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38th European Peptide Symposium
Vienna · 6-11 September 2026

AI-driven discovery of cross-kingdom peptide ligands

CysTopoFold Exact probabilistic disulfide-topology prediction for cysteine-rich peptides

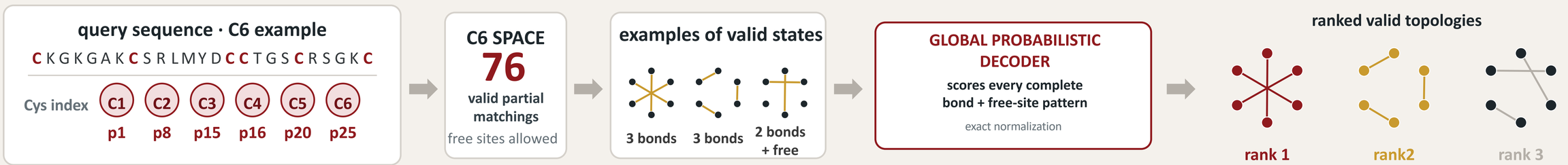
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BACKGROUND & CHALLENGE

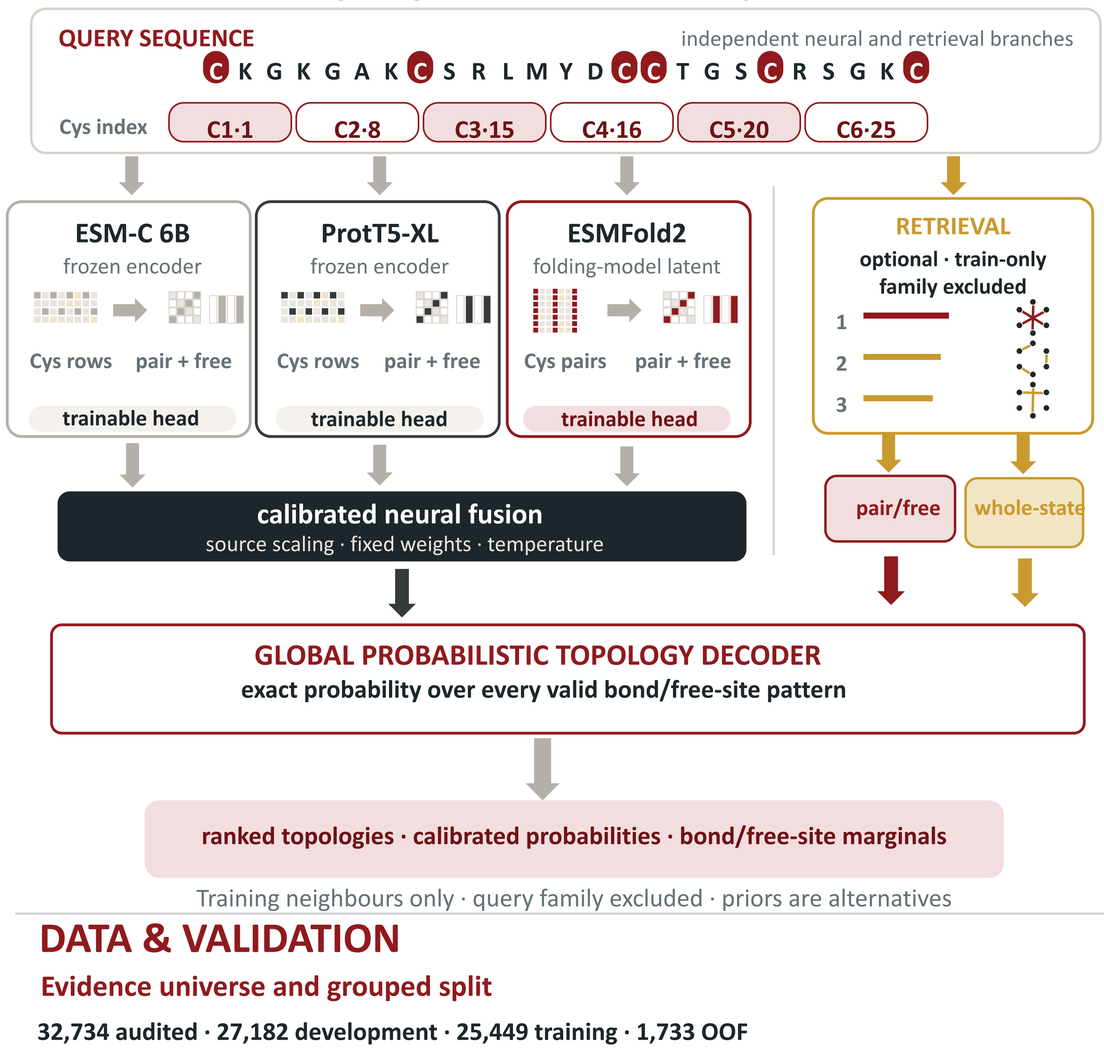
One peptide sequence can encode many valid disulfide connectivities

Connectivity determines peptide fold and stability. One sequence can admit many valid bond patterns, including free cysteines and odd cysteine counts.



Output: ranked topologies · calibrated probabilities · bond/free-site marginals · bond-count uncertainty

METHOD · How CysTopoFold learns and predicts

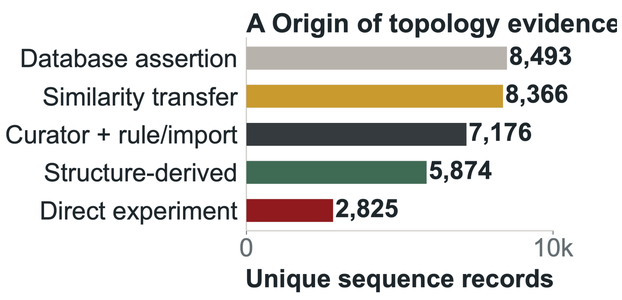


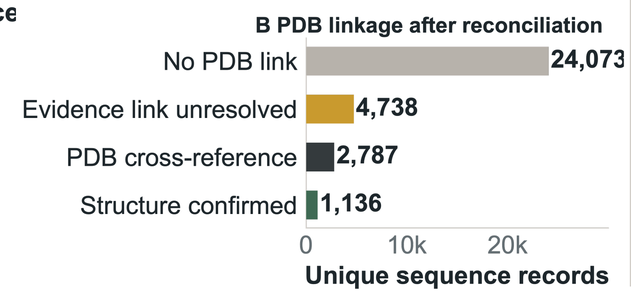
Training neighbours only · query family excluded · priors are alternatives

DATA & VALIDATION

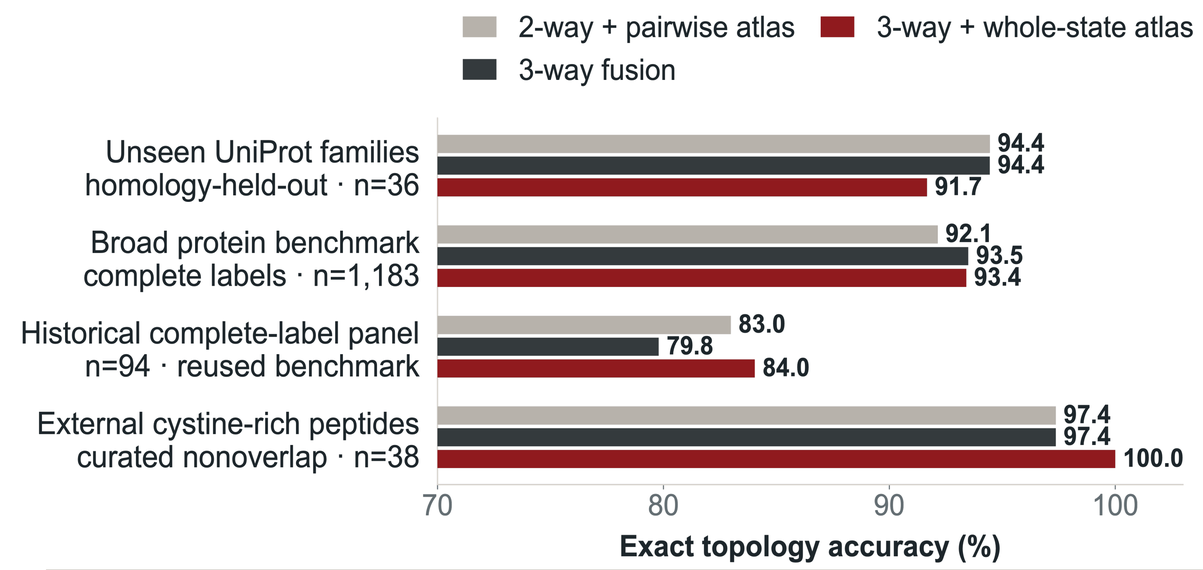
Evidence universe and grouped split

32,734 audited · 27,182 development · 25,449 training · 1,733 OOF

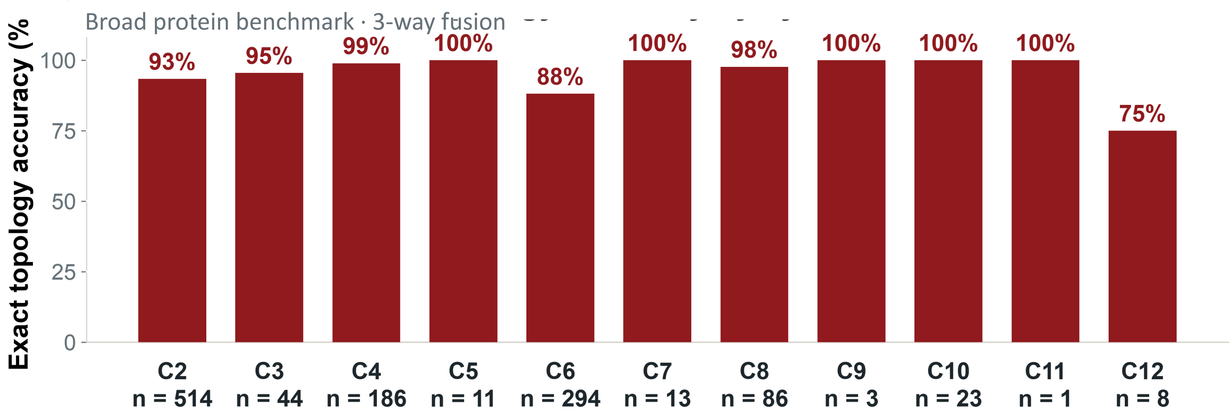




RESULTS · Performance across complementary cohorts

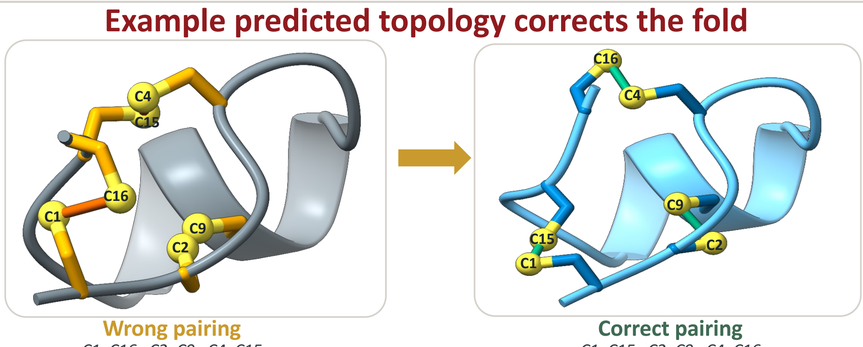


Cysteine-count audit



All C2-C12 groups shown · C9 (n=3) and C11 (n=1) are descriptive

Example predicted topology corrects the fold

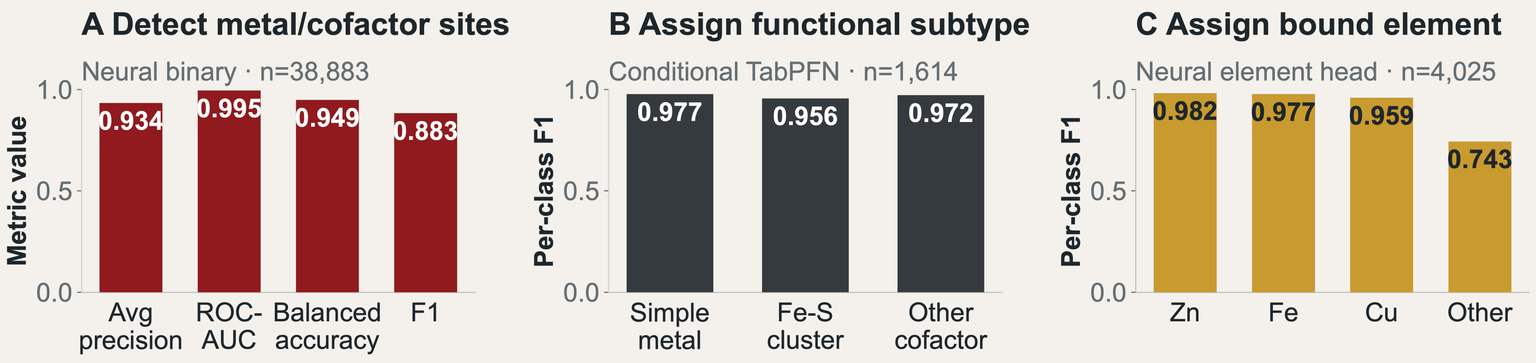


Wrong pairing
C1–C16 · C2–C9 · C4–C15

Correct pairing
C1–C15 · C2–C9 · C4–C16

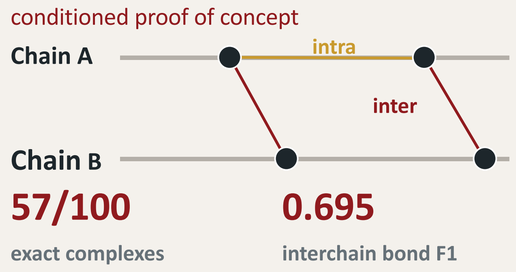
ADDITIONAL PREDICTIONS · Metal and interchain

Cysteine metal roles · three separate predictors



Interchain disulfides

conditioned proof of concept



57/100 exact complexes

0.695 interchain bond F1

Input: two sequences, eligible cysteines, bond count.
Exact: every typed bond correct.

CONCLUSIONS

Global decoding yields valid topologies and calibrated uncertainty.

Neural and retrieval evidence improve robustness across evaluation cohorts.

Next: prospective validation and joint endpoint discovery for interchain disulfides.


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Department of Drug Design and Pharmacology · University of Copenhagen

Pharmacoinformatics group

Research group · University of Copenhagen

drug.ku.dk/research-sections/pharmaceutical-informatics/pharmacoinformatics/

Related work: Hermes J, Matic M, et al. Peptide ligand discovery of G protein-coupled receptors. Nat Rev Methods Primers 6, 52 (2026). doi:10.1038/s43586-026-00503-5

For Center for Pharmaceutical Data Science Education check cpdse.dk

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Project questions, collaboration and updates

Scan to connect