Protein Language Model-based Assignment of NMR ^{1}H-^{15}N Chemical Shifts

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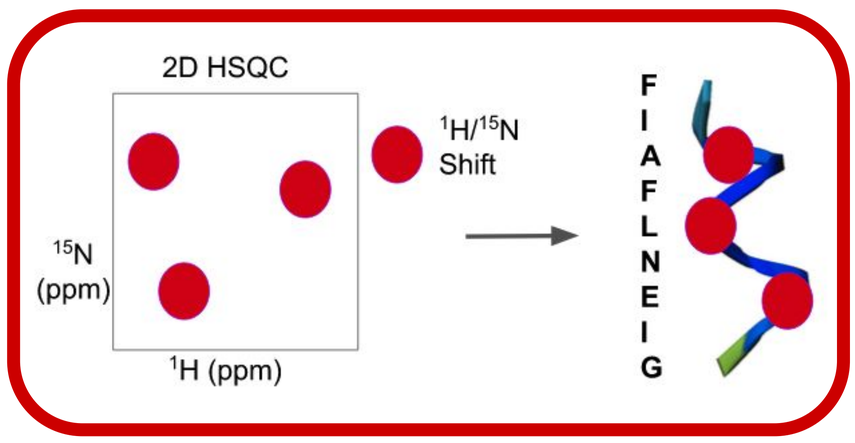
SHORT SUMMARY

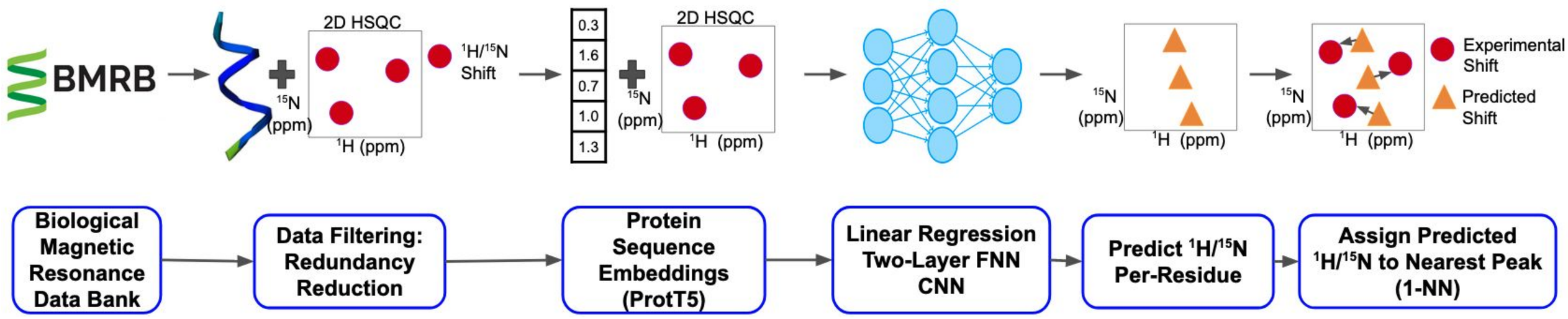
NMR ^{1}H-^{15}N chemical shift assignments with **Deep Learning** based only on protein sequence encodings from the **protein language model** ProtT5 [1]



Traditional Approach:

1) cost expensive, highly concentrated samples (^{13}C required)
2) time-consuming (3-6 d) spectrum acquisition and manual assignment of backbone resonances

New Deep Learning Approach:



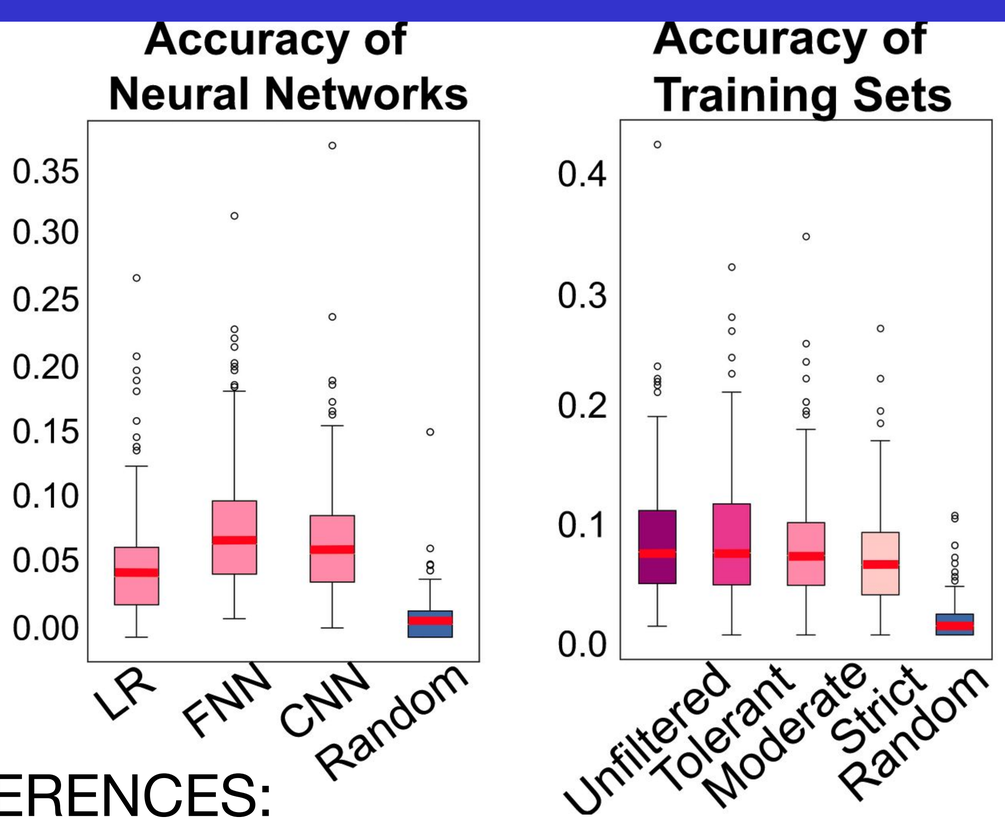
INTRODUCTION

- **Goal:** Assign ^{1}H/^{15}N shifts to the protein sequence without the need to measure additional ^{13}C backbone resonances
- Assignment is only based on the protein sequence encoded with a protein language model ProtT5 [1] and Deep Learning models
- **Benefits**: light-weight, fast alternative reducing the spectrum acquisition and assignment from 3-6 days to 20min-4h by avoiding the dependency on ^{13}C shifts

METHODS

- **Training:** protein sequence embeddings as input for Linear Regression/Two-Layer FNN/CNN
- **Inference:** Assigning predicted ^{1}H/^{15}N shifts to the closest experimentally measured shifts by 1-Nearest Neighbor
- **Data:** ^{1}H/^{15}N shifts from BMRB Database [2] redundancy reduced with mmseqs2 [3] with sequence identity 50% and coverage of 80%

PRELIMINARY RESULTS



OUTLOOK

- Simple linear and non-linear models seem not to be able to pick up the necessary information
- Although including information of protein 3D conformation in form of ProstT5 embeddings [4] did not show a significant improvement, incorporating **structure coordinates from PDB/AlphaFold2** [5,6] directly would be the next step
- **Cross-Attention** suggests to be a promising strategy to improve performance

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