



AntiFold

Improved antibody sequence design
using inverse folding

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* Equal contribution



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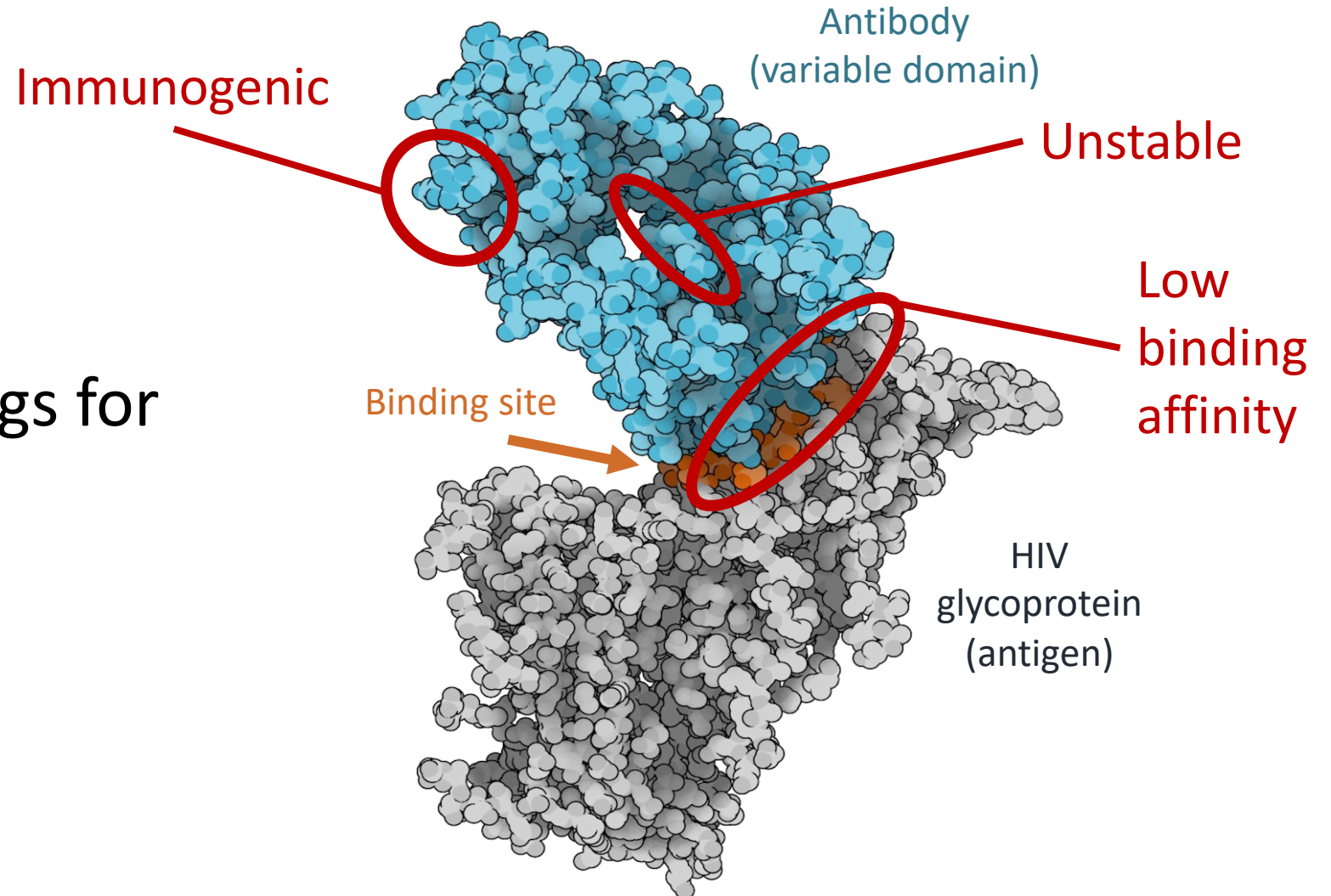


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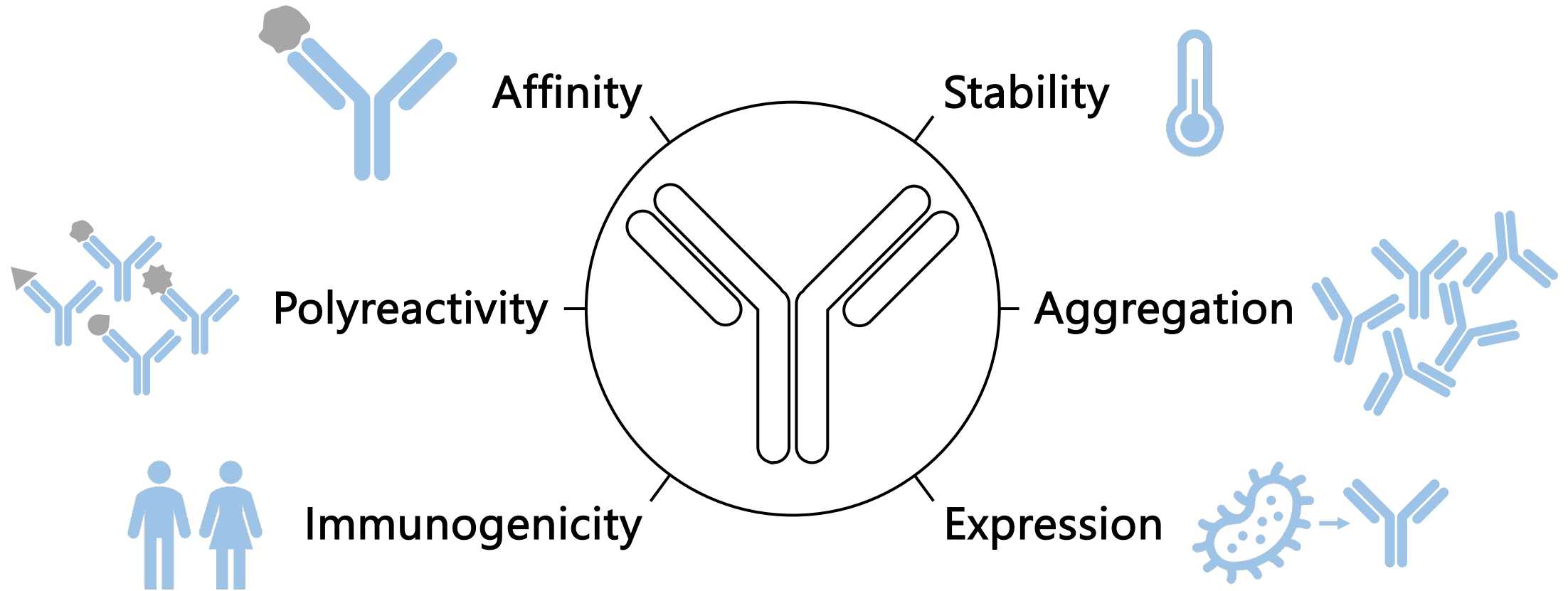


Antibodies play a key role in the immune system

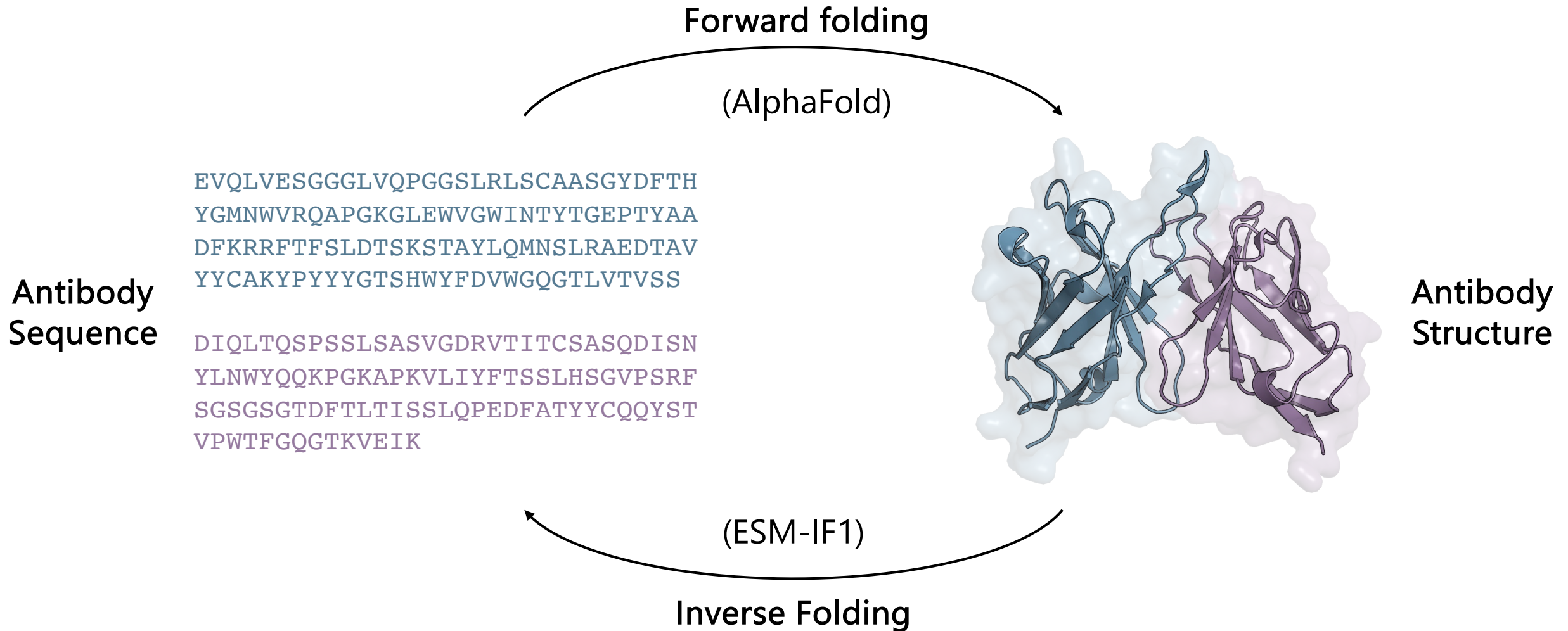
- Defend against pathogens
- Therapeutic drugs for a wide range of diseases



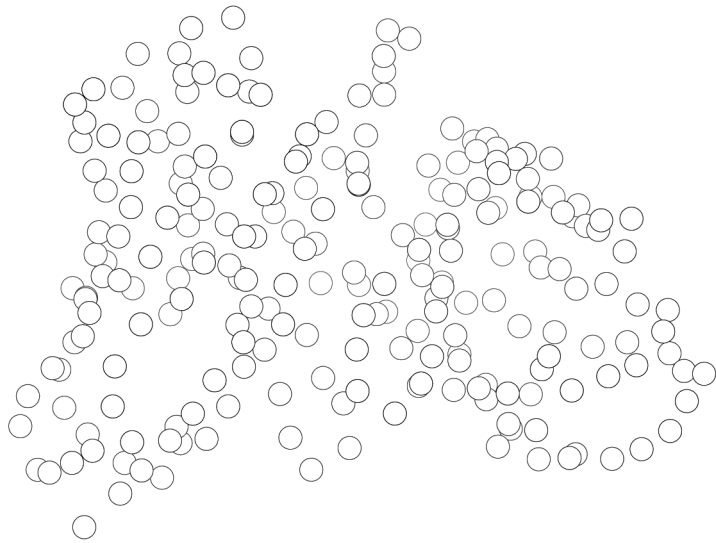
Reducing antibody “liabilities” requires optimizing a multi-parameter problem



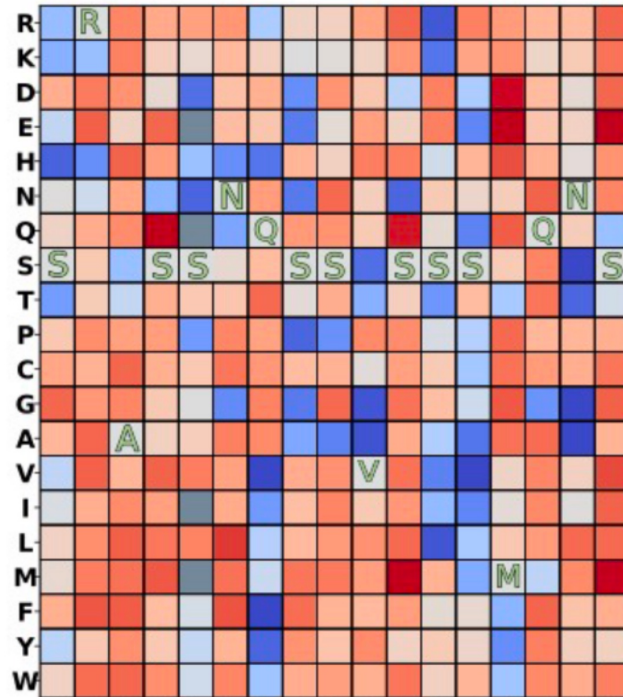
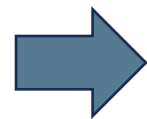
Inverse folding models predict sequence from structure



Inverse folding models predict mutational tolerance without changing structure



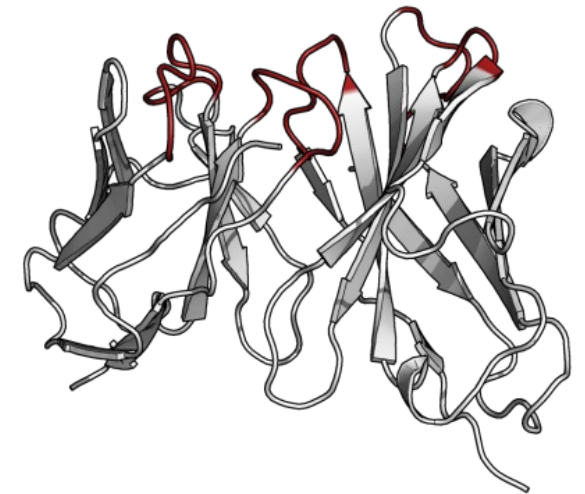
Input antibody
Backbone (Ca, C, N)



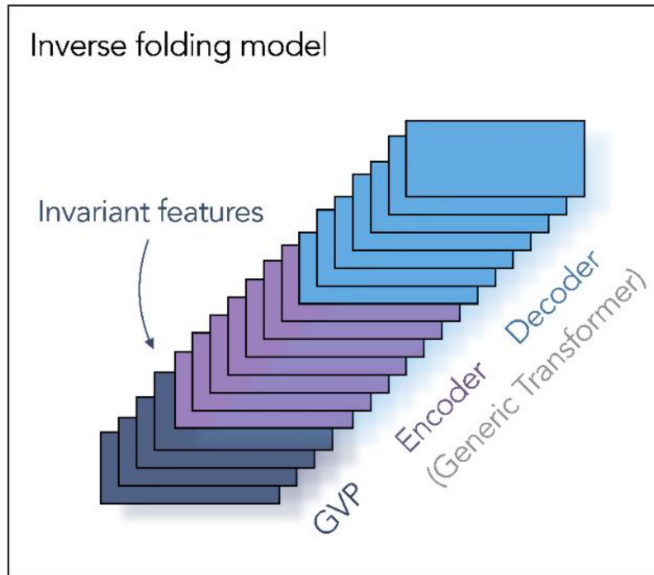
Inverse folding
probability distribution



Possible mutations
without changing structure

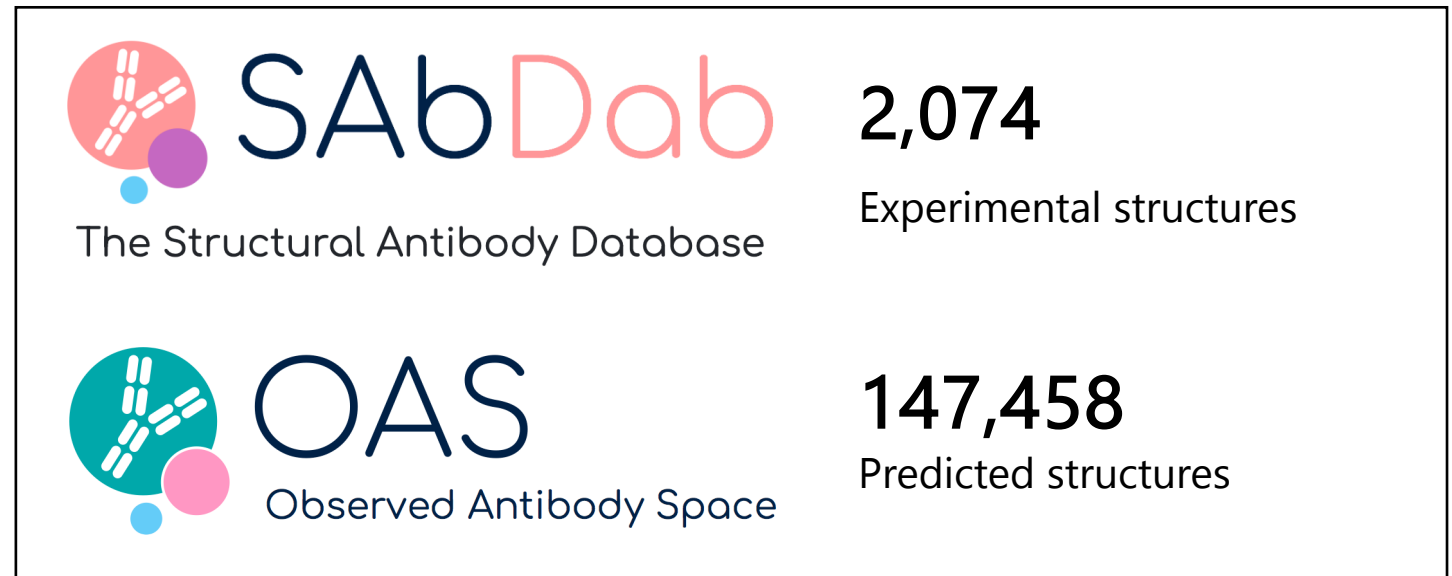


AntiFold is fine-tuned from ESM-IF1 on solved & predicted antibody structures



ESM-IF1
General protein model

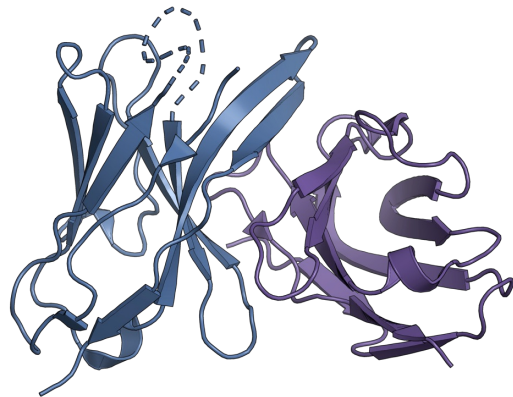
+



Antibody variable domain structures (paired VH/VL)

AntiFold is trained to predict masked residues

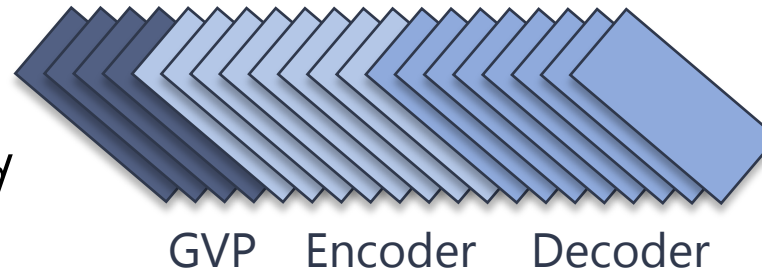
1. Mask structures



...TVTGYSXXXXXXXXXW...

2. Train antibody
inverse folding

*Predict
masked*



3. Sample sequences
with the same fold

...TVTGYSGYSATSNW...

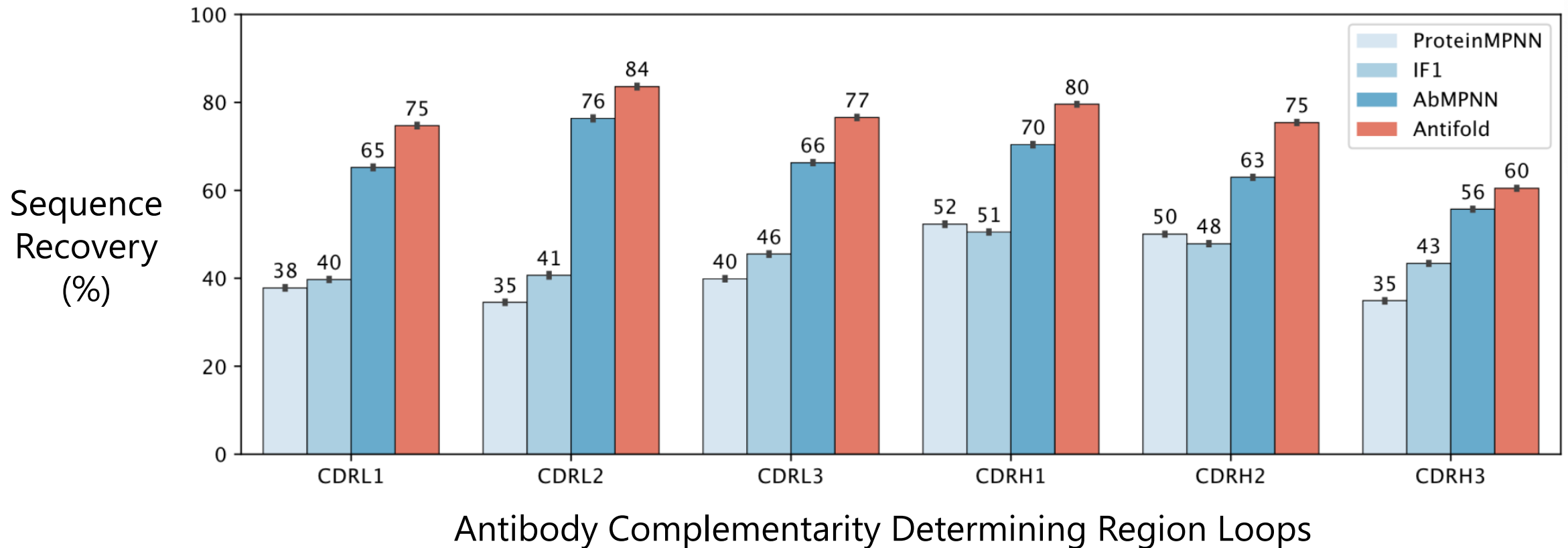
...TVTGYSGFTLSSFW...

...TVTGYSAYNVTTEW...

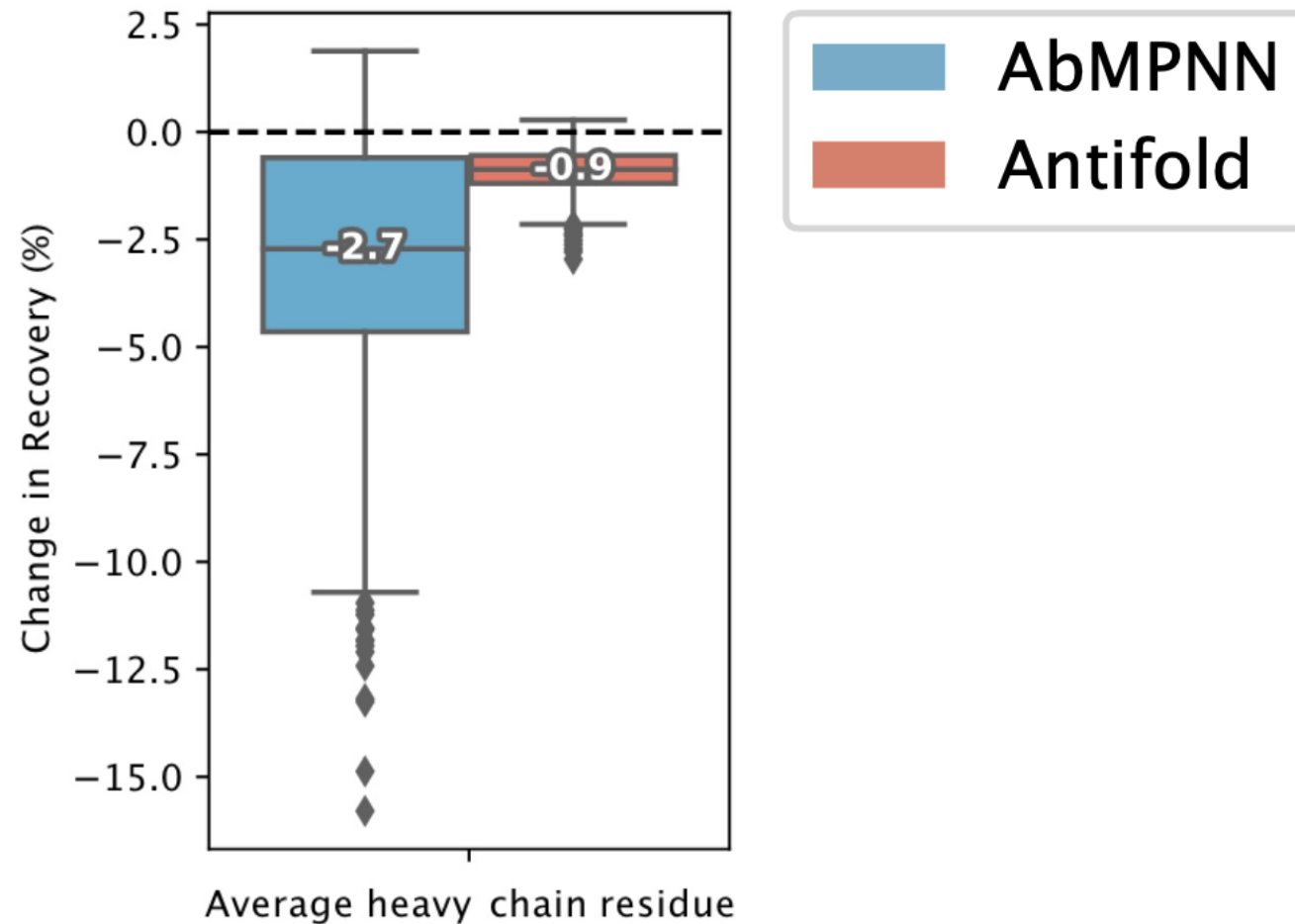
15% of coordinates are masked – mixture of single positions and spans

Selection of positions to mask biased towards variable CDR residues

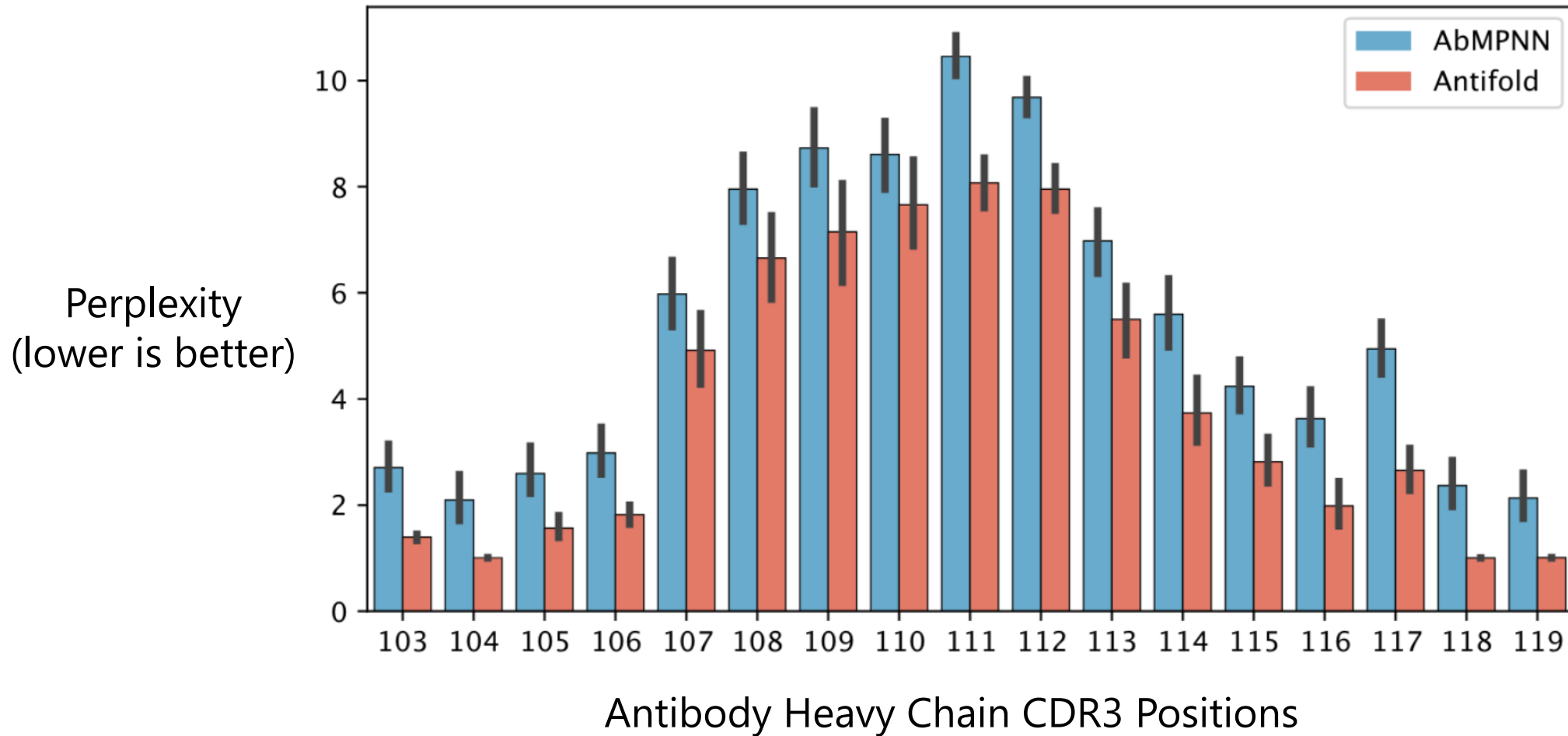
AntiFold outperforms general protein and antibody-specific inverse-folding models



Performance is maintained when modelled structures are given as input

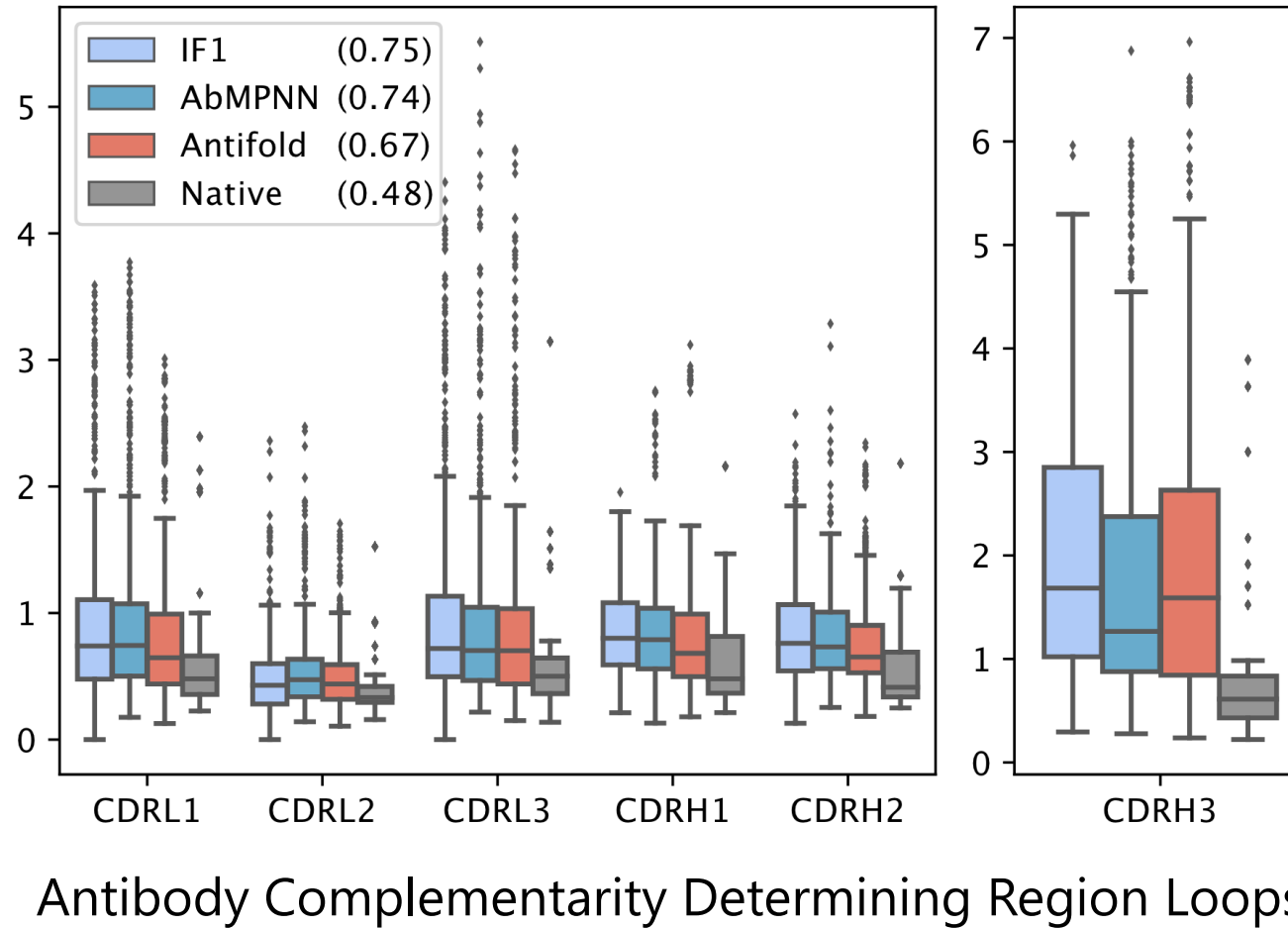


AntiFold suggests more confident amino acid distributions at CDRH3 positions, crucial for antibody binding



Designed antibody sequences re-fold into similar structures

Backbone deviation,
RMSD (Å)



AntiFold: Improved antibody sequence design using inverse folding



Poster #90
at 16:15

1. Improved design of antibodies while maintaining structure
2. Processes ~15 structures per minute (GPU)
3. Downloadable package freely available at: <https://opig.stats.ox.ac.uk/data/downloads/AntiFold/>

Acknowledgements



Poster #90
at 16:15

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Prof. Morten Nielsen

Prof. Charlotte M. Deane

