : 딥러닝 모델 구현
- rdkit : 분자 구조 처리

코드 실습

Github link: https://github.com/jeheon1905/gnn-molecular-ml-tutorial

```
# 코드 다운로드
git clone https://github.com/jeheon1905/gnn-molecular-ml-tutorial.git
cd gnn-molecular-ml-tutorial

# conda 환경 생성
conda create –y –n gnn-tutorial python=3.10

# 환경 활성화
conda activate gnn-tutorial

# PyTorch & PyG 설치
pip install torch==2.2.2 –index-url https://download.pytorch.org/whl/cpu
pip install “numpy<2.0”
pip install torch_geometric

# Dependencies 설치
conda install -y -c conda-forge rdkit seaborn
pip install scikit-learn==1.4.2 pandas matplotlib

# Jupyter kernel 등록
pip install jupyterlab ipykernel
python -m ipykernel install --user --name gnn-tutorial --display-name "Python (gnn-tutorial)“

# Jupyter lab 실행
jupyter lab notebooks/rdkit_molecular_graph_tutorial.ipynb
```

References

- CS224W: Machine Learning with Graphs
  Stanford / Fall 2025
  https://web.stanford.edu/class/cs224w/
- CSE 849: Deep Learning
  Vishnu Boddeti
  https://hal.cse.msu.edu/teaching/2024-spring-deep-learning/
- Topics in Artificial Intelligence (CPSC 532S): Multimodal Learning with Vision, Language and Sound
  https://www.cs.ubc.ca/~lsigal/532S_2018W2/Lecture18a.pdf
- GNN101: Visual Learning of Graph Neural Networks in Your Web Browser
  https://visual-intelligence-umn.github.io/GNN-101/
  https://www.youtube.com/watch?v=_0jXy4Zoh-o
- RDKit Cookbook
  https://www.rdkit.org/docs/Cookbook.html
- PyG (PyTorch Geometric) example codes:
  MoleculeNet (ESOL) GCN 학습 예제:
  https://github.com/pyg-team/pytorch_geometric/blob/master/examples/attentive_fp.py