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Predicting protein-small molecule interactions

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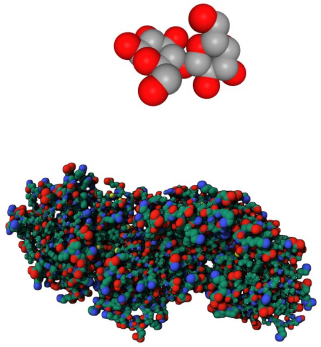
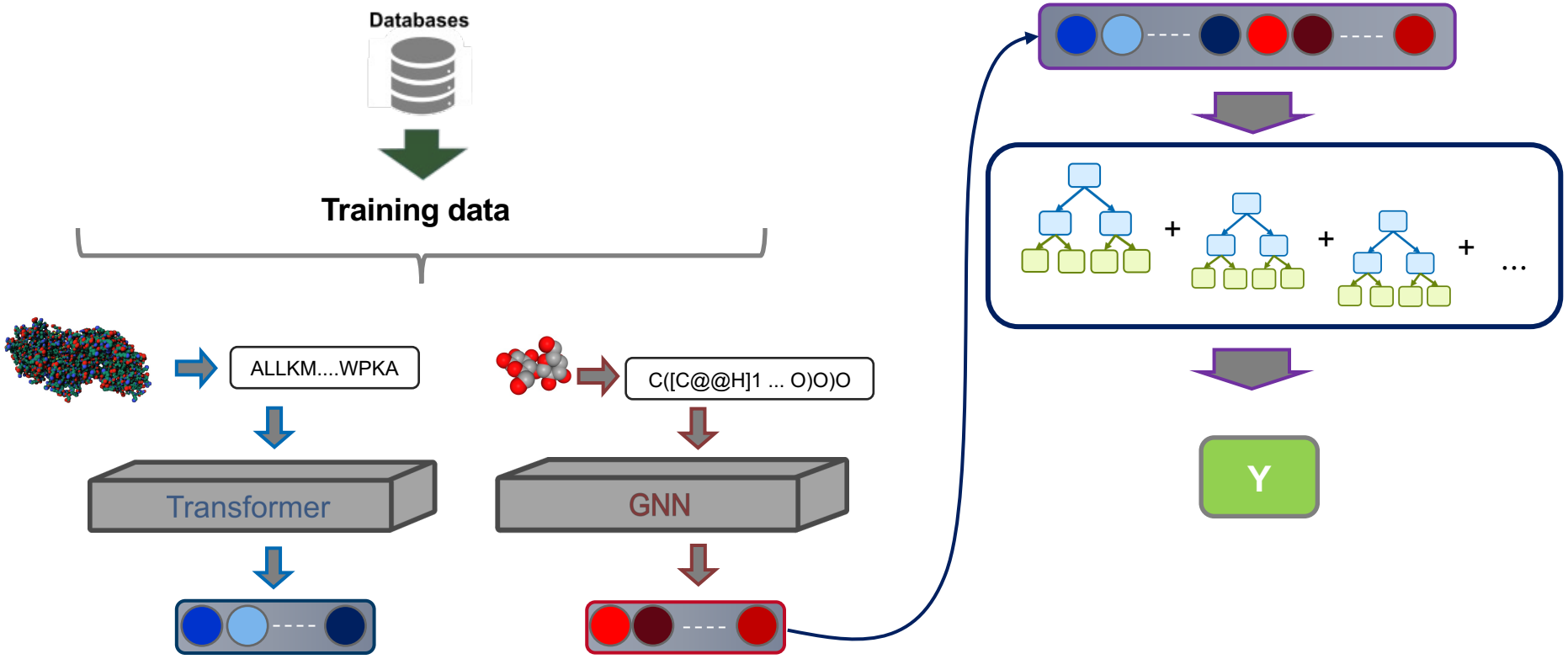


Prediction model

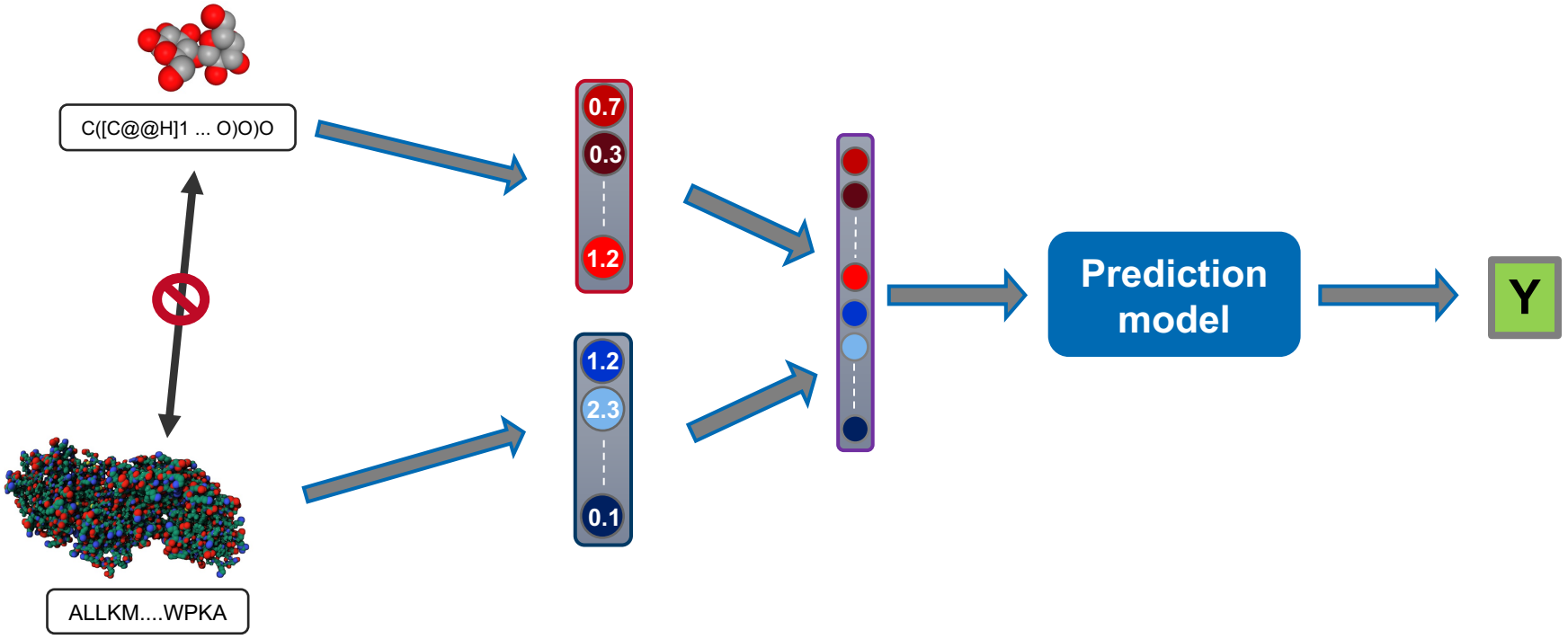
- **Enzyme-substrate pairs**
- **Transporter-substrate pairs**
- **Michaelis constants K_M**
- **Turnover numbers k_{cat}**
- **Drug-Target inhibition**
- **…**

Small molecule image: pubchem.ncbi.nlm.nih.gov/compound/6134#section=3D-Conformer; Protein image generated with: https://www.rcsb.org/3d-view

Typical Prediction Pipeline



Missing Information Exchange



Small molecule image: pubchem.ncbi.nlm.nih.gov/compound/6134#section=3D-Conformer; Protein image generated with: https://www.rcsb.org/3d-view

Multimodal Transformer Networks (1)

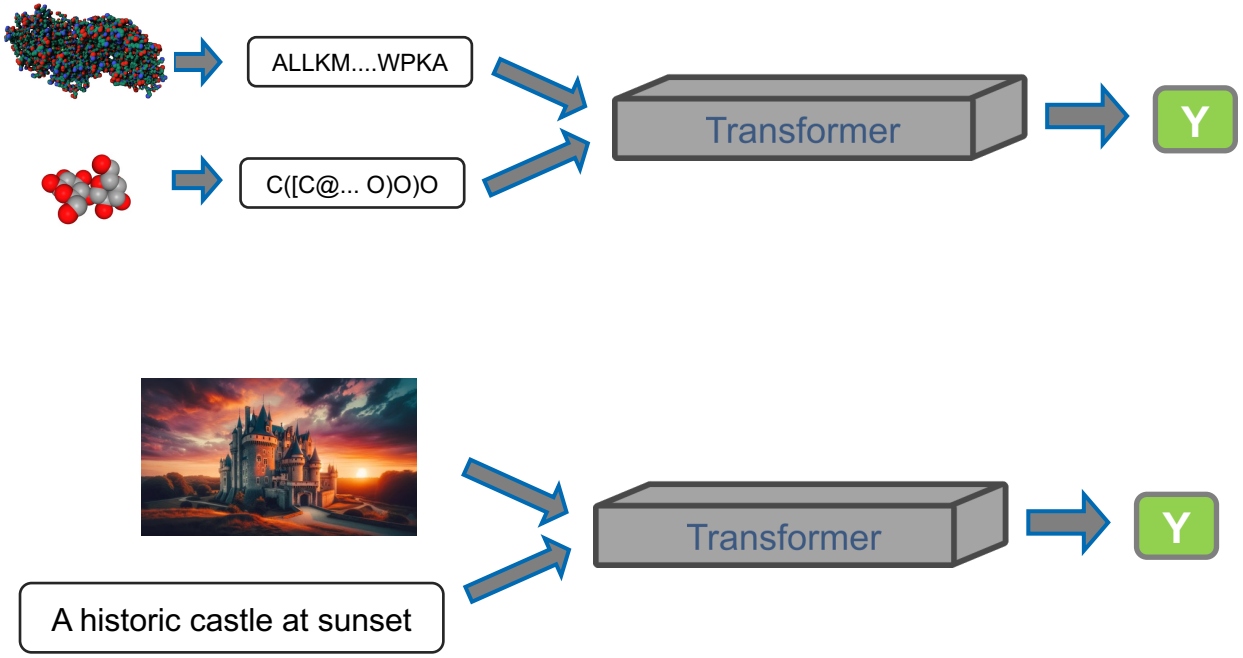
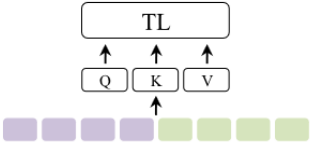


Image generated with DALL-E

Multimodal Transformer Networks (2)

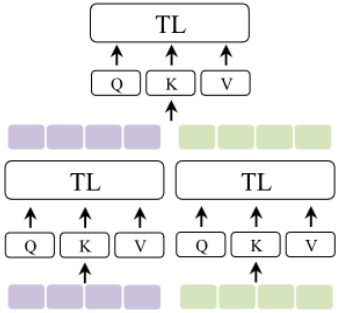
= 1st input type/modality (e.g., text or protein)

= 2nd input type/modality (e.g., image or small molecule)



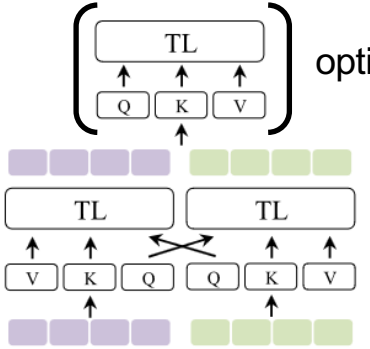
Concatenating both initial input sequences

- Generating a joint vocabulary for tokens of both input types
- Concatenated sequences is input for single Transformer



Concatenating sequence embeddings after separate processing

- Each input sequence is input of separate Transformer layers
- Resulting embeddings are used as the input of shared Transformer layers



Cross-attention between both sequences

- Using embeddings from other input type to calculate attention scores
- No self-attention

Xu, P., Zhu, X., & Clifton, D. A. (2023). Multimodal learning with transformers: A survey. IEEE Transactions on Pattern Analysis and Machine Intelligence.

ProSmith – Protein-Small Molecule Transformer

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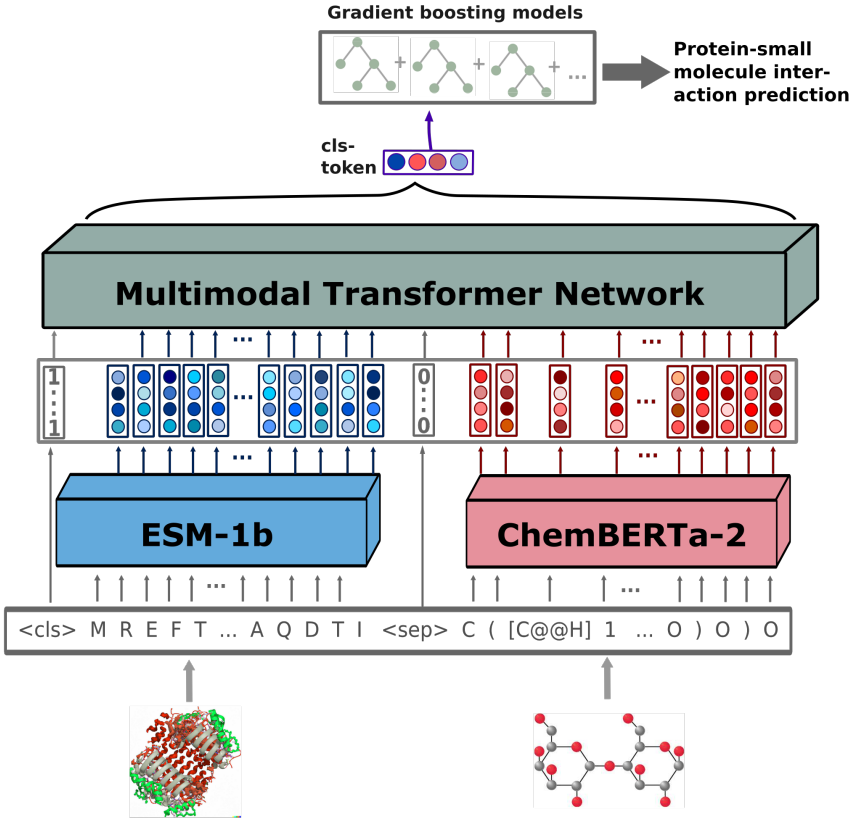

Kroll, A., Ranjan, S., & Lercher, M. J. (2024). A multimodal Transformer Network for protein-small molecule interactions […] *PLOS Comp Biol*, *20*(5), e1012100.