

# Computational Structural Biology of Biomolecular Interactions

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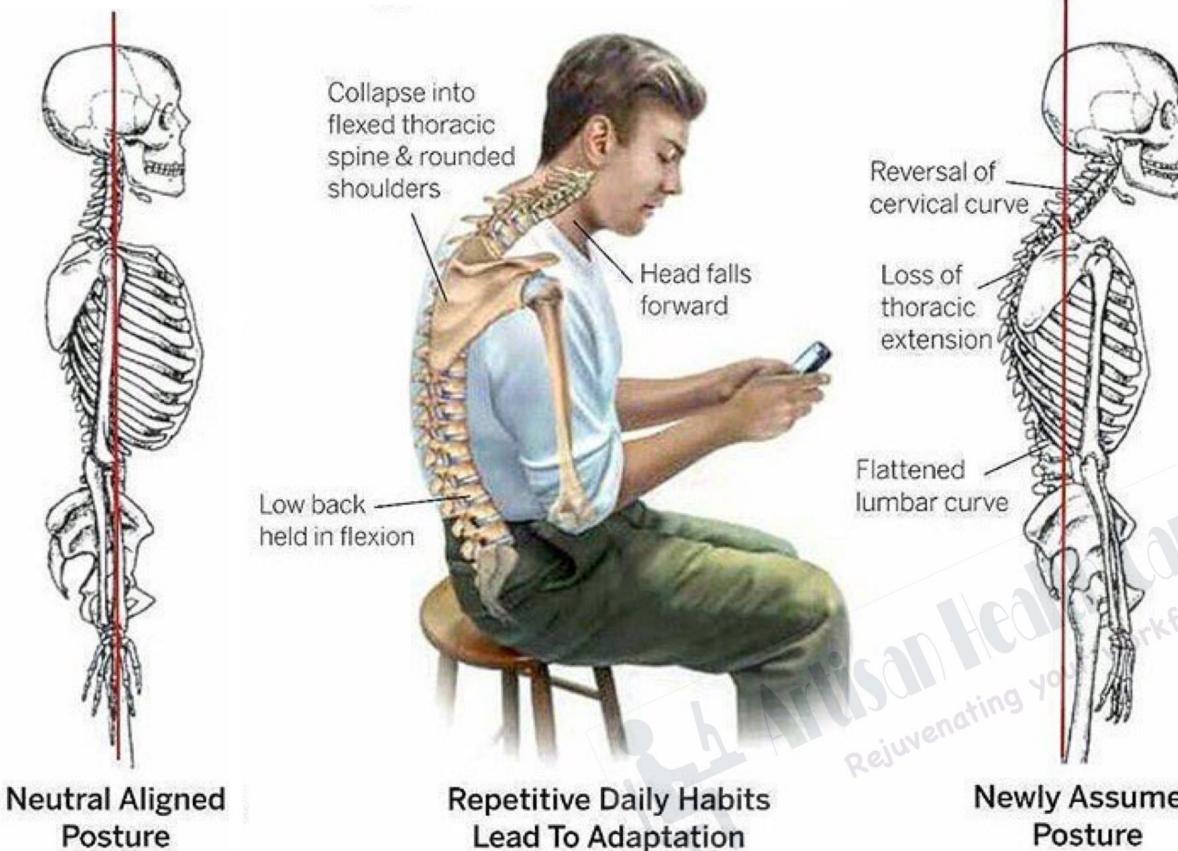


**Computational Structural Biology Lab - Karaca Lab**

25.04.2023

# Understanding molecular machines: Why?

## FORM FOLLOWS FUNCTION!



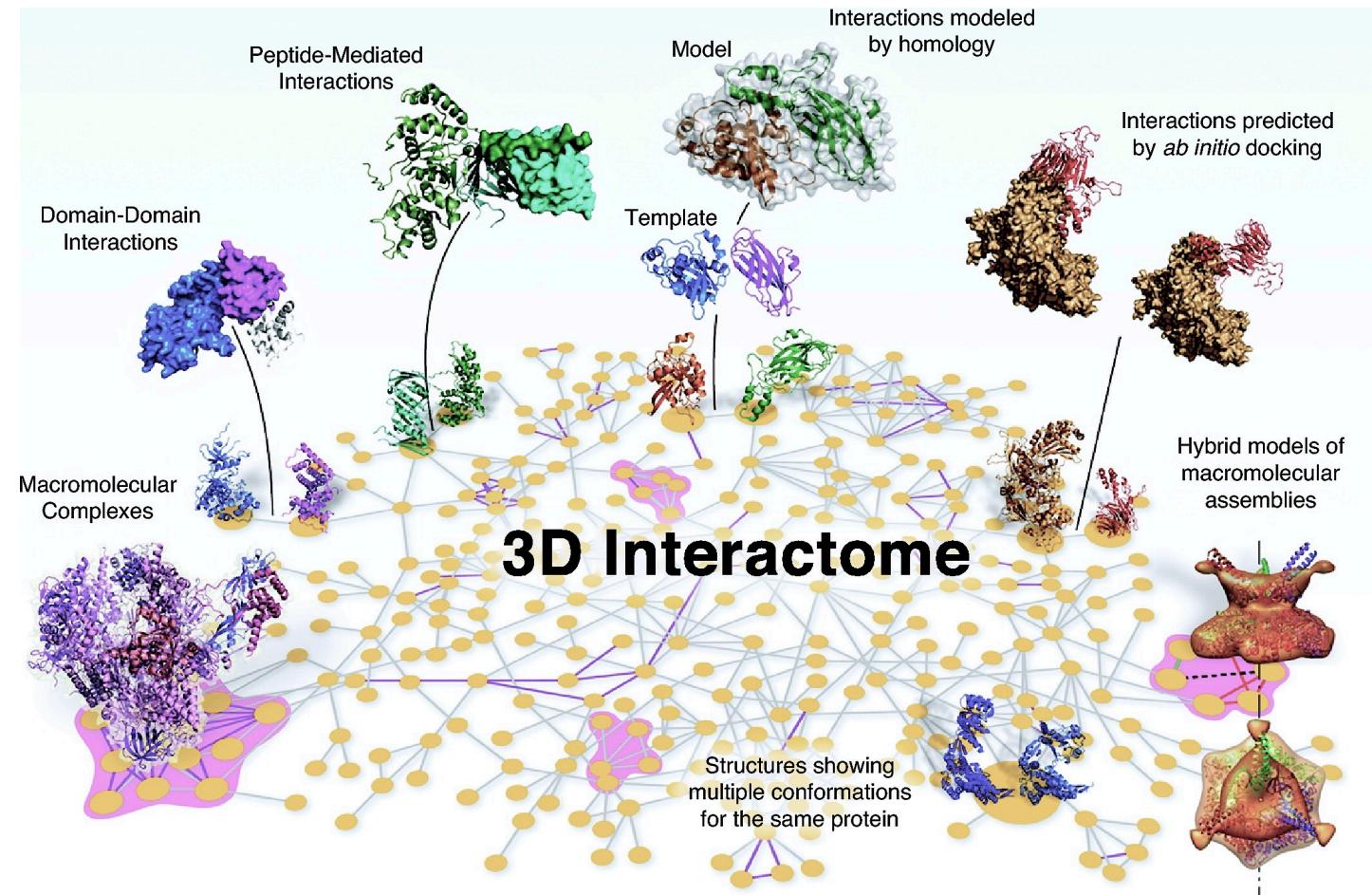
# Structural Biology of Complexes

## Experimental Structures Computational Models

X-Ray Cryst.

NMR Spec.

Electron Mic.



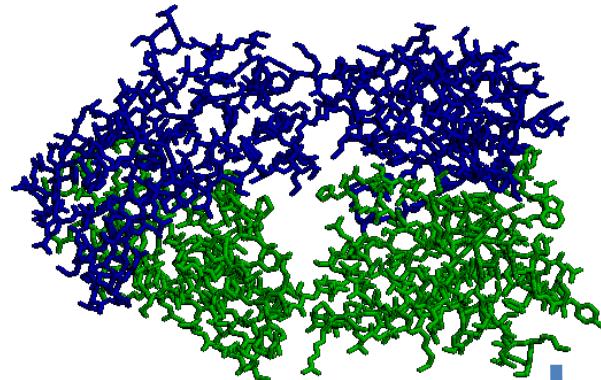
Homology Modeling

Docking

Integrative Modeling

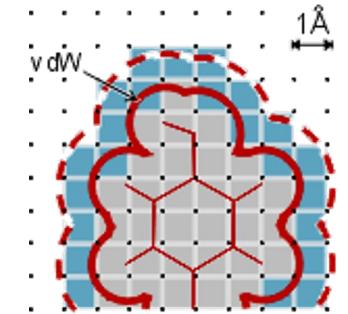
DL-based modeling

# How to represent the system *in silico*?

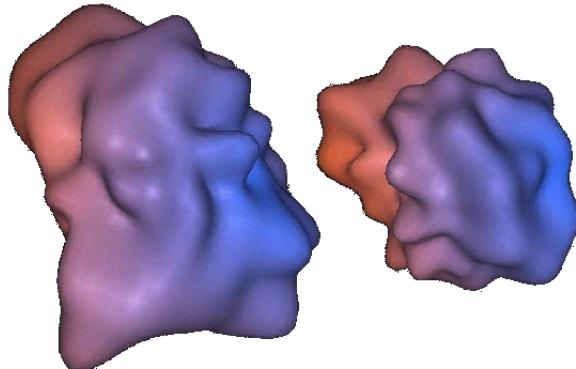
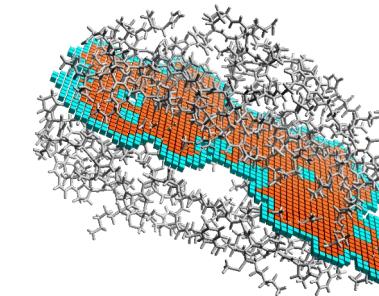


Explicit

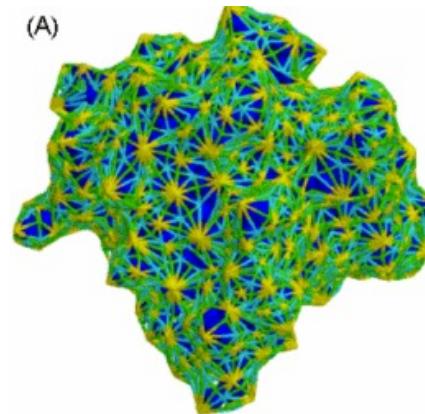
Mixed



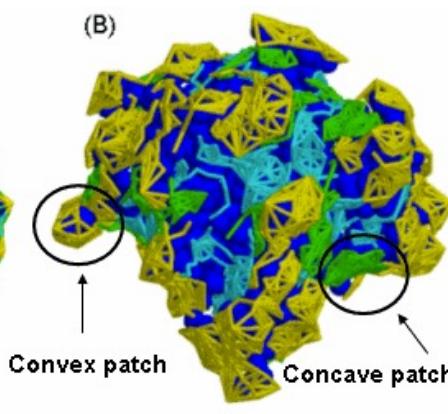
Grid Representation



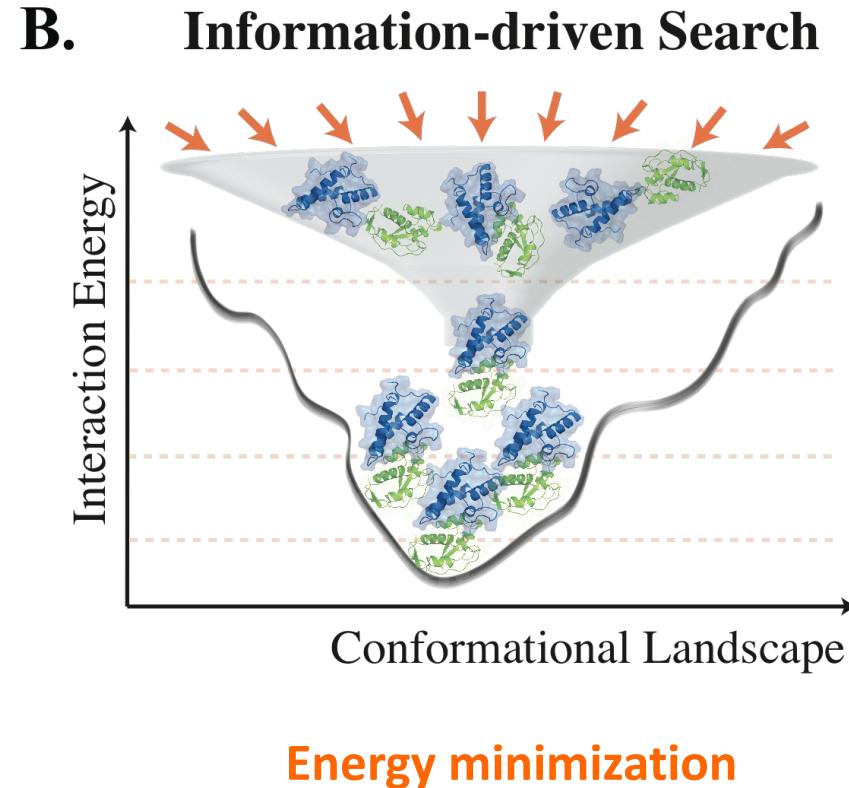
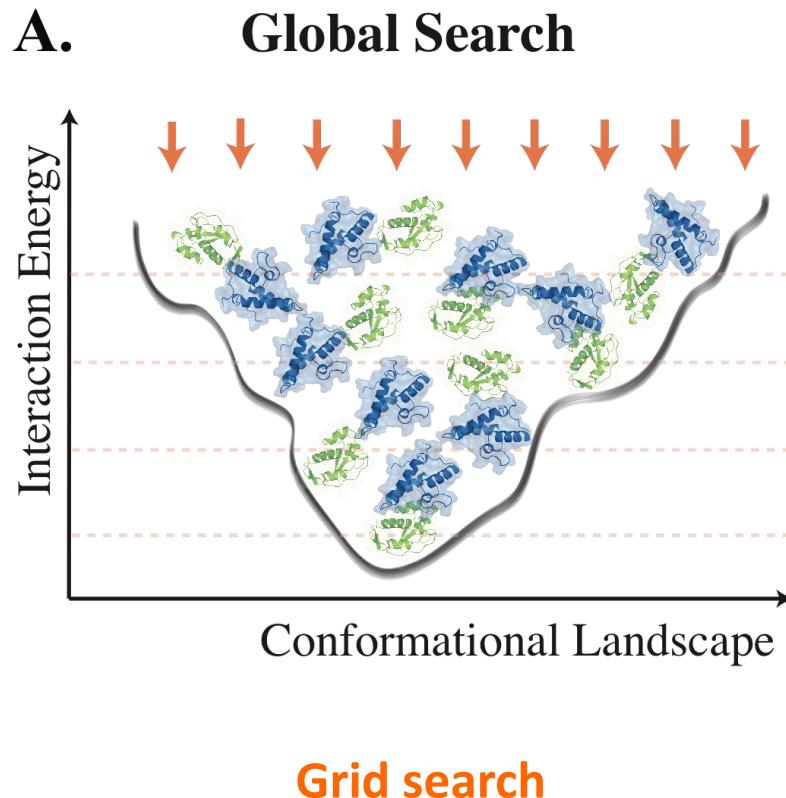
Spherical Harmonics



Geometric Hashing

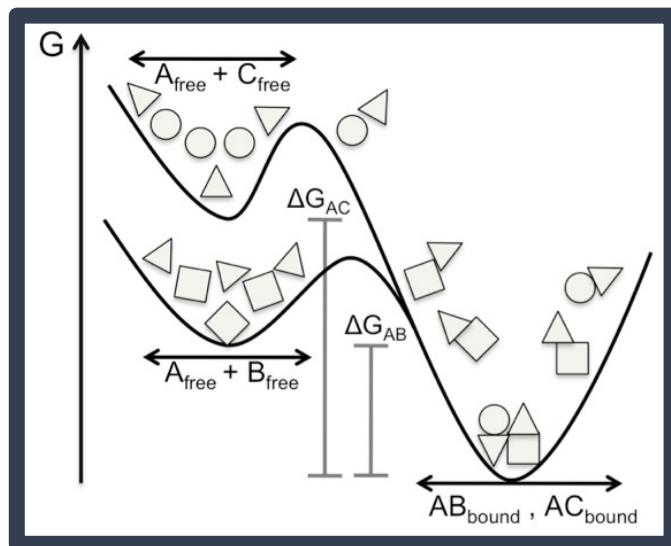


# What are the available search methods?



# How to pick the right model?

- Scoring based on a biophysical function
  - Force field terms
  - Buried surface area
  - Interaction propensities

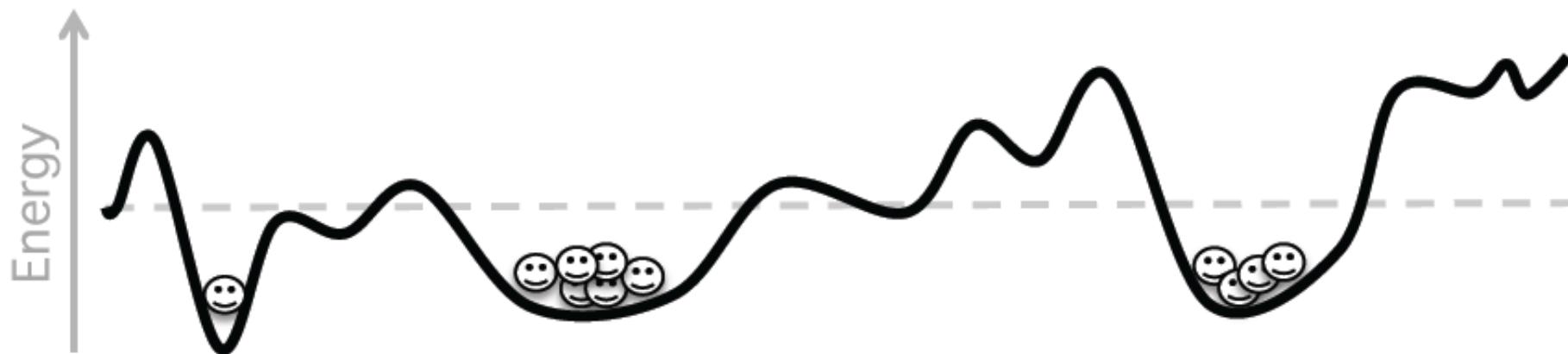


Filtering based on exp. data

Incorporating  $E^{\text{restr}}$  violations

# To check MODEL precision

- Clustering



Measure: Root Mean Square Deviation (RMSD)

or

Fraction of Common Contacts (FCC)

# How to assess the models?

Check accuracy and precision at the same time.

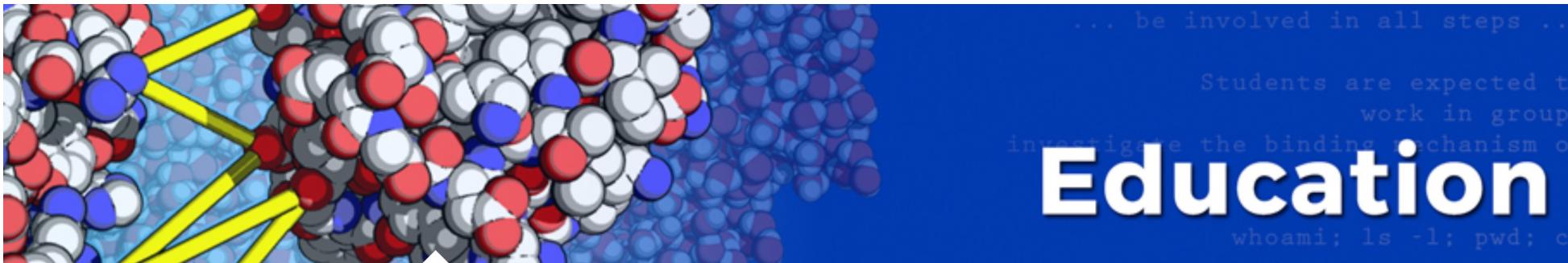


Accurate  
Precise

NOT Accurate  
Precise

NOT Accurate  
NOT Precise

# HADDOCK Tutorials



Computational Structural Biology group focusing on dissecting, understanding and predicting biomolecular interactions at the molecular level.

- [Email](#)
- [Github](#)
- [Youtube](#)
- [Subscribe](#)

Supported by:



## HADDOCK Tutorials for version 2.4

In this page you can find links to tutorials on the usage of our software and webportal [HADDOCK 2.4](#).

- [\*\*HADDOCK2.4 local installation tutorial\*\*](#): A tutorial demonstrating the installation and use of a local installation of HADDOCK2.4. It demonstrates various docking scenarios. You will need for this a valid license of HADDOCK2.4.
- [\*\*HADDOCK2.4 basic protein-protein docking tutorial\*\*](#): A tutorial demonstrating the use of the HADDOCK web server to model a protein-protein complex using interface information derived from NMR chemical shift perturbation data. This tutorial does not require any Linux expertise and only makes use of our web server and [PyMol](#) for visualisation/analysis.
- [\*\*HADDOCK2.4 basic antibody-antigen docking tutorial\*\*](#): This tutorial demonstrates the use of HADDOCK2.4 for predicting the structure of an antibody-antigen complex using information about the hypervariable loops of the antibody and NMR data identifying the epitope. This tutorial does not require any Linux expertise and only makes use of our web servers and [PyMol](#) for visualisation/analysis. The complex is also modelled using AlphaFold2 and the results compared to those obtained with HADDOCK.
- [\*\*HADDOCK2.4 MS cross-links tutorial\*\*](#): A tutorial demonstrating the use of cross-linking data from mass spectrometry to guide the docking in HADDOCK. This tutorial builds on our [DisVis tutorial](#) and illustrates various scenarios of using cross-linking data in HADDOCK. This tutorial does not require any Linux expertise and only makes use of our web server and [PyMol](#) for visualisation/analysis.

<https://www.bonvinlab.org/education/HADDOCK24/>

# Hands-on videos

## Demonstrations and hands-on session for working with HADDOCK

PRACE Autumn School 2021



BioExcel CoE  
3.2K subscribers



<https://www.youtube.com/watch?v=2niUg-t2DZg>

## Basics of docking for drug design and Introduction to HADDOCK

PRACE Autumn School 2021



BioExcel CoE  
3.2K subscribers



<https://www.youtube.com/watch?v=PiiEyRyO07g>

# HADDOCK forum for your questions and problems

[Sign Up](#)[Log In](#)

Feel free to create new topics related to your questions!

The HADDOCK category is meant for discussing any topic related to the use of the HADDOCK software, either as a local installation or via the [HADDOCK web portal](#). For details about HADDOCK please refer to <https://www.bonvinlab.org/software/haddock2.4>

<https://ask.bioexcel.eu/c/haddock/6>

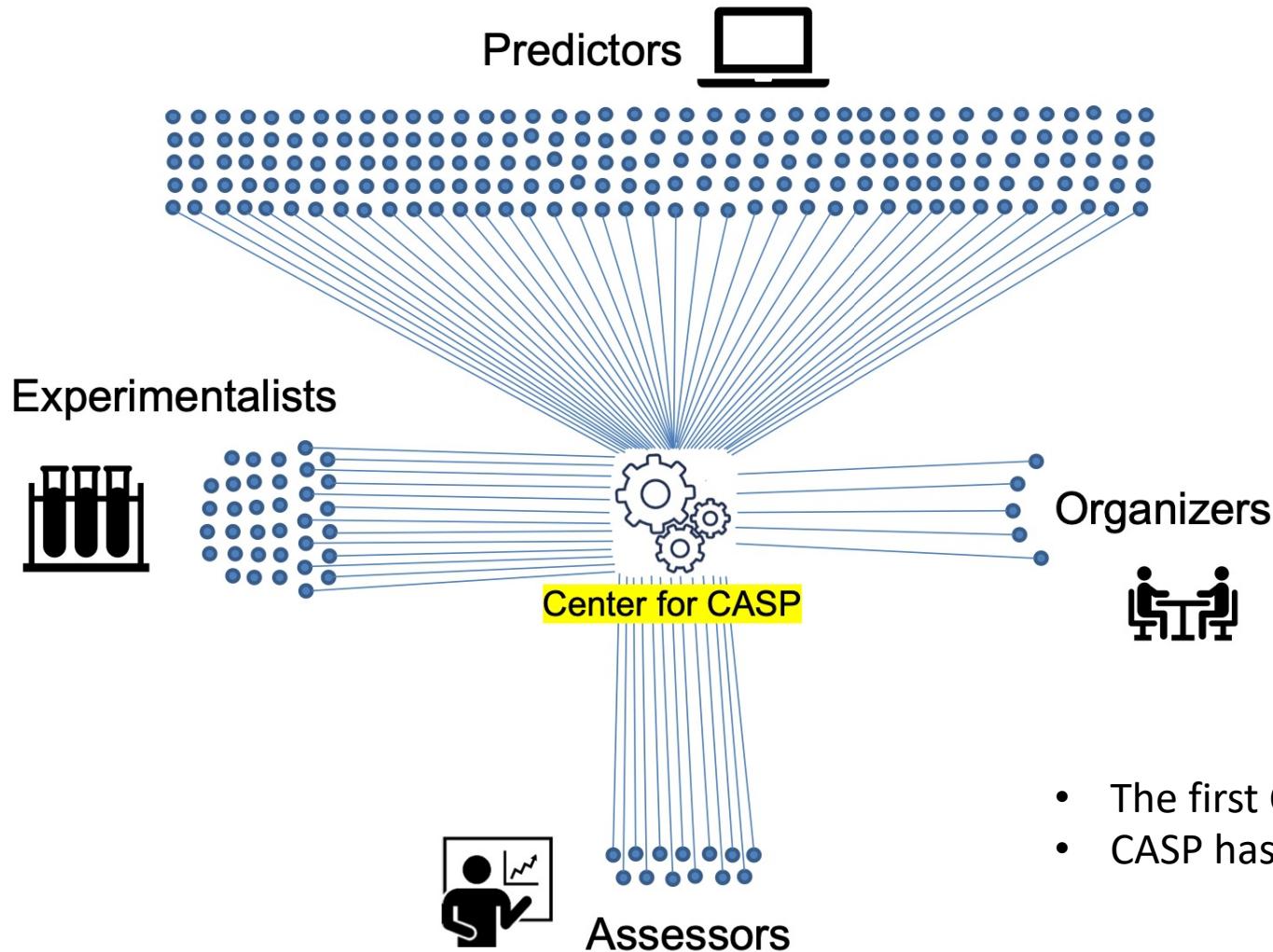
**HOW**



How to evaluate the accuracy of protein structure prediction methodologies?

How to evaluate improvements in the methods of identifying protein structure from sequence?

# CASP (Critical Assessment of Protein Structure Prediction)



- The first CASP in 1994
- CASP has been organized every 2 years

# CASP14 (2020) - Assessors

- Topology
- High accuracy modeling
  
- Refinement
- Contacts
  
- Accuracy estimation
- Assemblies
  
- CAPRI
- Function

Nick Grishin, Lisa Kinch



Andrie Luples, Joana Pereira, Marcus Harman



Dan Rigden



Alfonso Valencia, Rosalba Lepore



Chaok Seok



Ezgi Karaca



Burcu Ozden

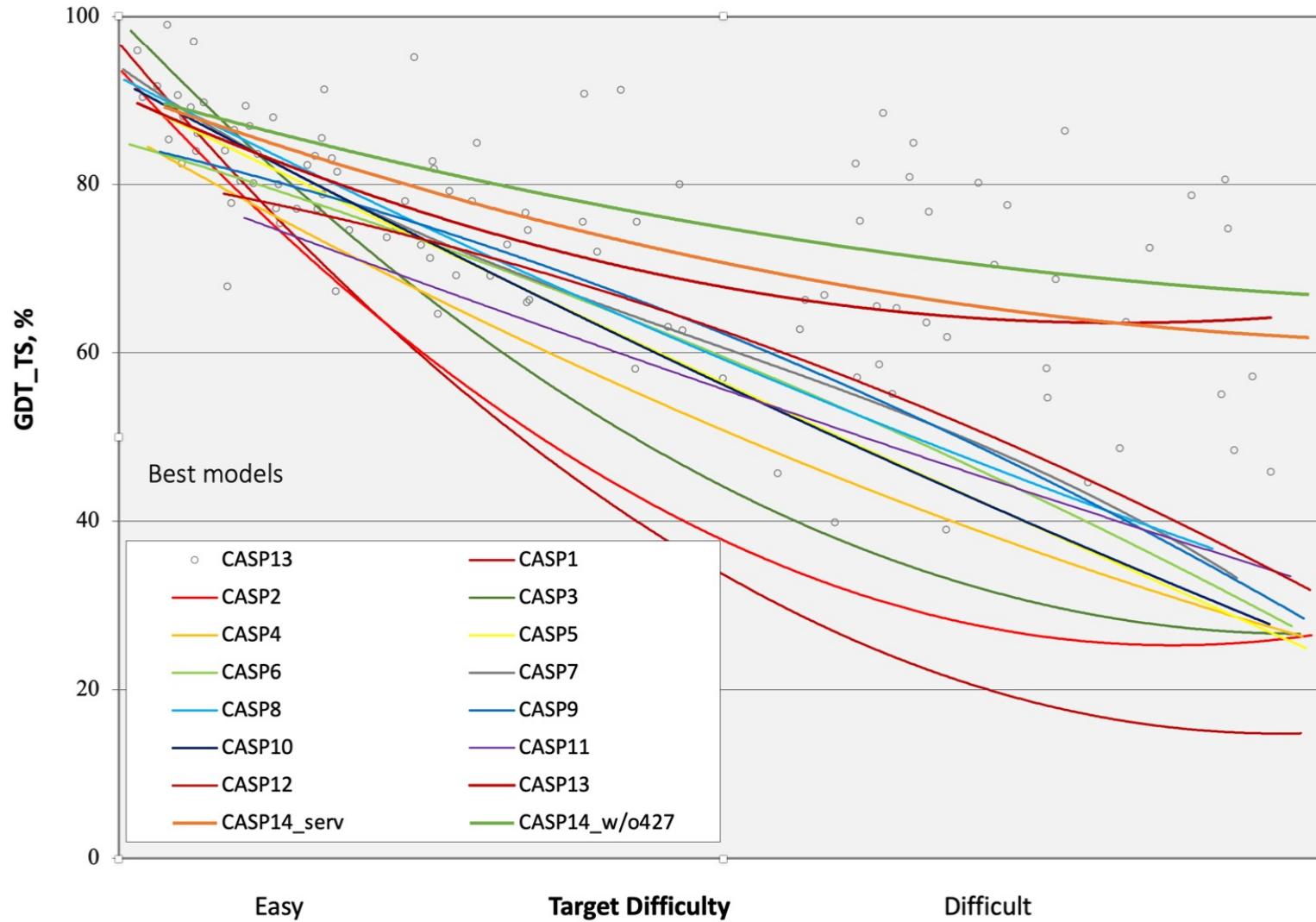


Marc Lesink, Shoshana Wodak

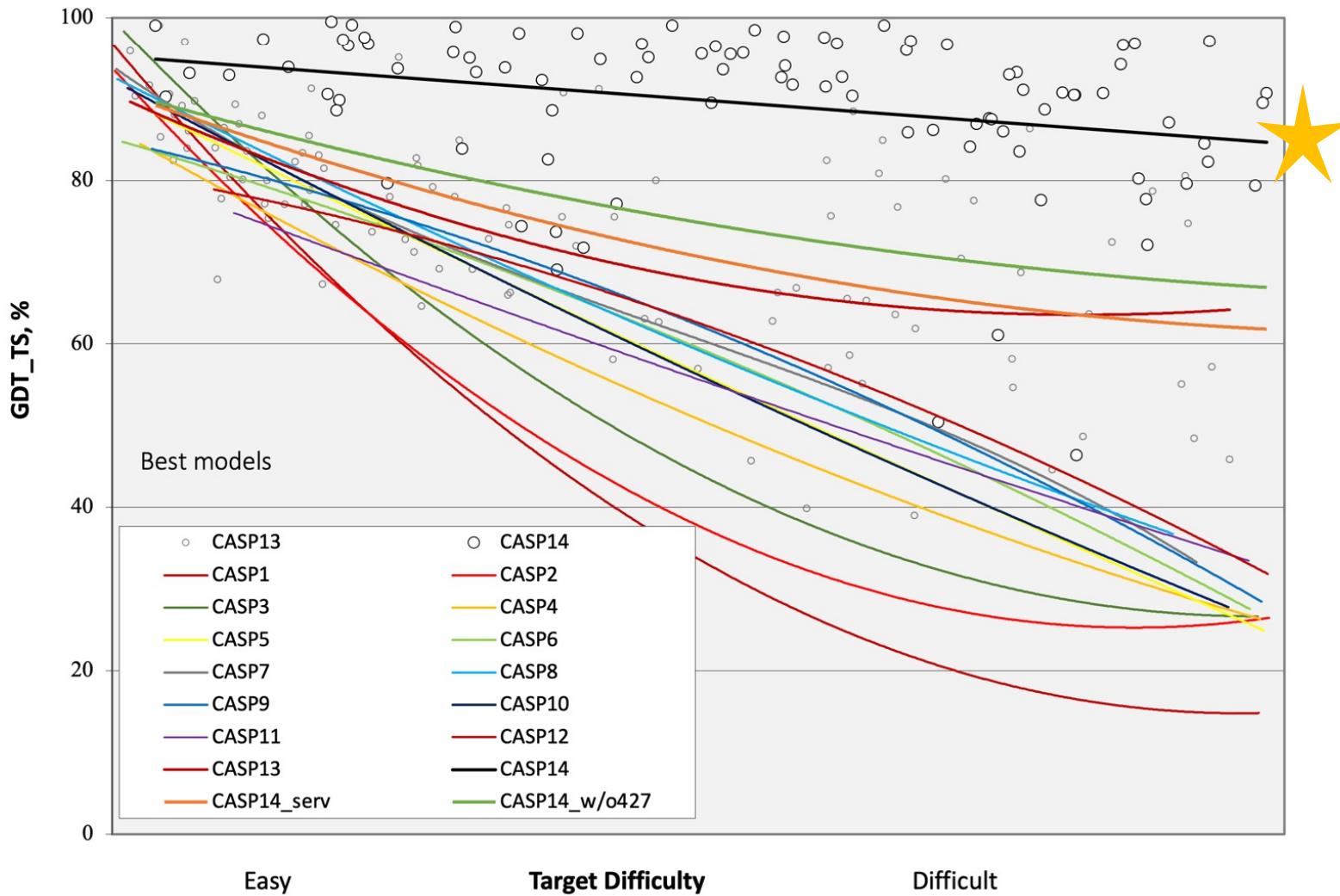
Sandor Vadja, Dima Kozakov



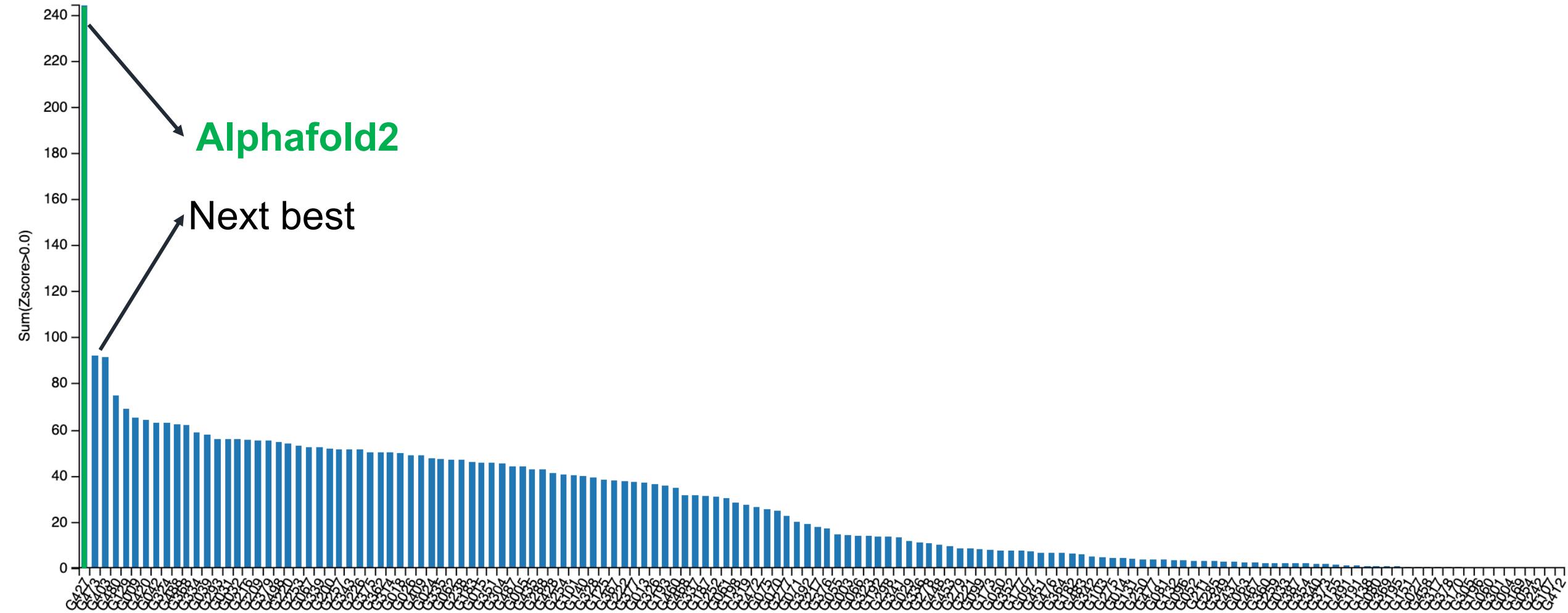
# Tertiary structure prediction rates over years...



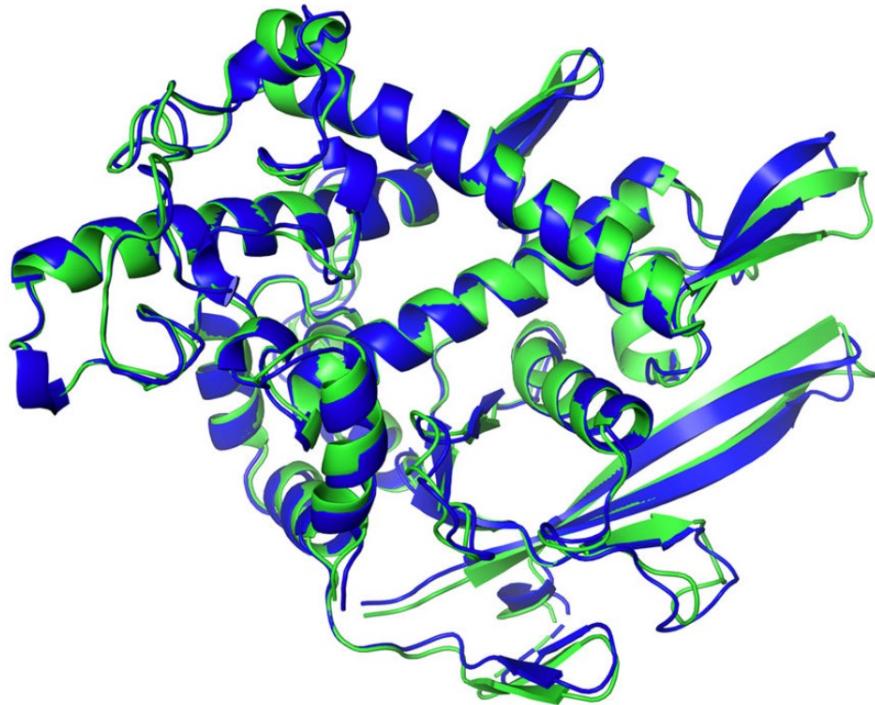
... with AlphaFold2



# AlphaFold's Success in 2020 in CASP14



# Revolution in Structure Prediction!



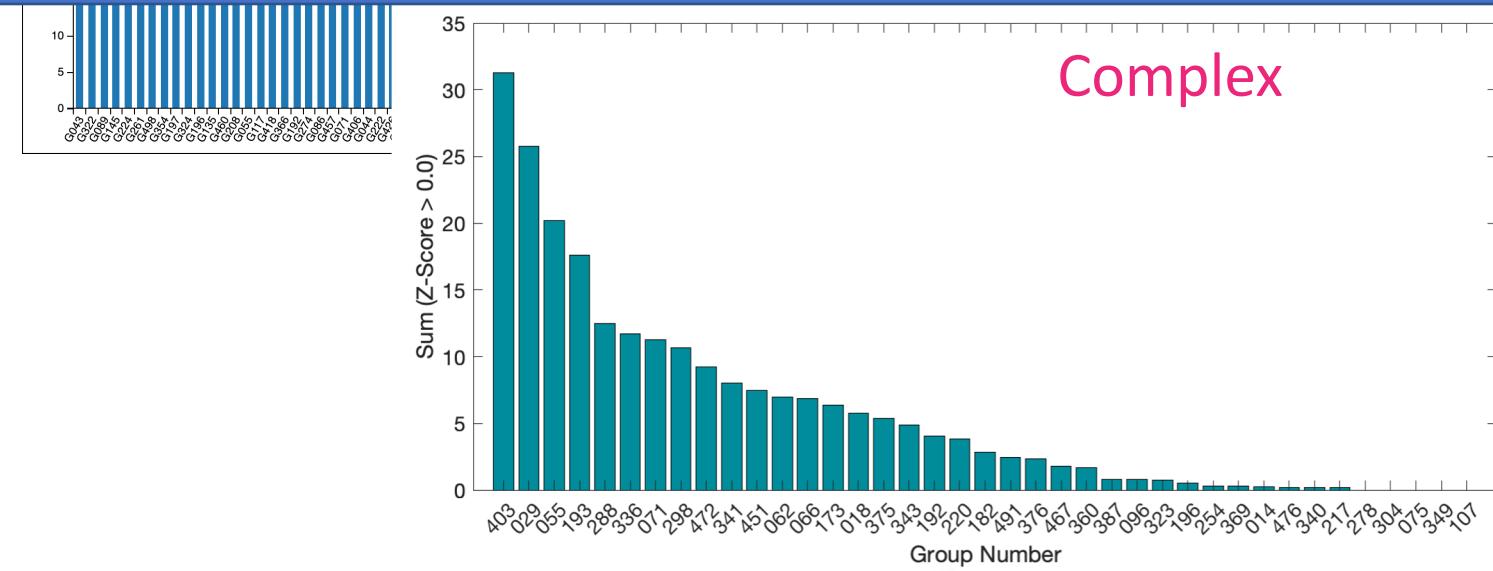
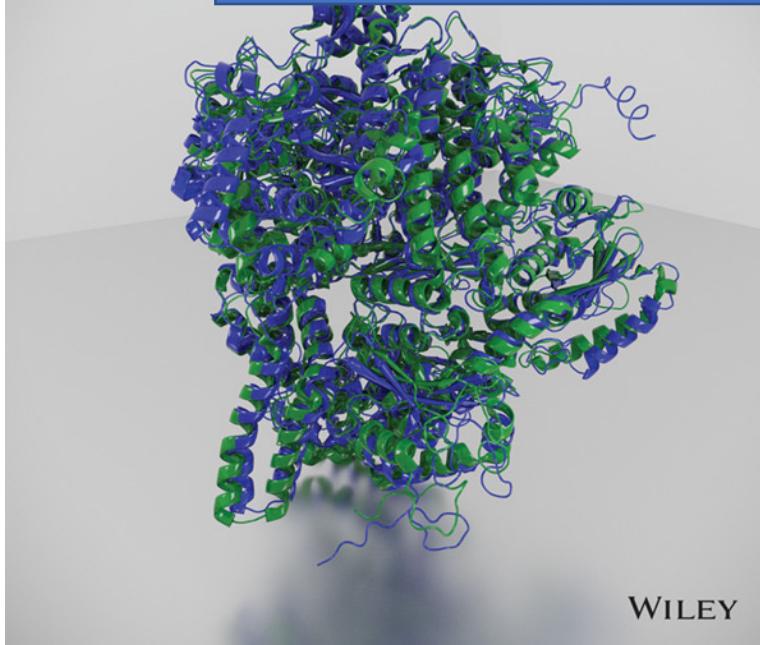
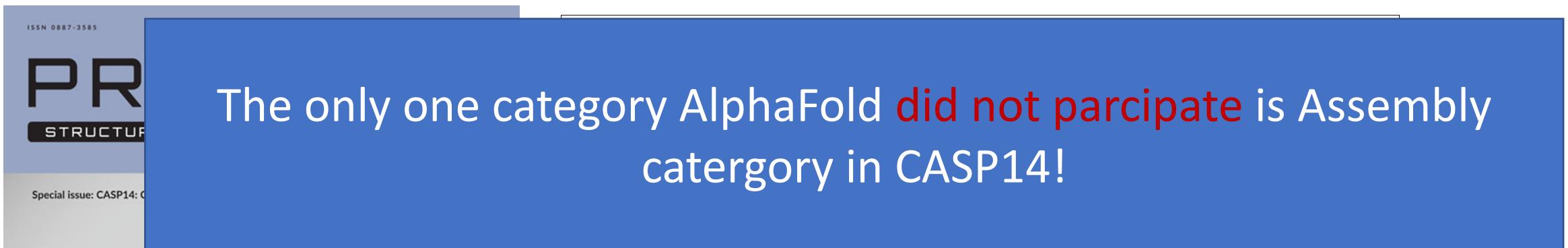
AlphaFold2  
Experimental

Structures of a protein that were predicted by artificial intelligence (blue) and experimentally determined (green) match almost perfectly. DEEPMIND

**'The game has changed.' AI triumphs at solving protein structures**

By Robert F. Service | Nov. 30, 2020 , 10:30 AM

# A paradigm shift on its way!



RESEARCH ARTICLE

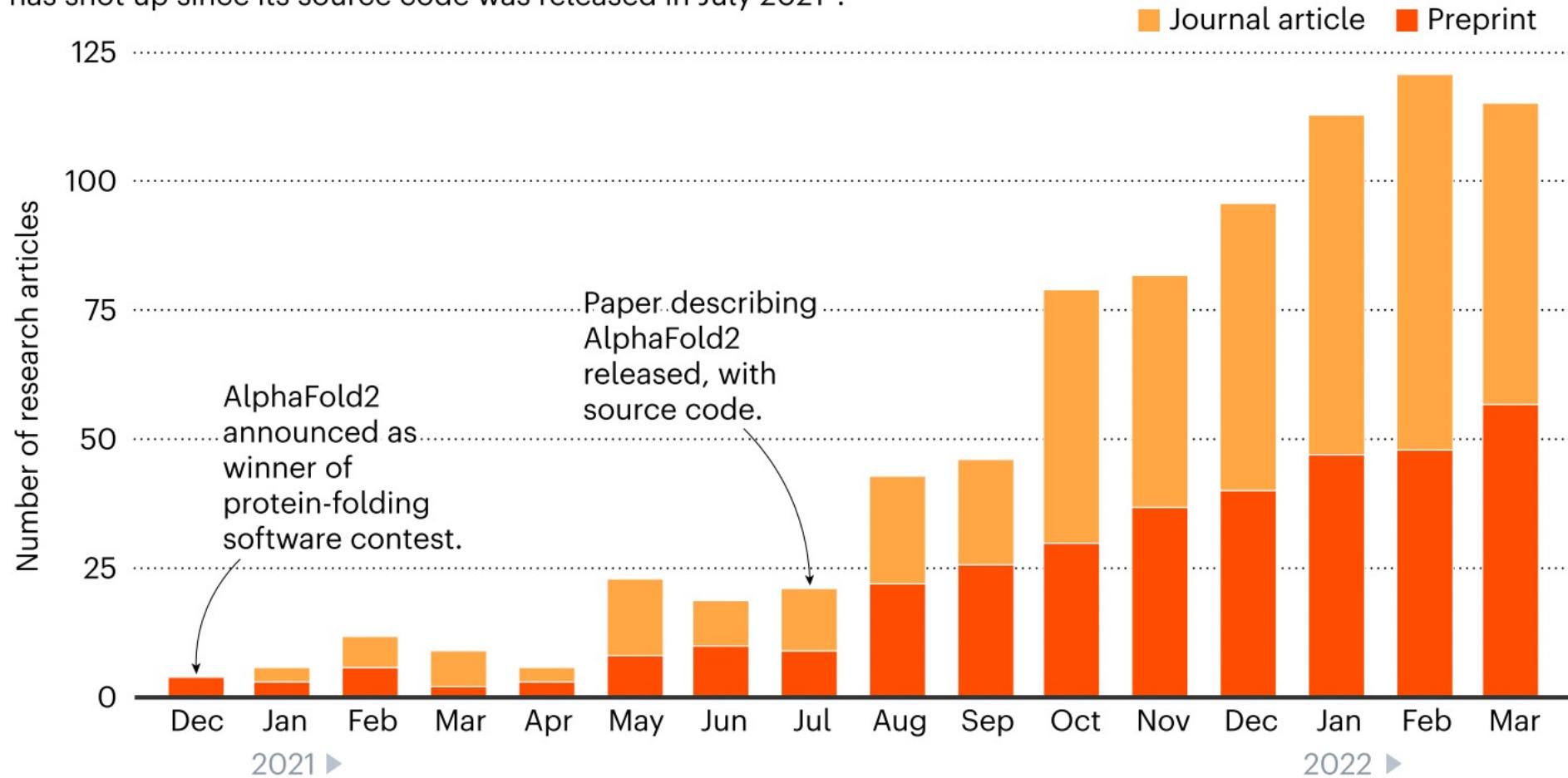
Assessment of the CASP14 assembly predictions

Burcu Ozden<sup>1,2</sup> | Andriy Kryshtafovych<sup>3</sup> | Ezgi Karaca<sup>1,2</sup>

PROTEINS  
WILEY

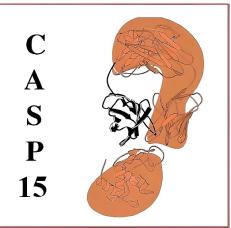
# What happened since AF2 release

The number of research papers and preprints citing the AlphaFold2 AI software has shot up since its source code was released in July 2021\*.



Ewen Callaway, Nature, 2022

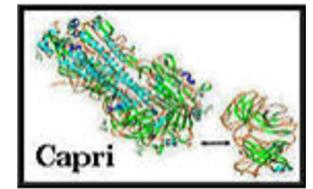
What about the  
DL methods in assembly prediction?



# CASP15 Assembly Assessment Team



Ezgi Karaca



Burcu Özden



Marc Lensink



Andriy Kryshtafovych



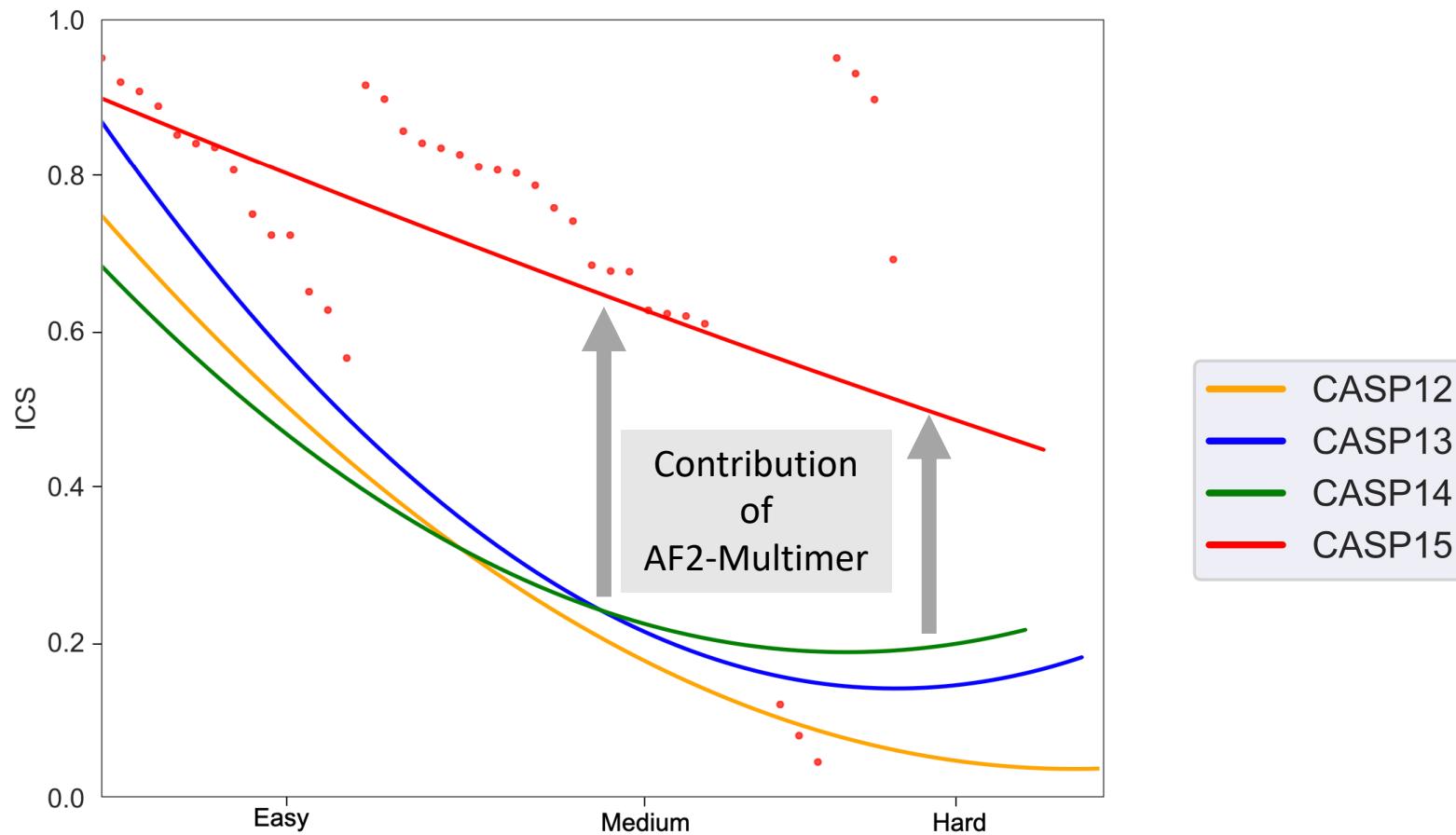
Shoshana Wodak

CASP15 was held in Antalya!

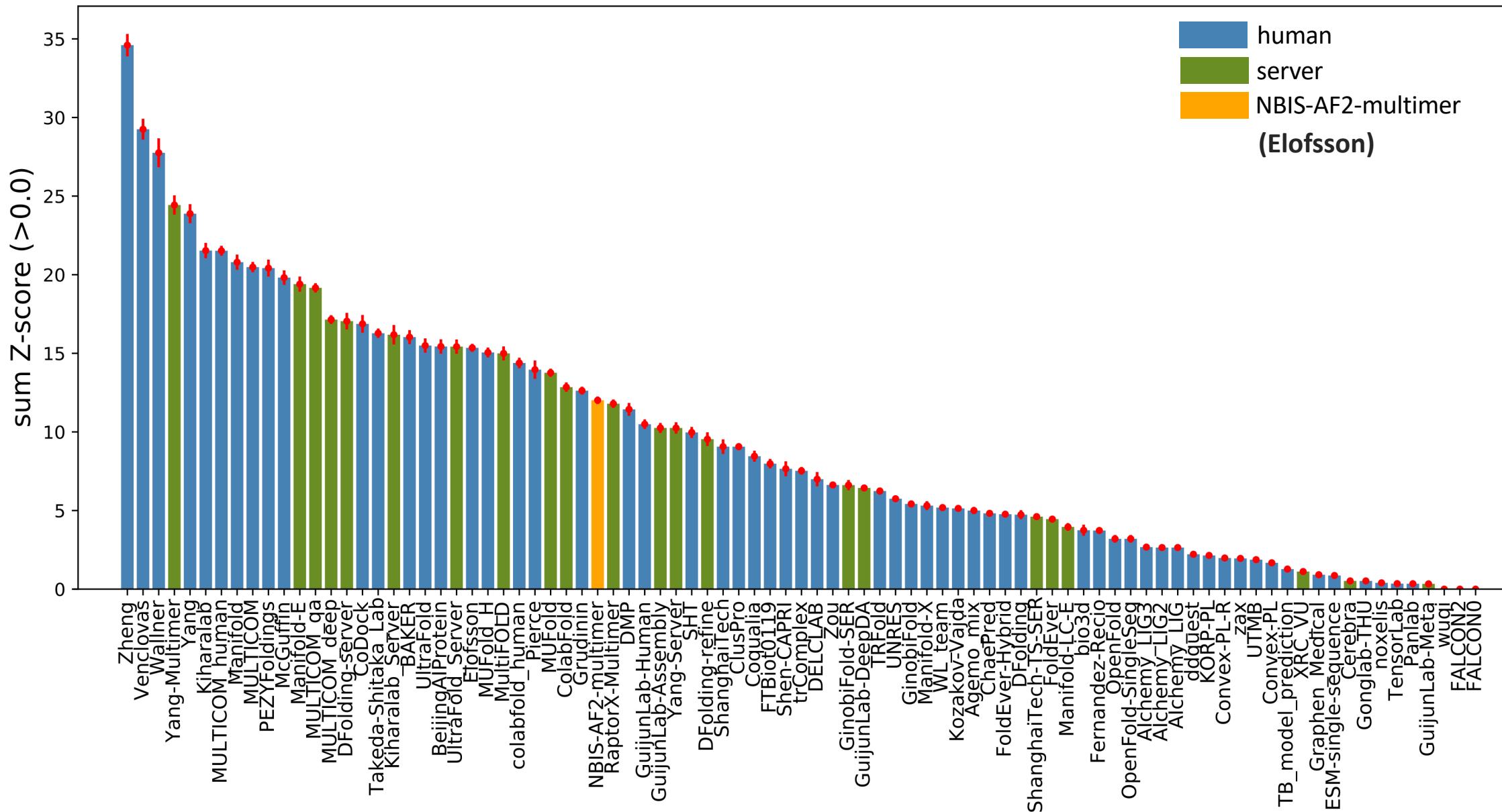


<https://predictioncenter.org/casp15/index.cgi>

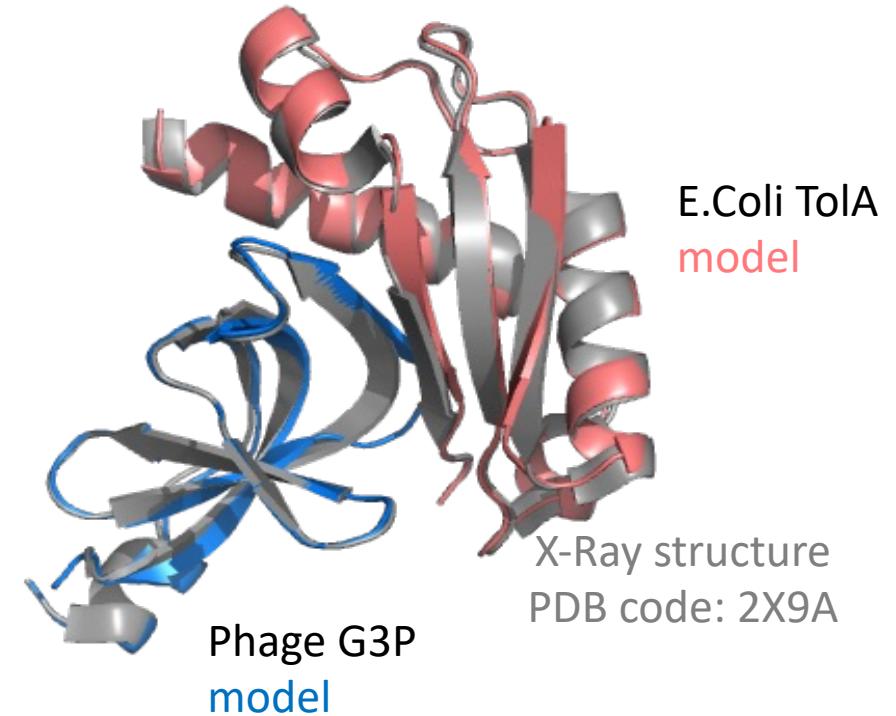
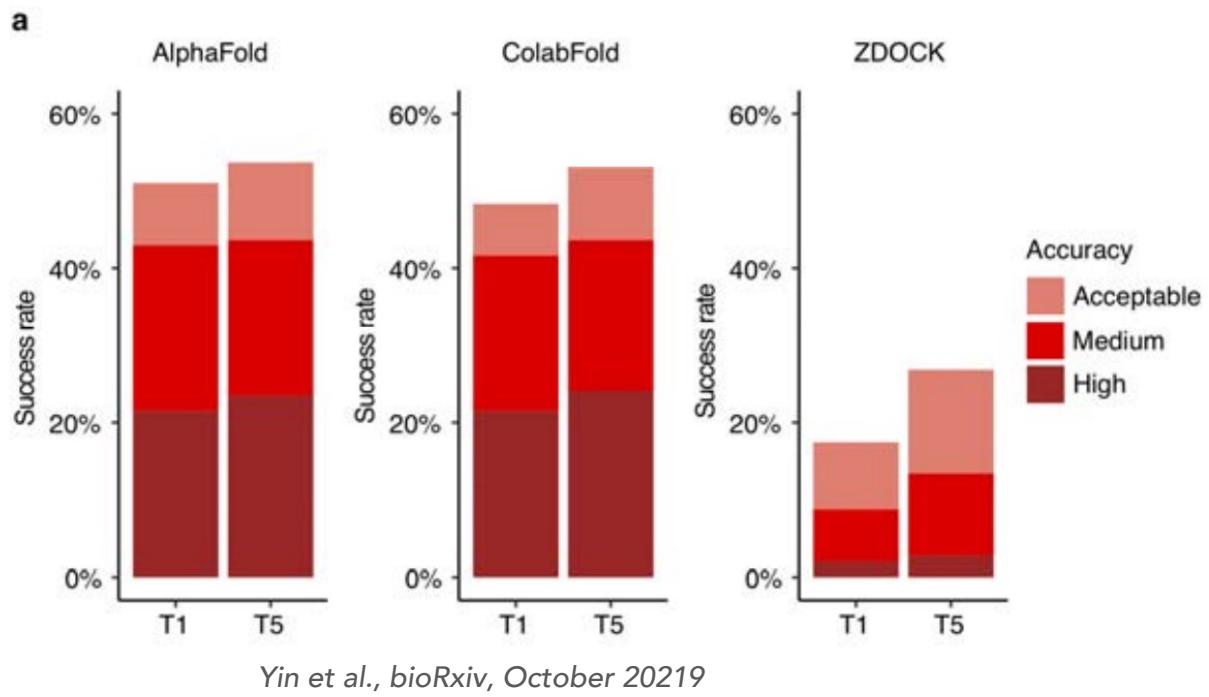
# Assembly performance over years in CASPs



# CASP15 Assembly group ranking



# How well will be the oligomers predicted?



Link for the workshop:

<https://github.com/CSB-KaracaLab/CSB-WS>

