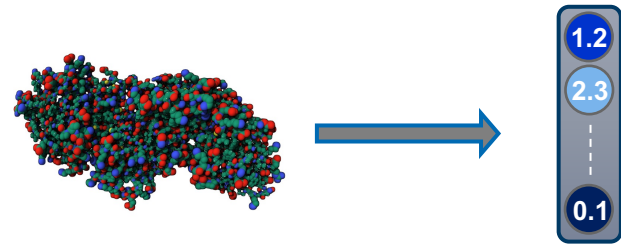# Utilizing protein 3D structures for predictions

3D CNNs for processing protein structures

- We can encode all atoms in a 3D grid (3-dimensional array)
  - Each voxel (analogous to a pixel in a 2D image) stores the information which atom is present at this position
    - One channel for each atom type
      (carbon, nitrogen, sulfur, oxygen, phosphor)
- 3D objects can be processed using convolutional neural networks (CNNs)
  - Similar to CNNs for images
    - Instead of 2D convolutional filters moving along the x- and y-axes, we have 3D filters also moving along the z-axis
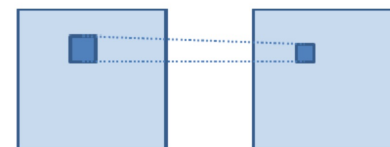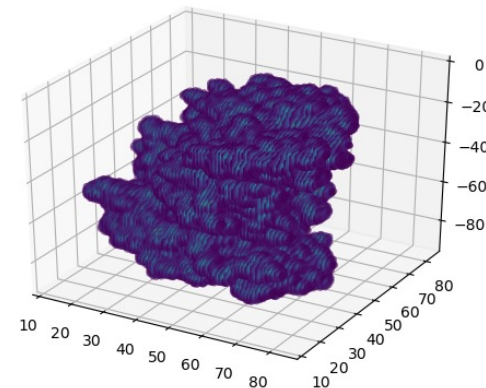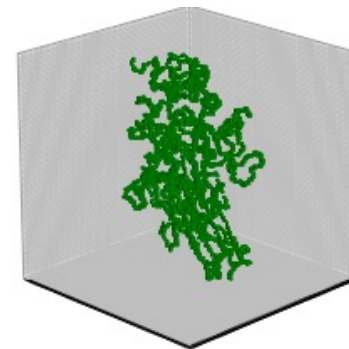

(a) 2D convolution

(b) 3D convolution

hhu.de
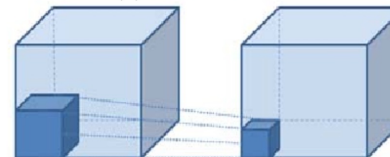
Examples of 3D CNNs for proteins

- Examples for existing 3D CNNs for proteins
    - EnzyNet (2017):
        - Side chain information is ignored
        - 3DCNN for full protein for EC number prediction

    - 3DCNN_MQA (2018):
        - Encodes all atoms in the protein in a 3D grid
        - CNNs for quality assessment of predicted protein structures

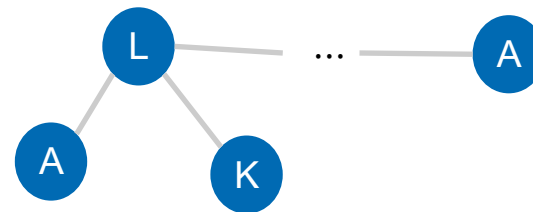# GNNs for processing protein structures (1)

- Transformer Networks are graph neural networks (GNNs)

### Transformer Network
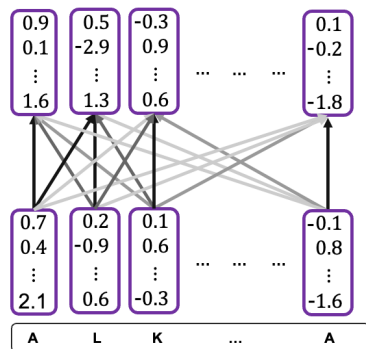
Graph Neural Network

- Transformers are a special type of GNNs
  - Protein Transformers mostly attend to amino acid tokens that are close in the 3D structure
  - We can aid the model in doing this by using a GNN with edges between amino acids that are close in the 3D structure

GNNs for processing protein structures (2)

- Initialization of amino acid representations in GNNs:
  - In principle, node representations could be learned during training
  - We can use representations learned from protein language models
- Examples for protein GNNs for protein function prediction:
  - DeepFRI (2021):
    - LSTM was trained on 10M proteins for masked token prediction
    - GNN nodes initialized with LSTM representations
    - 3-layered GNN: Edges between close amino acids (predicted)

  - ESM-GearNet (2023):
    - Using ESM-2 to compute node presentation for the GNN
    - Using AlphaFold 2 to compute edges between amino acids
    - Architecture: 6 layers of GNN with 512 as hidden dimension
    - Training:
      - Pre-training using contrastive learning
      - Fine-tuned on protein function prediction tasks

hhu.de
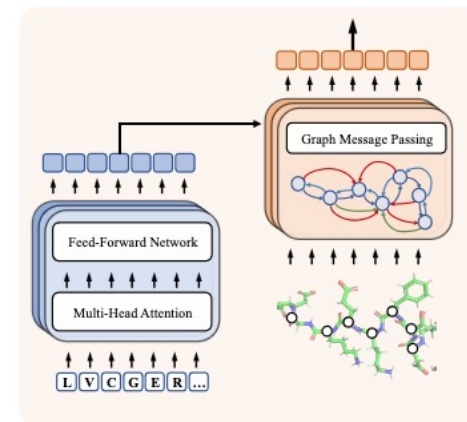
Performance & Limitations

- Performance of GNNs compared to protein language models (PLMs):

Method	PLM	Struct. Info.	EC	GO-BP	GO-MF	GO-CC	PSR	MSP
			F_{max}	F_{max}	F_{max}	F_{max}	Global ρ	AUROC
ProtBERT-BFD[1]	✓	✗	0.838	0.279	0.456	0.408	-	-
ESM-2-650M[1]	✓	✗	0.880	0.460	0.661	0.445	-	-
GearNet	✗	✓	0.730	0.356	0.503	0.414	0.708	0.549
ESM-GearNet								
- w/ serial fusion			**0.890**	**0.488**	**0.681**	0.464	0.829	**0.685**

- Potential limitation:
  - Only encodes proximity between amino acids but not the exact 3D confirmation of all atoms