A Foundational Architecture for Protein Structure Prediction

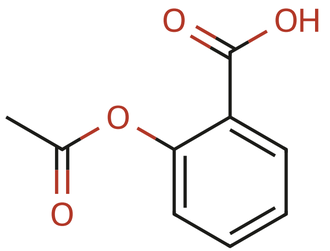
Jeffrey Ouyang-Zhang

08.27.26

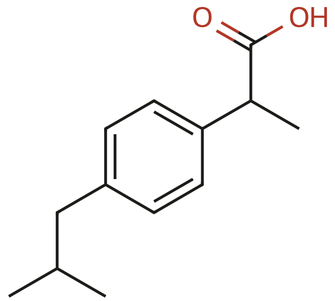
Small molecules power modern medicine

- 90% of drugs sold globally*

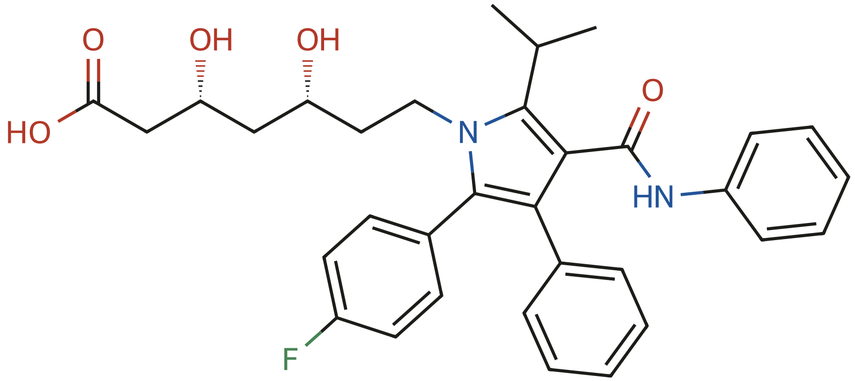
Aspirin



Ibuprofen



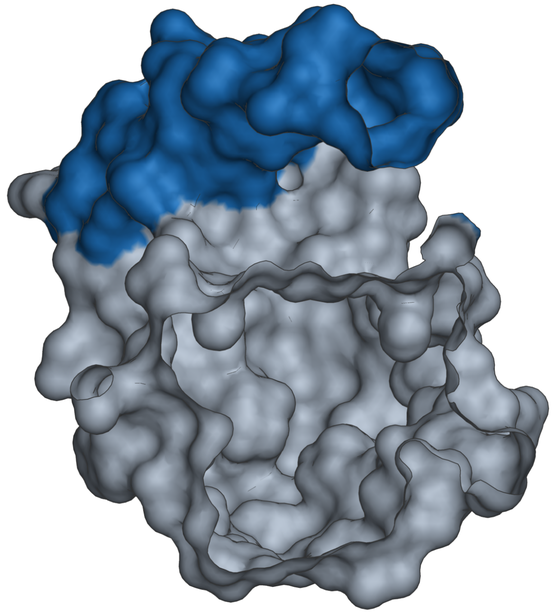
Atorvastatin



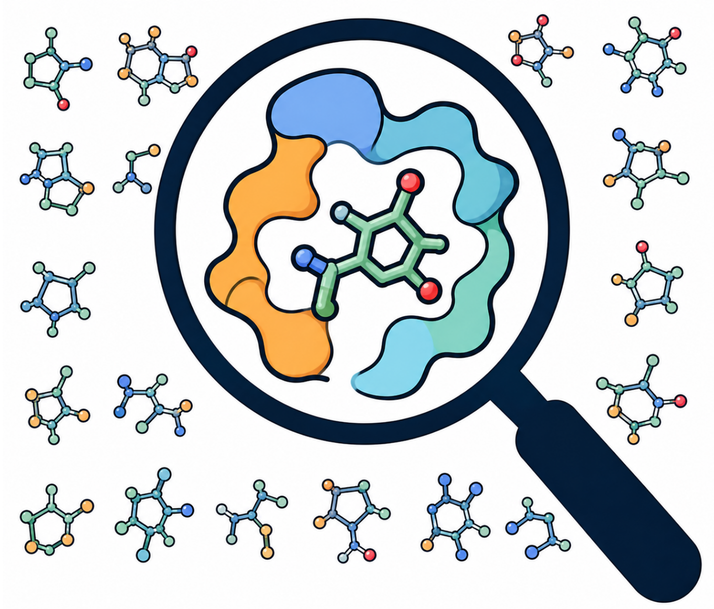
*Makurvet 2021. Biologics vs. small molecules: Drug costs and patient access

Drug discovery is a search problem

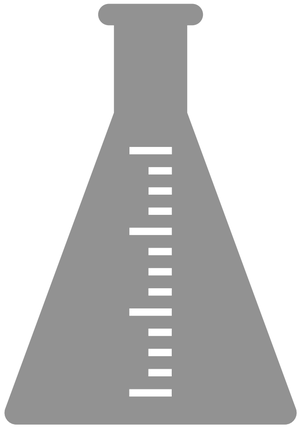
1. Identify a target protein



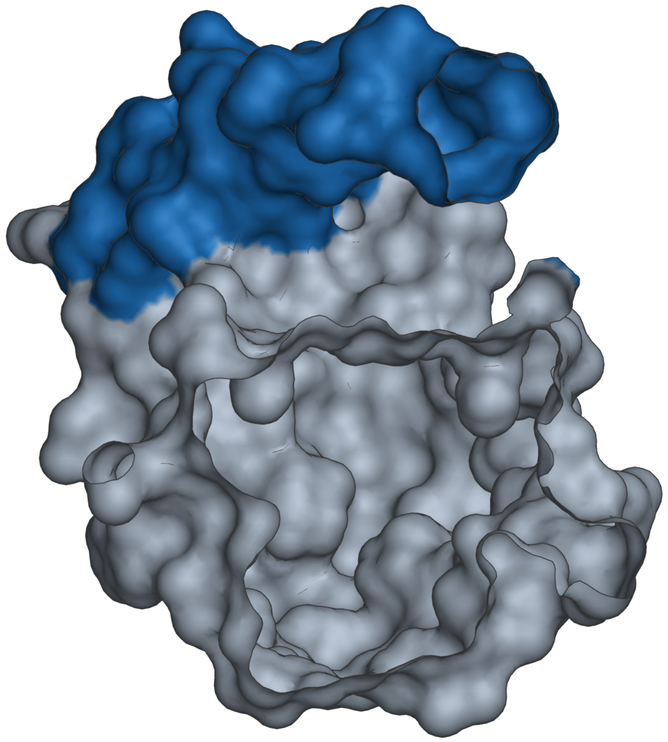
2. Screen candidate molecules



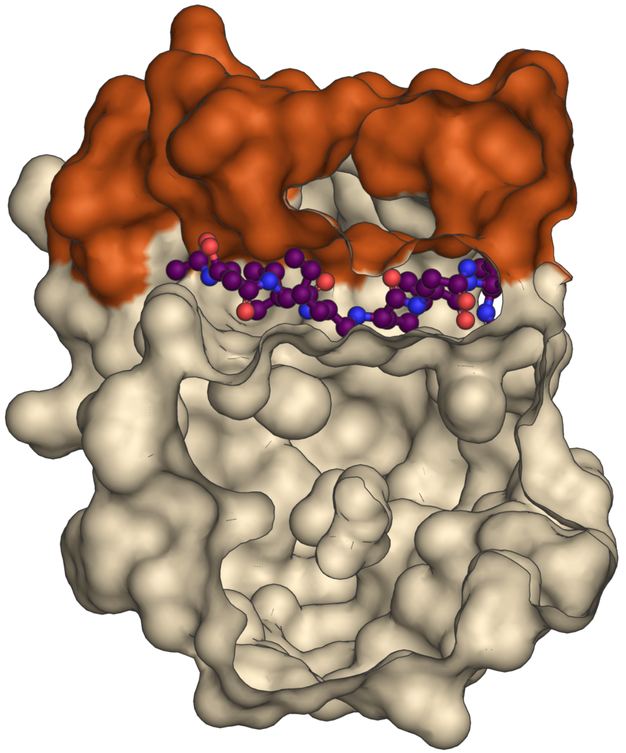
3. Experimentally validate hits



But proteins move

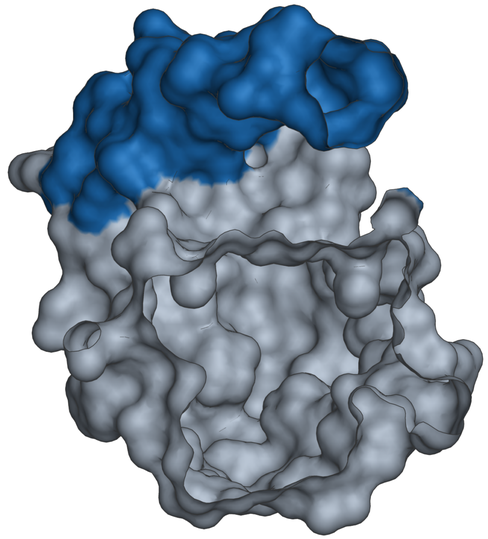


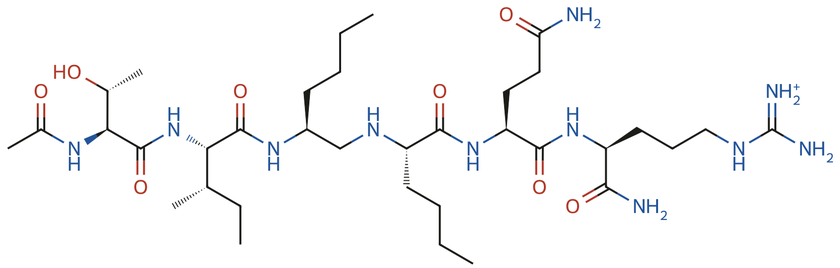
apo 1HHP



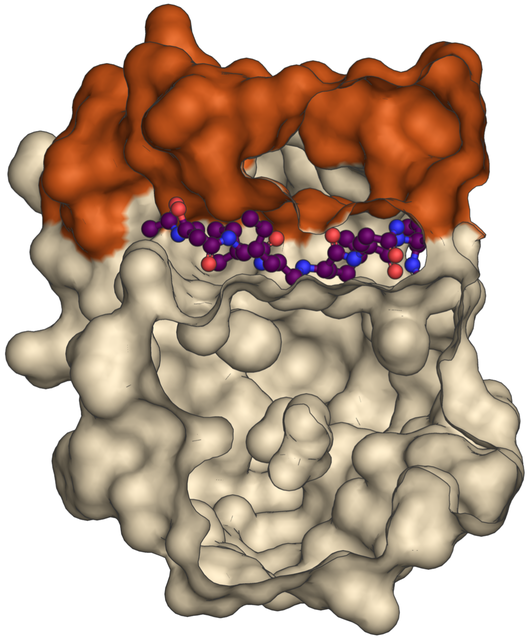
MVT-101 complex 4HVP

Alphafold in virtual screening





AlphaFold3



Alphafold in virtual screening



more accurately represents the interaction



much slower and more expensive

- **1min/molecule * 1M molecules = 15K GPU hours**

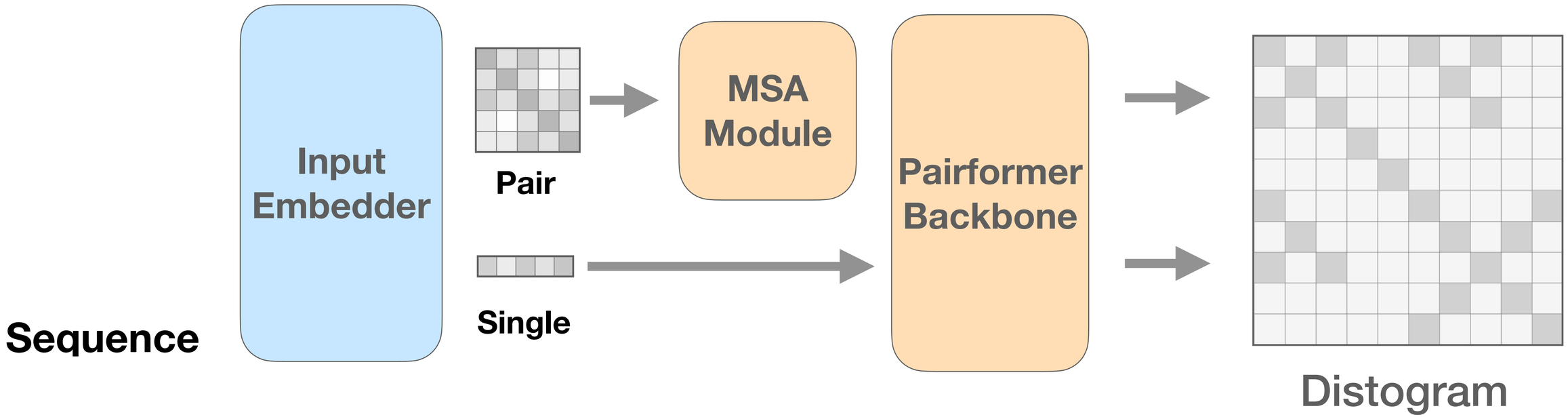
Accelerating AlphaFold

- simplified architecture
    - same accuracy
    - faster inference
    - **foundational modules**
- **collaboration in machine learning and drug discovery**

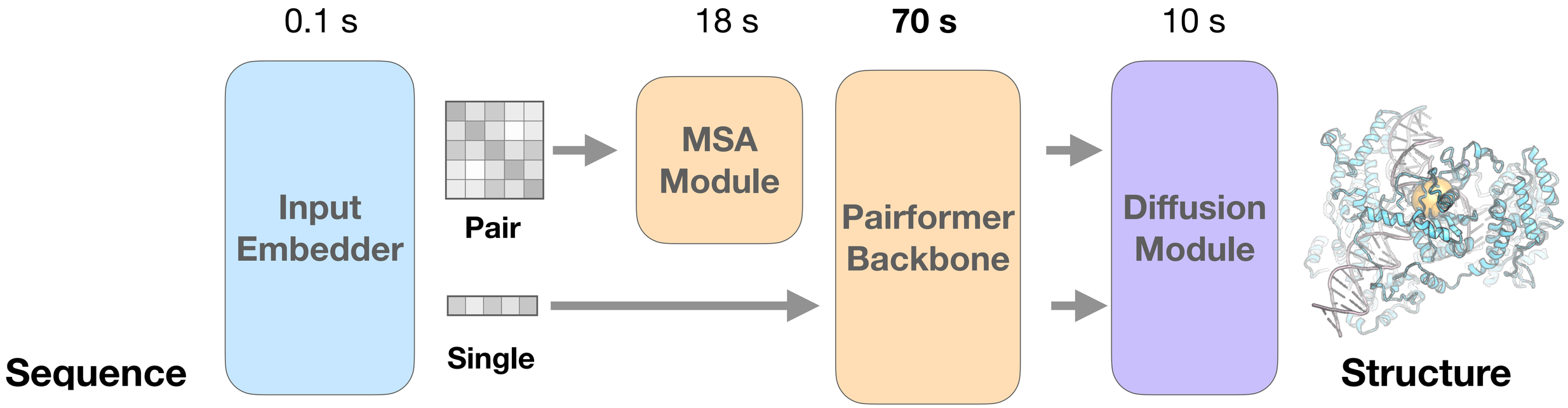




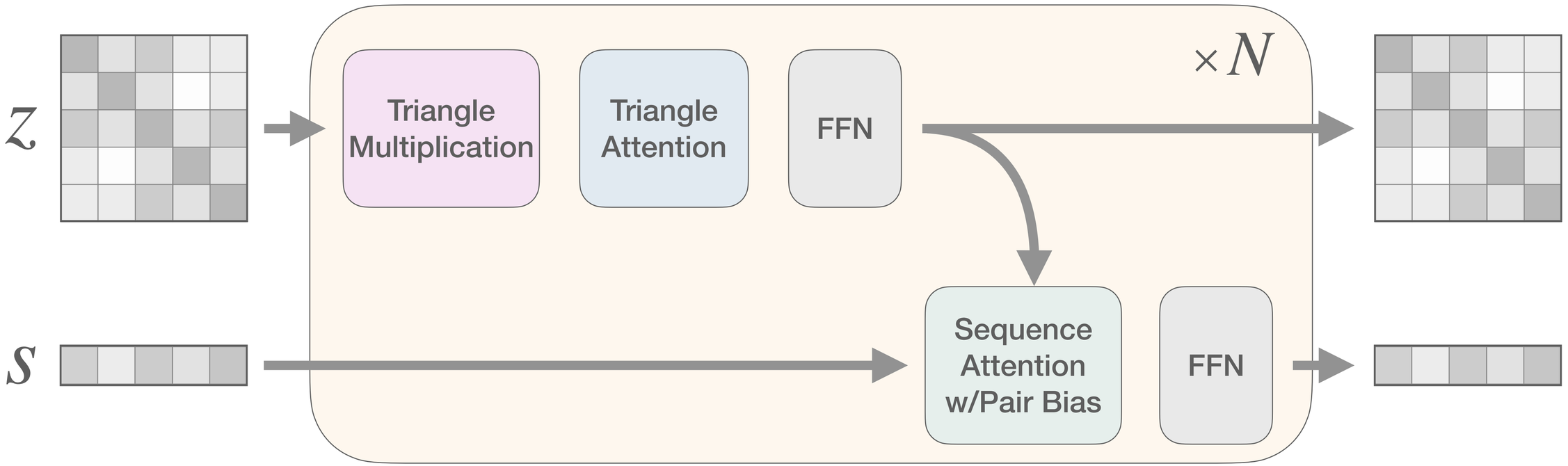
AlphaFold3 architecture



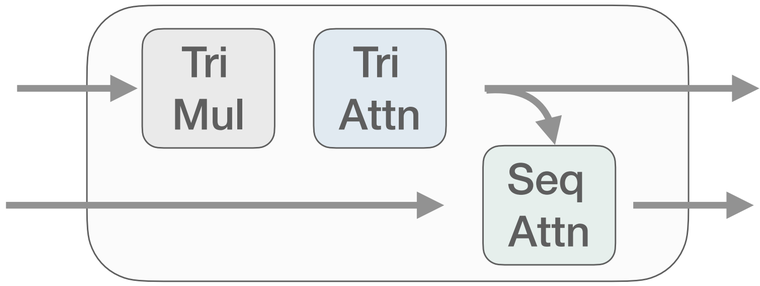
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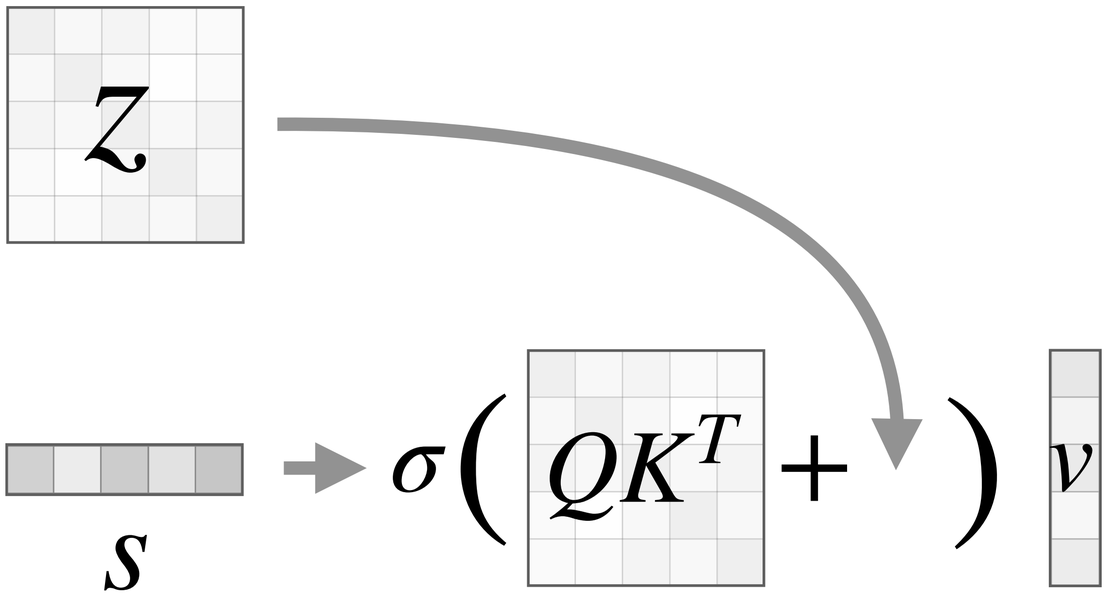
Pairformer Backbone



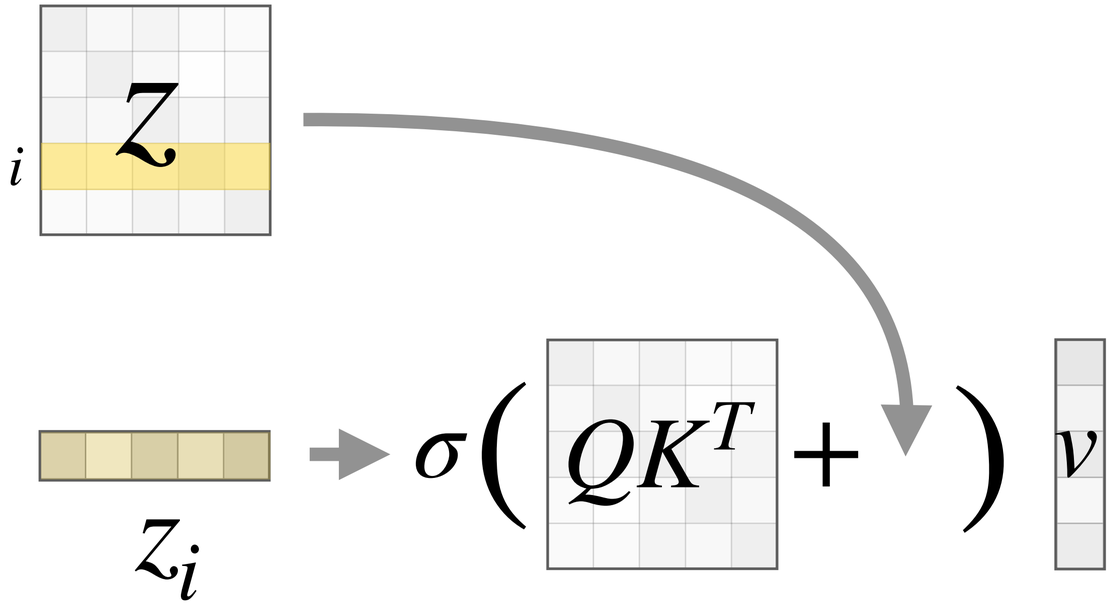
Triangle attention learns sparse interactions



Sequence Attention w/Pair Bias

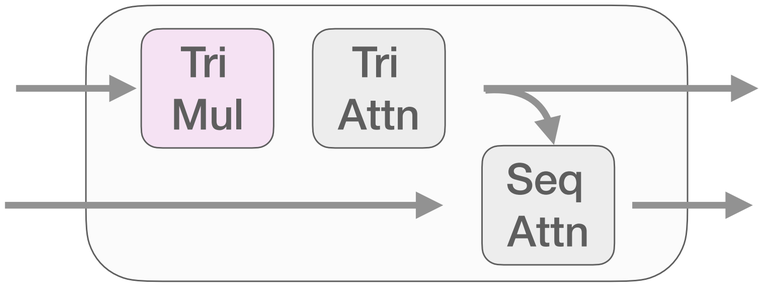


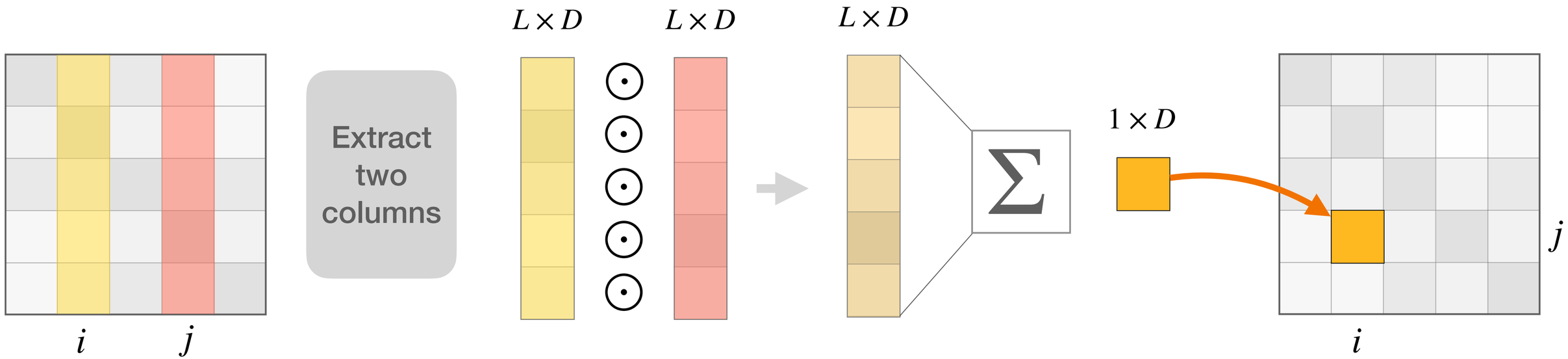
Triangle Attention



Computes Sequence Attention L times

Triangle Multiplication learns triplets





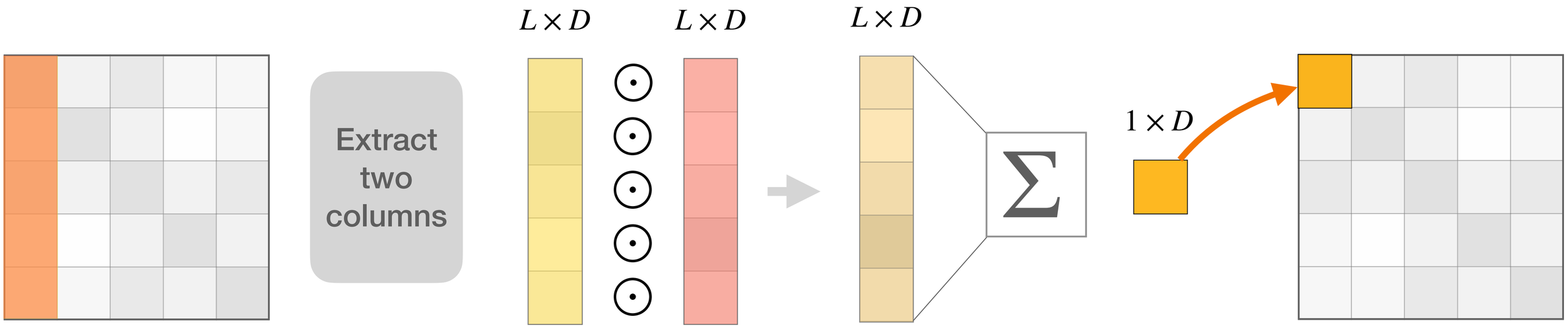
$$\mathbf{z} \in \mathbb{R}^{L \times L \times D}$$

$$\mathbf{z}_{ki} \odot \mathbf{z}_{kj}$$

$$\mathrm{TriMul}(\mathbf{z})_{ij} = \sum_k \mathbf{z}_{ki} \odot \mathbf{z}_{kj}$$

Figure inspo: Akiyama et al. Scaling down protein language modeling with MSA Pairformer. 2025.

Triangle Multiplication

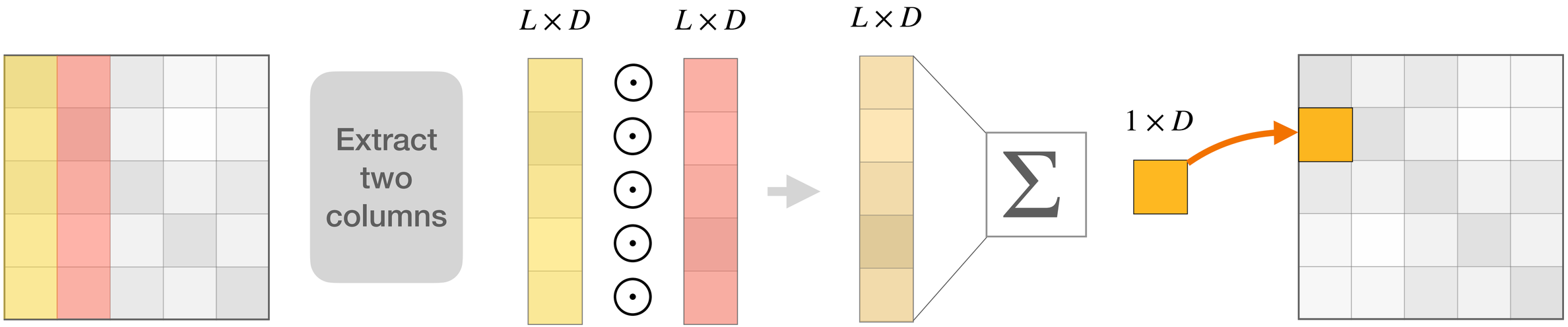


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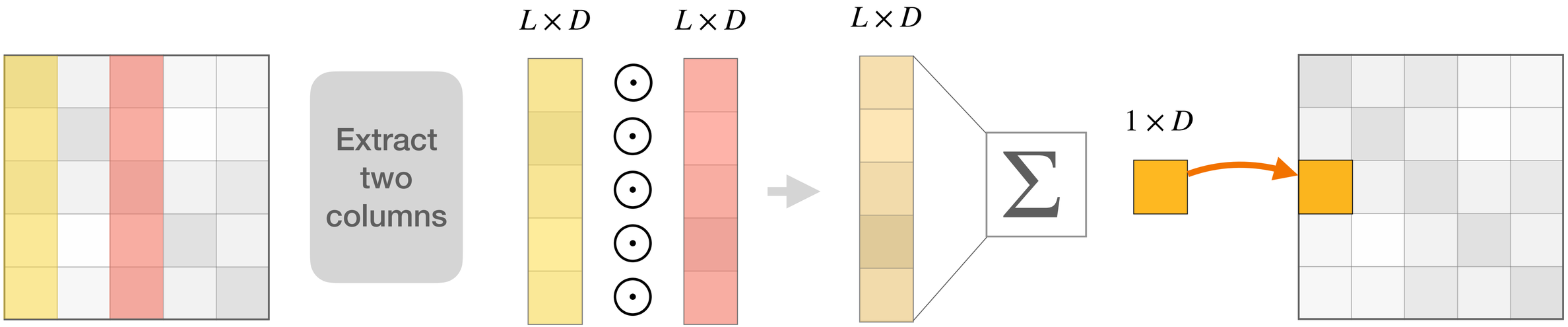


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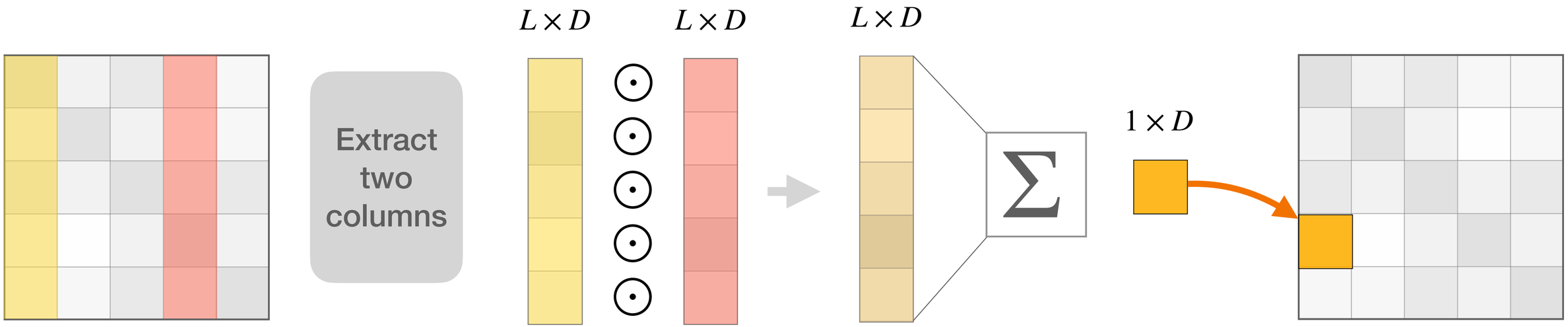


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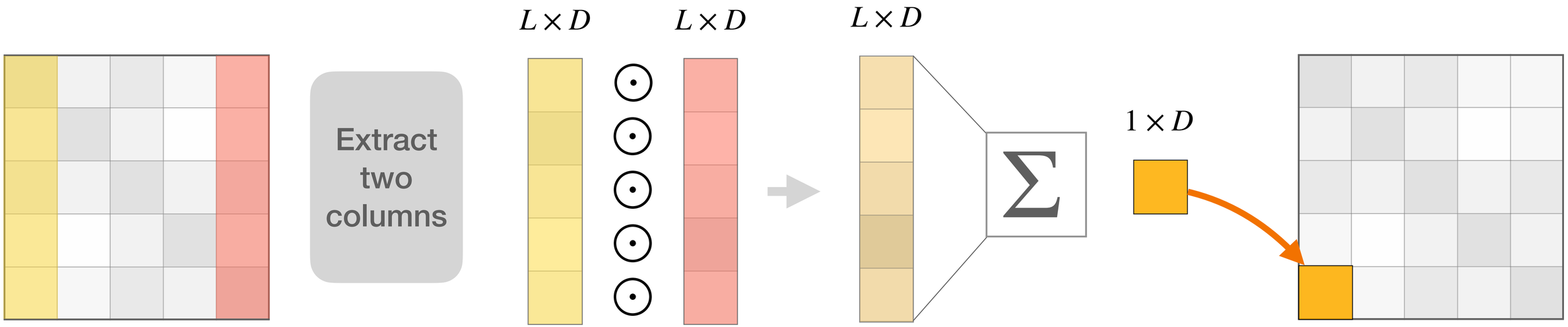


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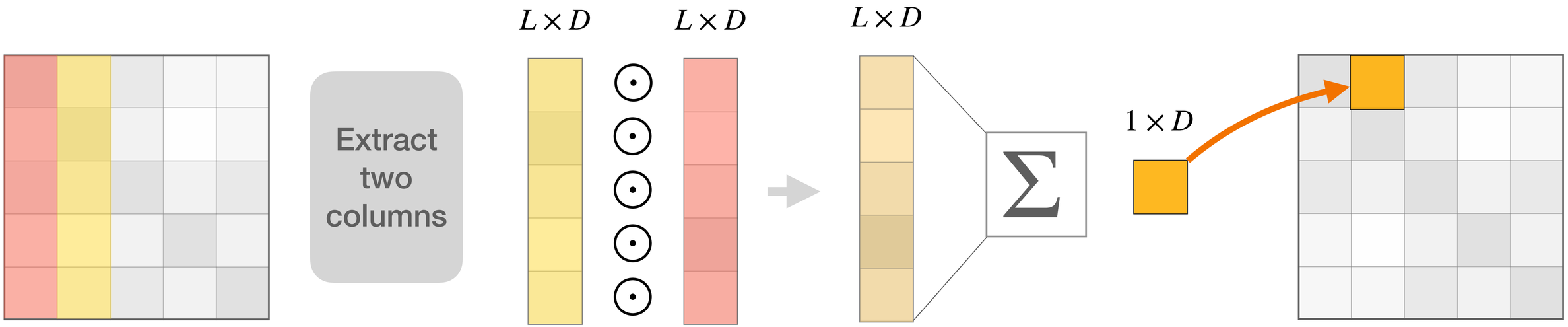


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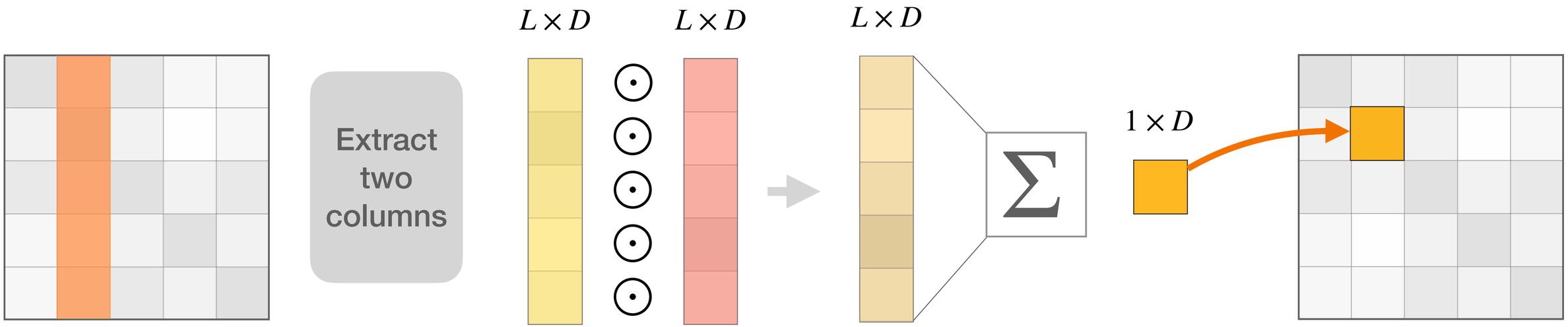


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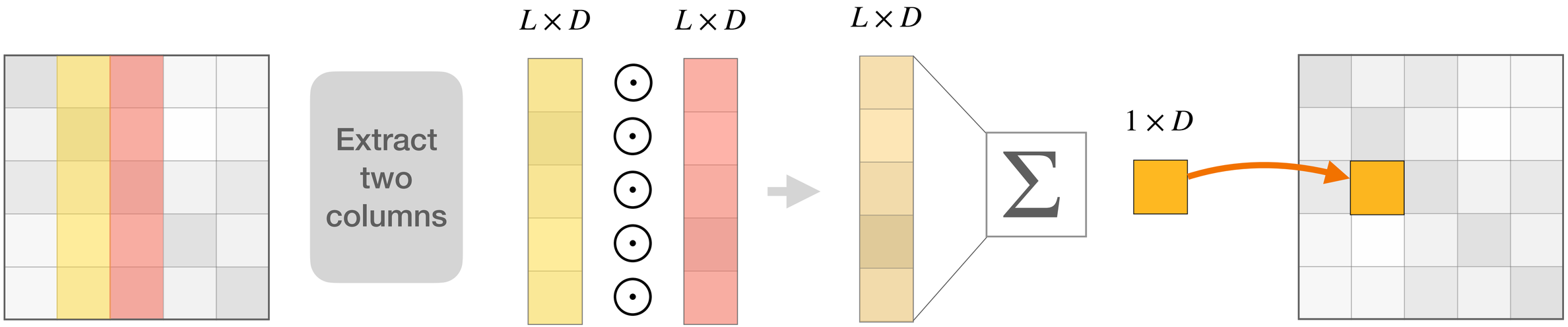


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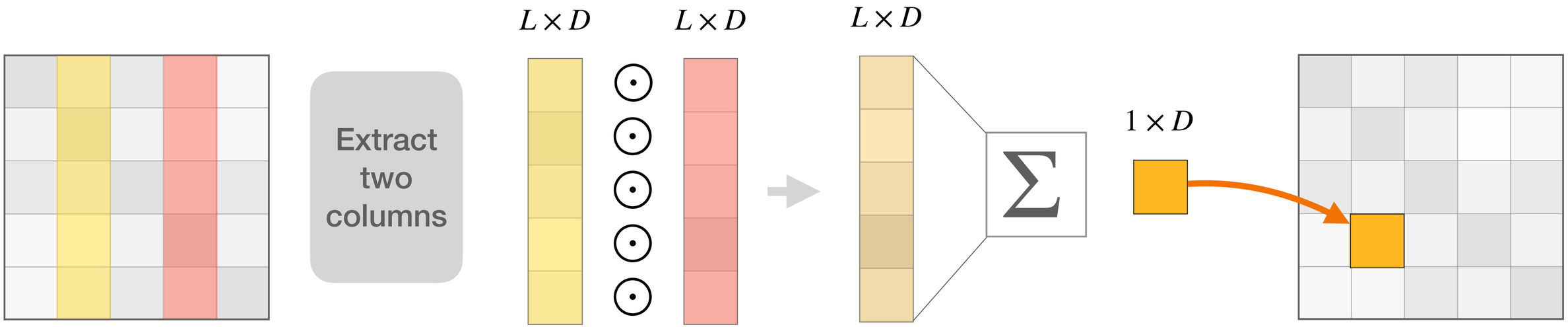


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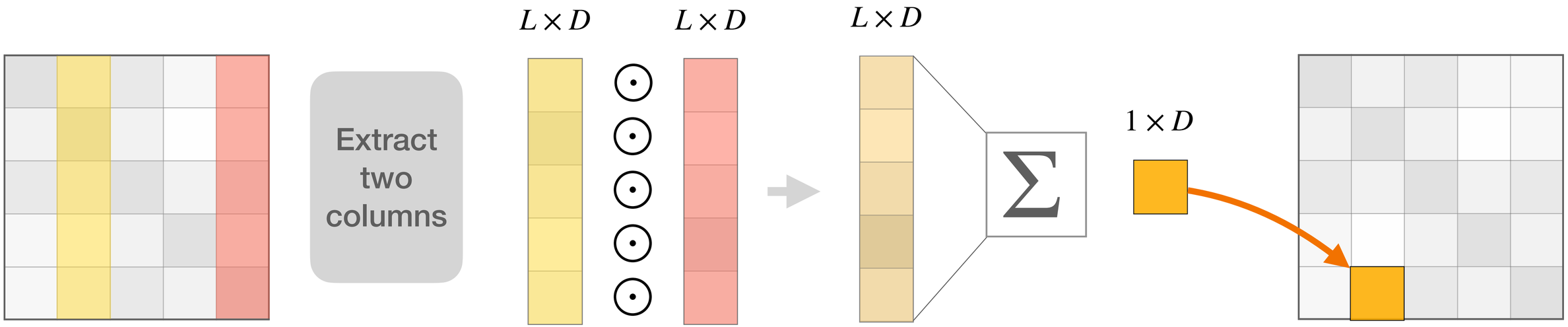


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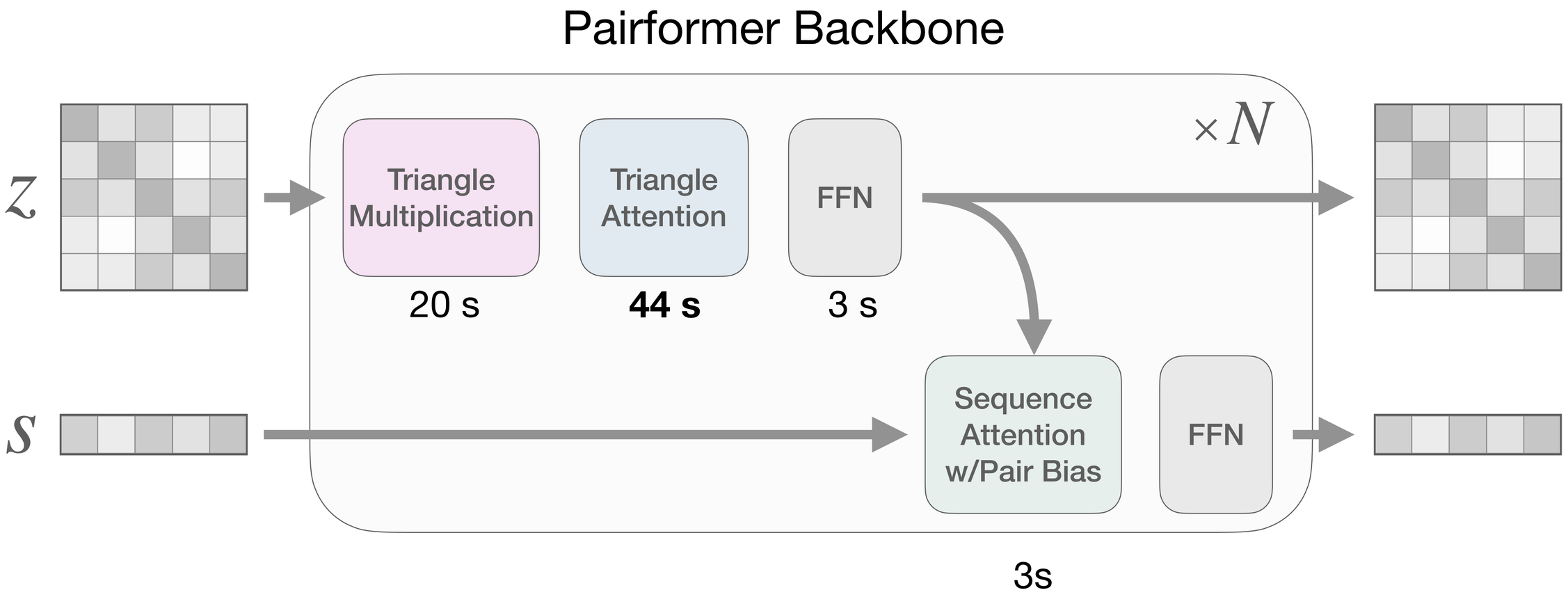


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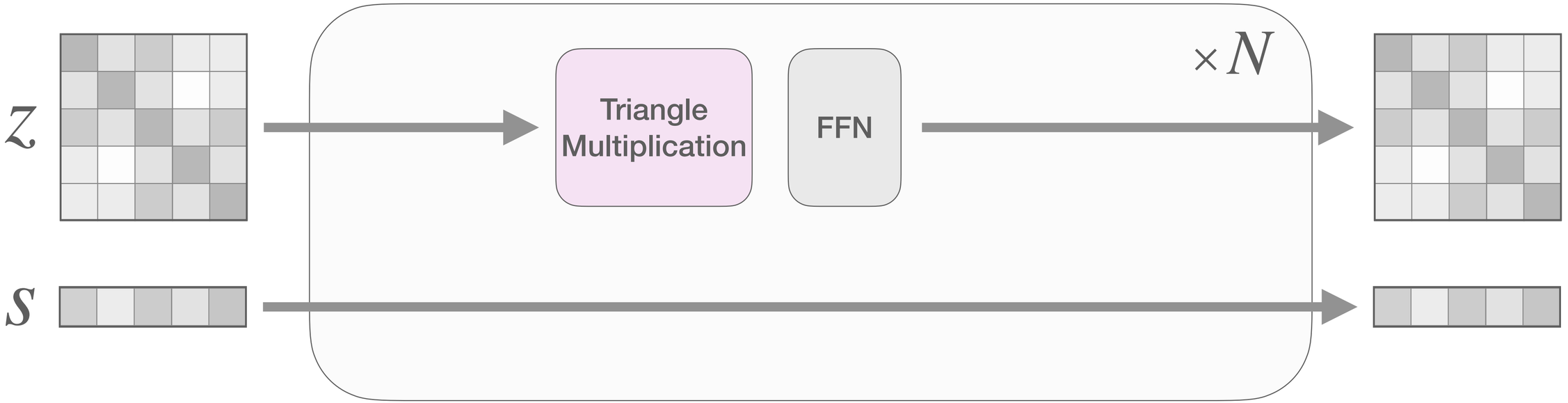
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Triangle Attention dominates runtime

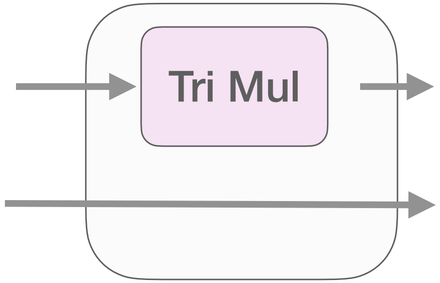


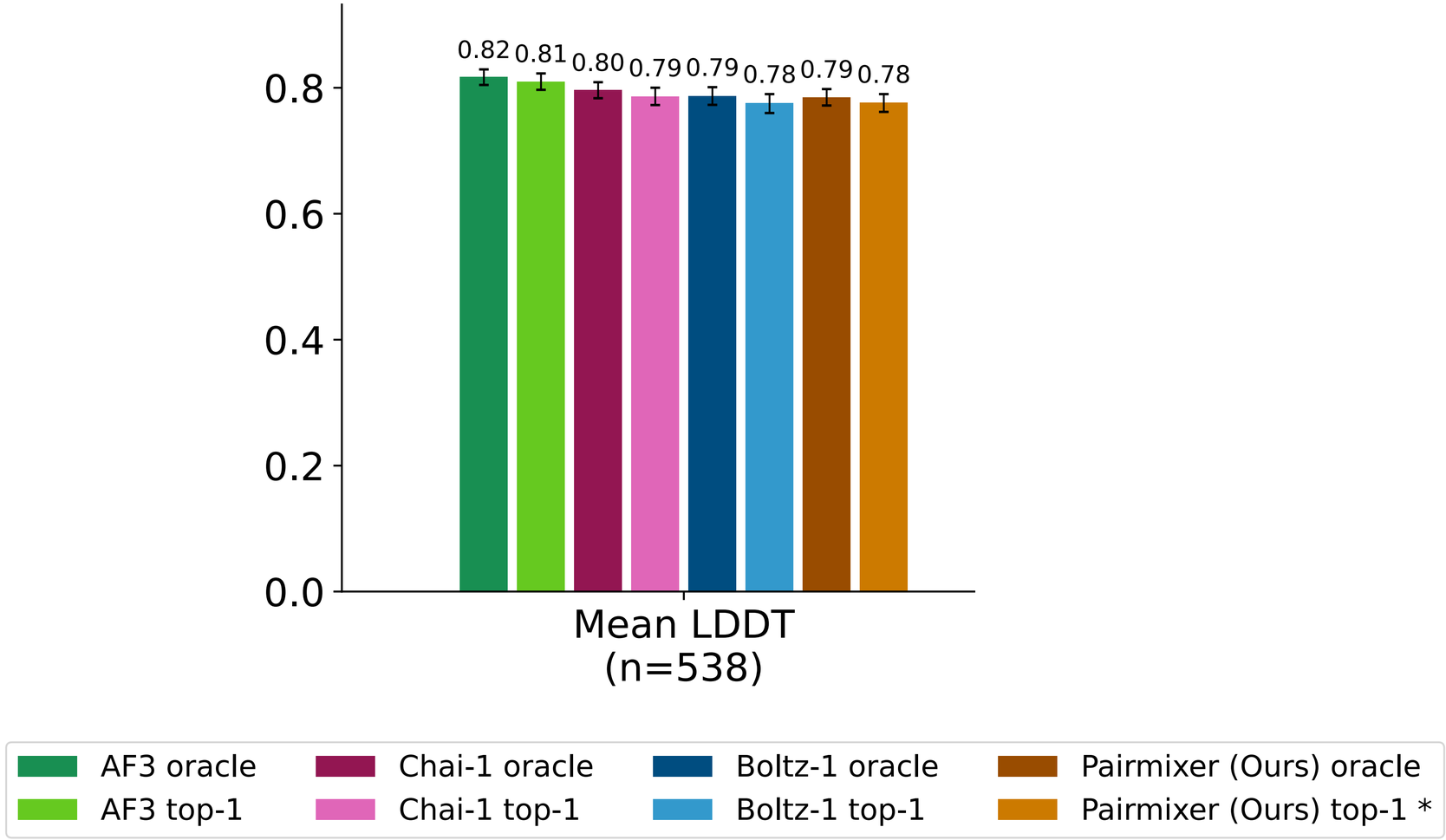
Pairmixer Backbone



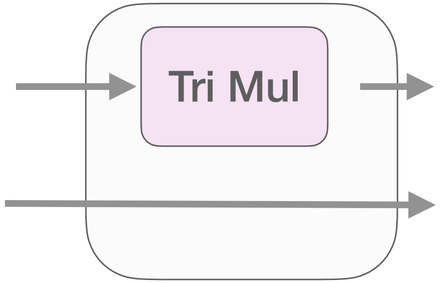
***Ouyang-Zhang**,et al. 2025. Triangle Multiplication Is All You Need For Biomolecular Structure Representations*

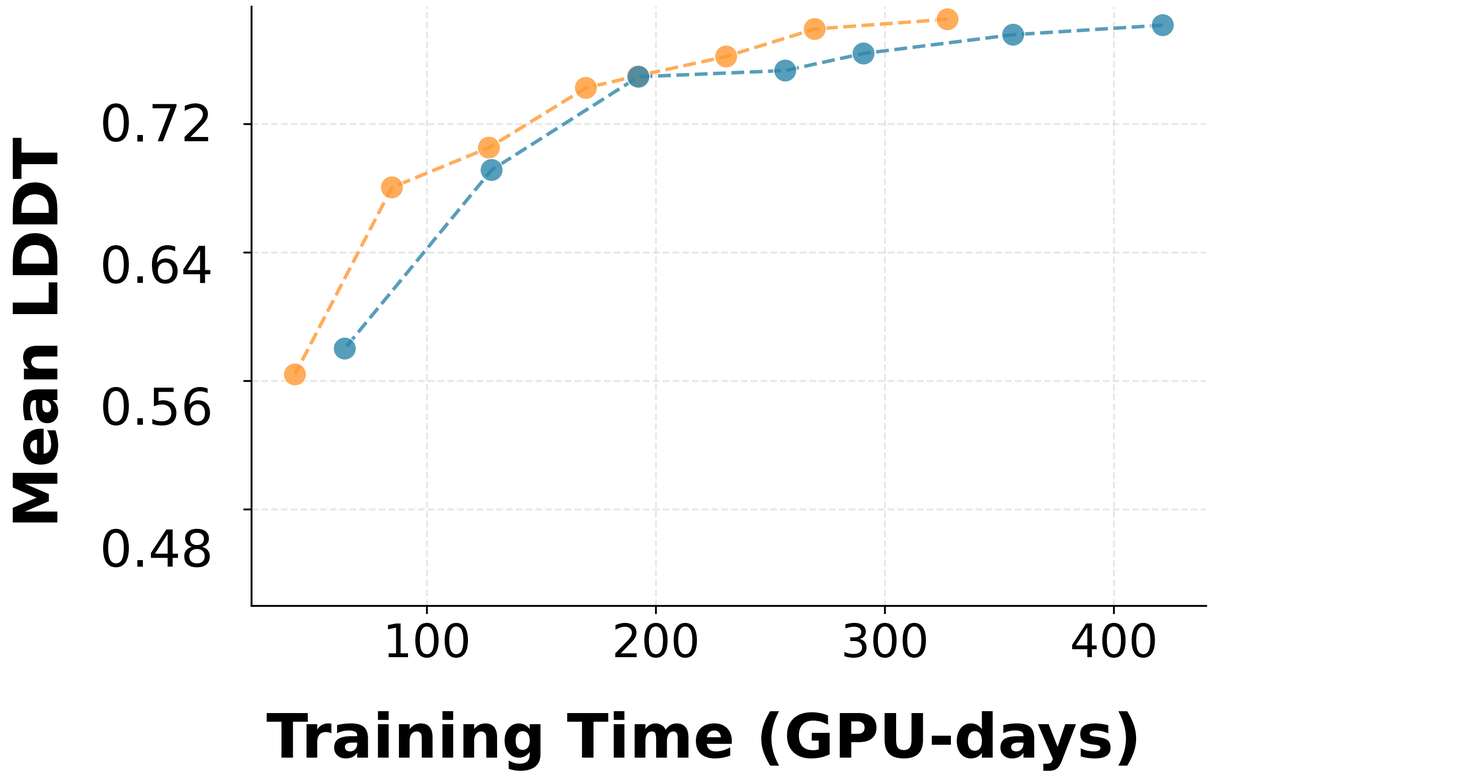
Equally performant



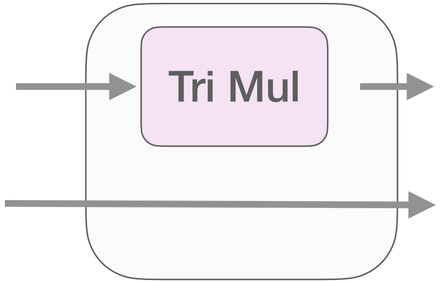


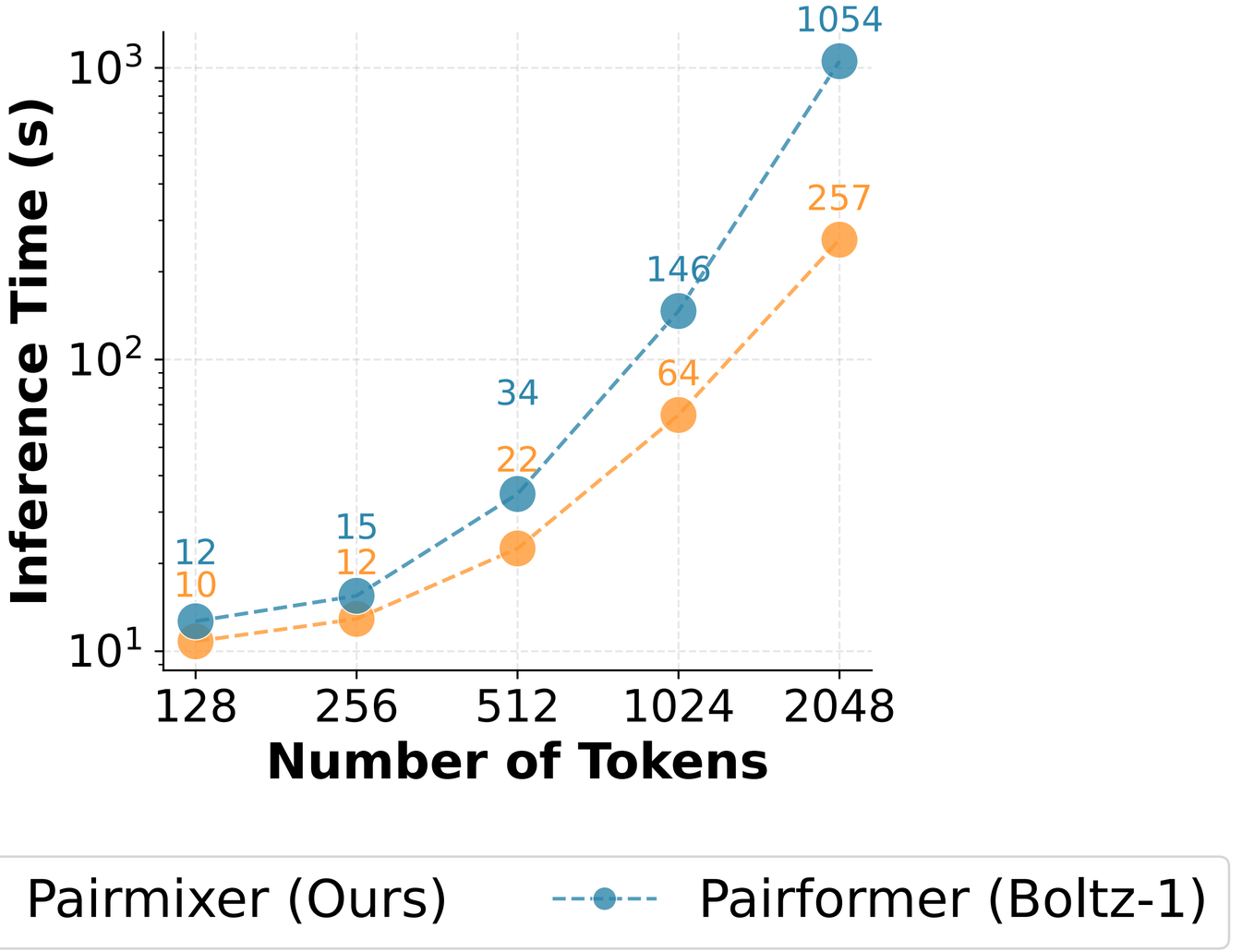
Trains Faster



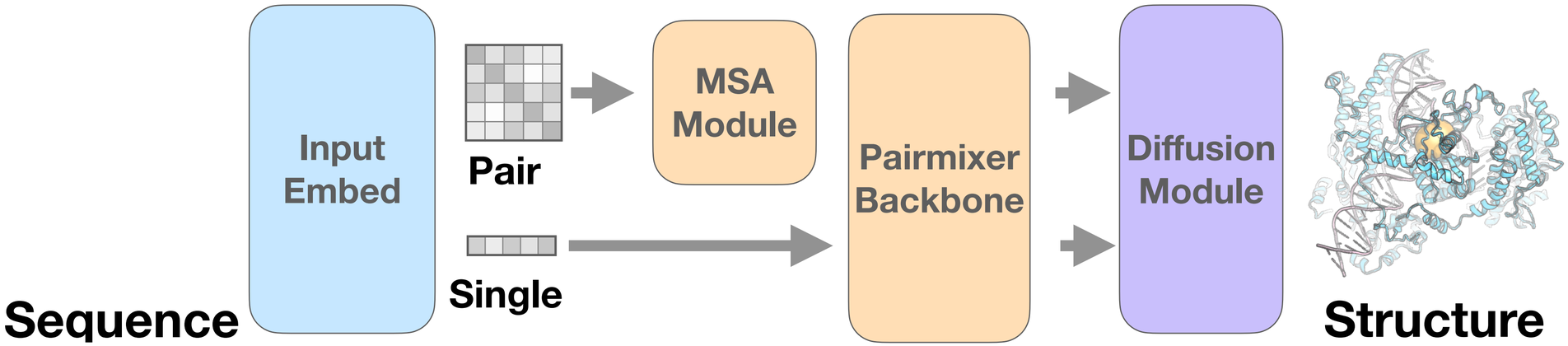


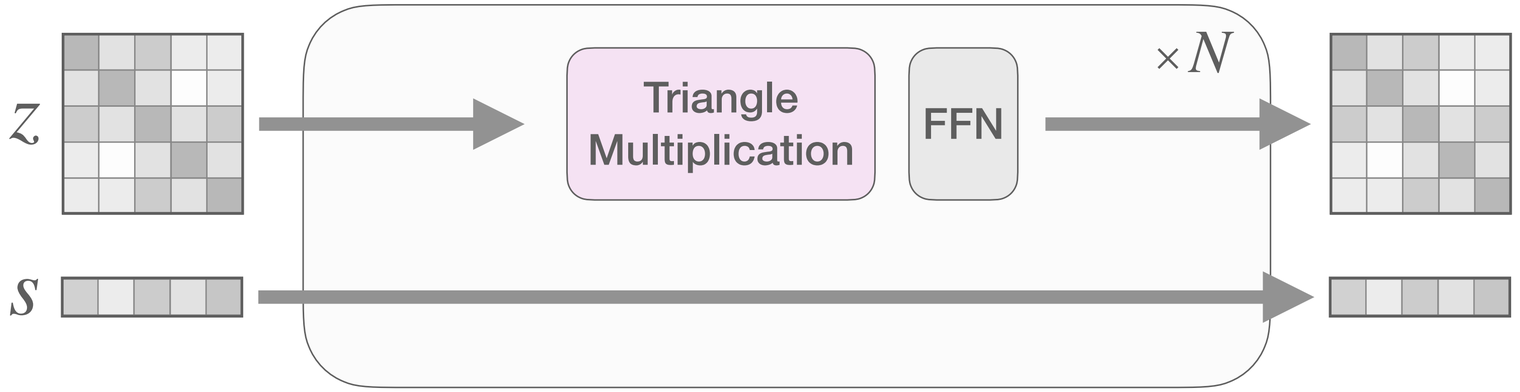
Samples Faster



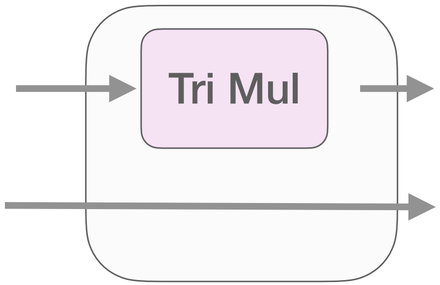


Pairmixer is a fast, efficient structure predictor





Acknowledgements



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The University of Texas at Austin

Genesis
RESEARCH

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