Joint CASP16-CAPRI57 assembly prediction round of 2024

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CAPRI and CASP

CAPRI	**CASP**
Since 2001	Since 1994
Critical **A**ssessment of **PR**edicted **I**nteractions	**C**ritical **A**ssessment of **S**tructure **P**redictions

Joint prediction rounds since 2014:

25 Targets	Round 30	CASP11	2014
10 Targets	Round 37	CASP12	2016
21 Targets	Round 46	CASP13	2018
12 Targets	Round 50	CASP14	2020
37 Targets	Round 54	CASP15	2022
34 Targets	Round 57	CASP16	2024

Prediction rounds on a “rolling” basis	Prediction season
Fits with publication schedule	Intense 2 to 3 months
3 to 4 weeks per prediction round	
Fixed assessor team, established metrics	Varying assessors, varying metrics

Difference in targets

Mostly hetero-dimers or -trimers Peptides, sugars, water positions	Mostly obligate, many homo-oligomers Very large assemblies
Incites method development	**Large-scale testing of methodologies**

Website

CAPRI

Since 2001

Critical **A**ssessment of
PRedicted **I**nteractions

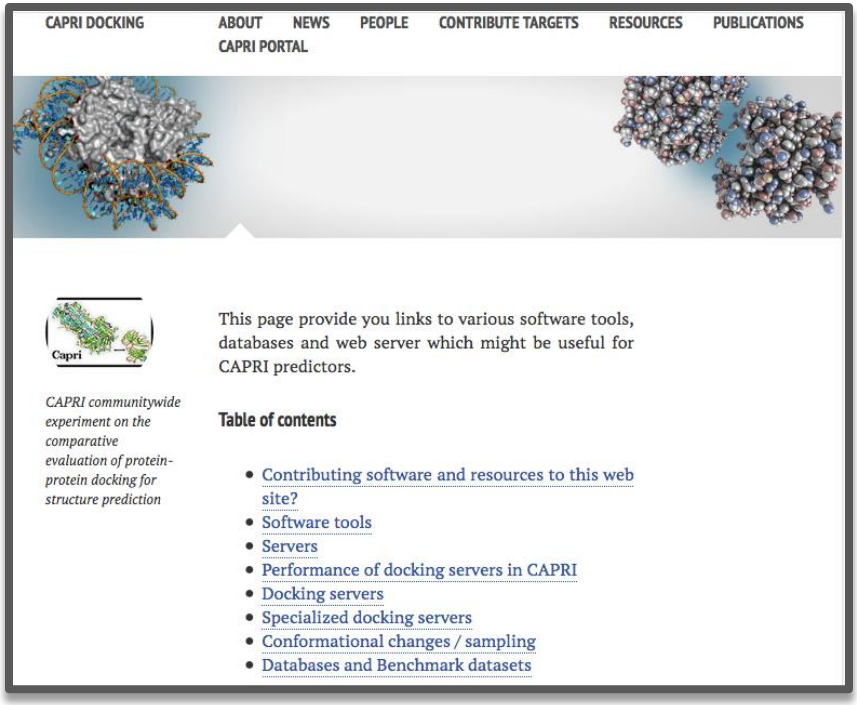
Protein Docking *and* Scoring

https://www.pdbe.org/capri

(for prediction submission)

https://www.capri-docking.org/

(community exchange portal)

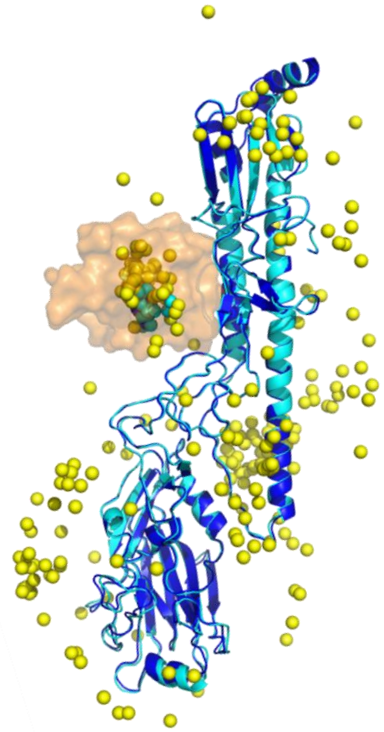


@CAPRIdock.bsky.social

CAPRI

Community-wide double blind experiment modelled after CASP, launched in 2001, aimed at assessing the performance of protein docking and scoring algorithms.

Prediction of the structure of an unpublished **protein-protein**, **protein-DNA/RNA**, **protein-peptide**, **protein-sugar** complex, or **multi-domain** protein; extended to the prediction of **binding affinity** and **interface water position**.



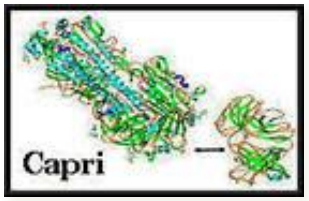
Marc  assessment

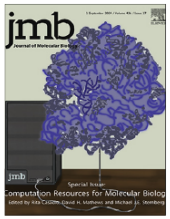
Alexandre  organization

Guillaume  website

Sameer  operations

EBI  infrastructure

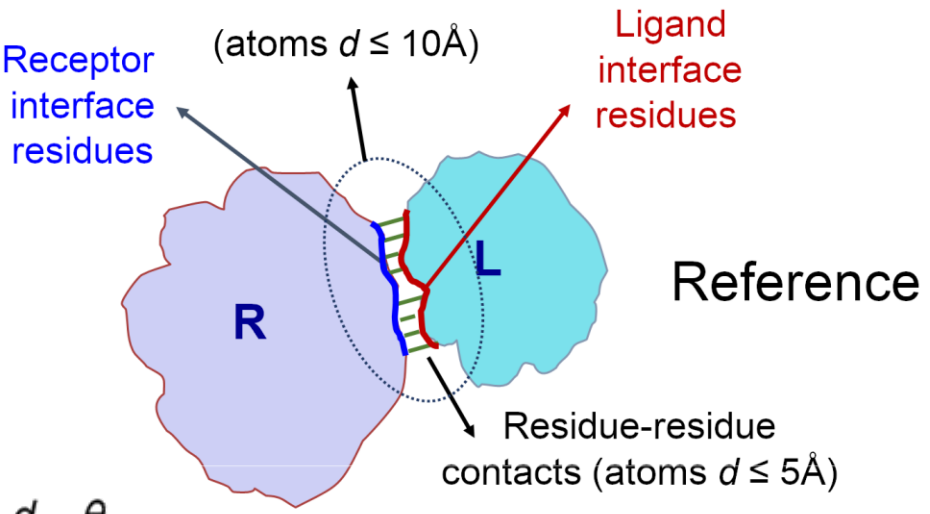


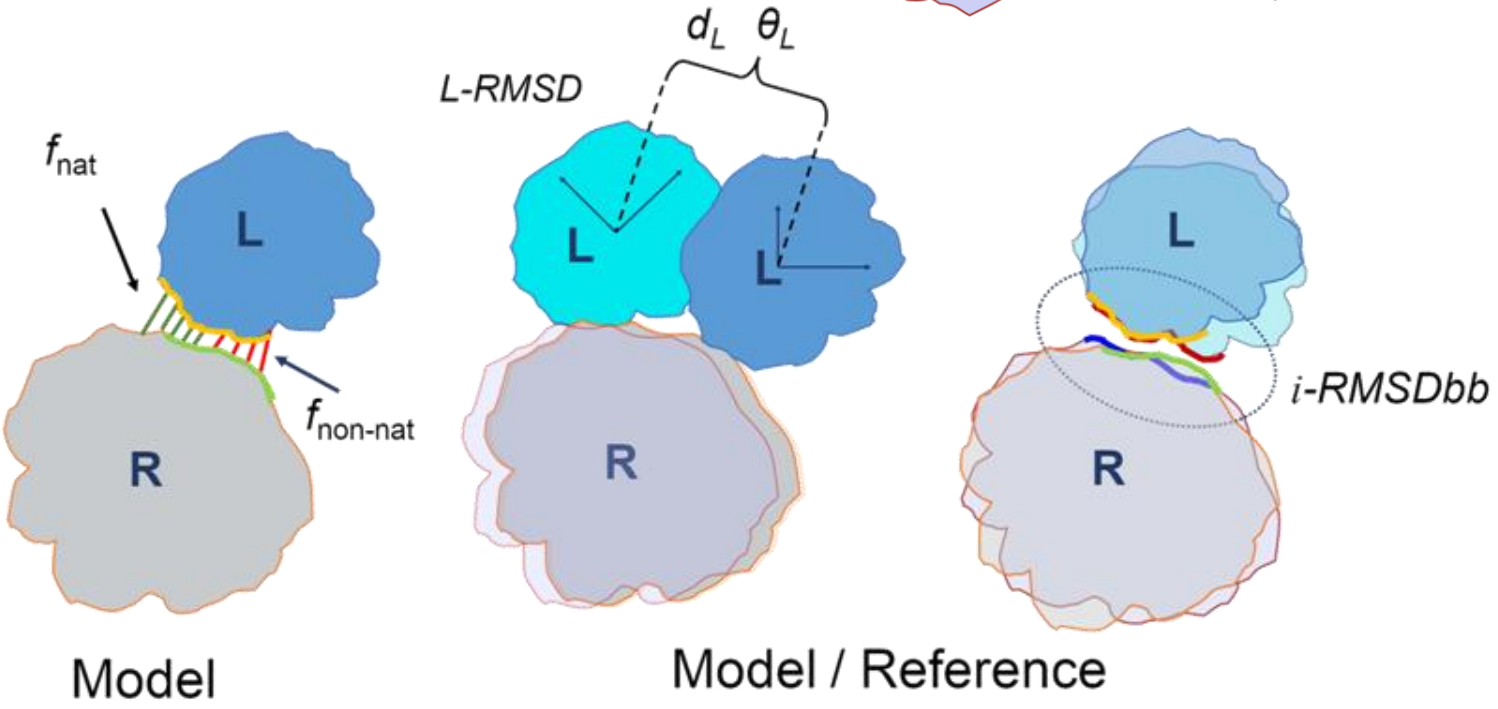


CAPRI-Q: The CAPRI resource evaluating the quality of predicted structures of protein complexes

Keeley W. Collins [1], Matthew M. Copeland [1], Guillaume Brysbaert [3], Shoshana J. Wodak [4], Alexandre M. J. J. Bonvin [5], Petras J. Kundrotas [1,*], Ilya A. Vakser [1,2,*] and Marc F. Lensink [3,*]

J Mol Biol 2024;436:168540





CAPRI Assessment

1. CAPRI assessment is
   a) receptor/ligand and
   b) interface based
   - L-rms
   - *f*(nat); i-rms

2. Four assessment categories
   - incorrect, acceptable, medium, high

3. For multimeric targets, each interface is assessed separately; depending on complexity, targets may then be split up into several assessment units (AU), with an AU representing a combination of individual interface scores
   - Either an AverageOf or BestOf

4. Final predictor score is the sum of these scores

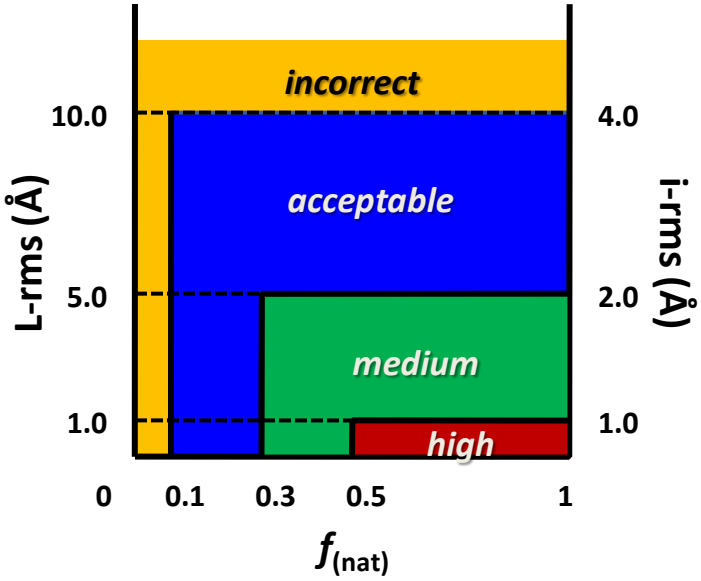
$$\text{Score} = \omega_1 \cdot N_{ACC} + \omega_2 \cdot N_{MED} + \omega_3 \cdot N_{HIGH}$$

$\omega_1 = 1$; $\omega_2 = 2$; $\omega_3 = 3$

*Only **L-rms**, **i-rms** and f_{nat} are used to classify protein-protein interaction models in CAPRI.*

Additional quantities are being calculated, such as S-rms, which are useful quality measures for protein-peptide interaction models.

An additional condition may be placed on f_{nonnat} values in the future.



Timeline and Conventions

CASP	CAPRI	Duration
Stage0		
Stage1	CAPRI **R57**	2 weeks
MassiveFold input		
	CAPRI Scoring	1 week
Stage2	CAPRI **R58**	1 week

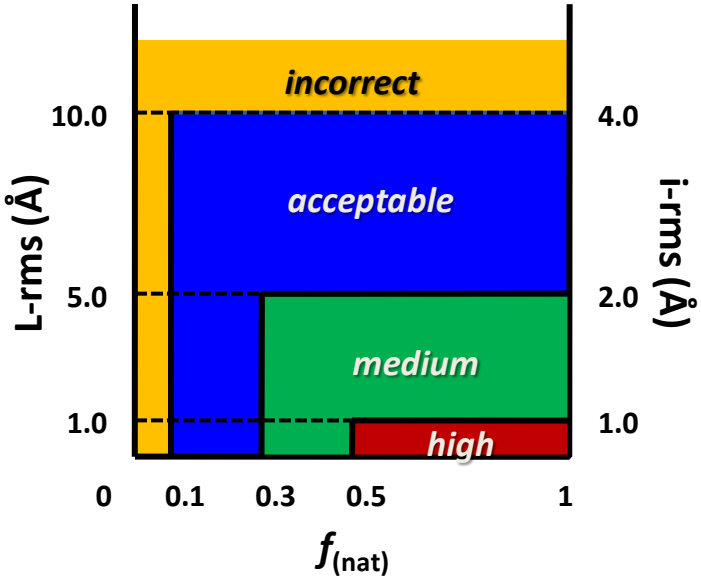
*Only **L-rms**, **i-rms** and f_{nat} are used to classify protein-protein interaction models in CAPRI.*

The rms thresholds are modified for protein-peptide interaction; high-quality requires:

$f_{(nat)}$	>=	0.8
L-rms	<=	1.0 Å
i-rms	<=	0.5 Å

1. Colors for the four assessment categories
   - **Incorrect**
   - **Acceptable**
   - **Medium**
   - **High**

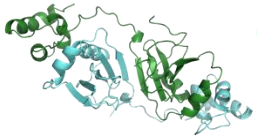
2. Font style for the predictor groups
   - Normal for human predictors
   - **ALL-CAPS (and boldface) for servers**
   - *S.Italics for scorer groups*
   - Name+ means "and their server"



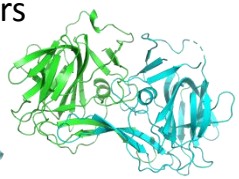
Statistics

CAPRI	T236 – T309		
CASP	T,H,M; 1201 – 2270		
Homo- and hetero-dimers	4	4	
Homo- and hetero-oligomers	4	15	
Antibodies and nucleic acids	10		
Number of targets	34		
Assessment units per stage	47	38	
Number of models (total)	88 198		
Number of models (top-5)	38 328		
MassiveFold models	430 486		
Total number of submitting groups	23	98	15
Submitting groups R57/stage1	15 – 22	23 – 77	11 – 13
Submitting groups R58/stage2	15 – 20	53 – 65	-
	CAPRI (included in CASP)	CASP	Scorers

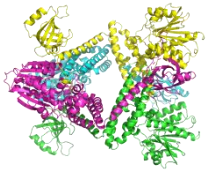
Homo-oligomers



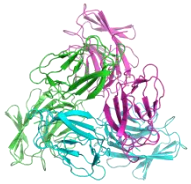
T236
T1201



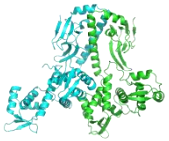
T242
T1206



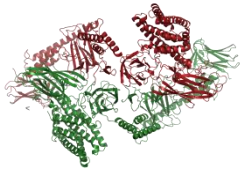
T282
T1237



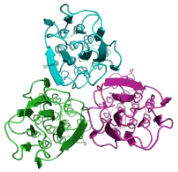
T286
T1240



T309*
T1298



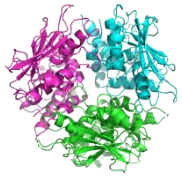
T260
T1218



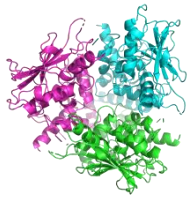
T298
T1259

* No MassiveFold

Conformers

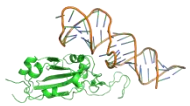


T250
T1249v1

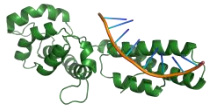


T252
T1249v2

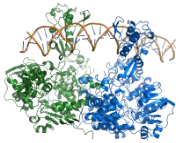
DNA and RNA binding



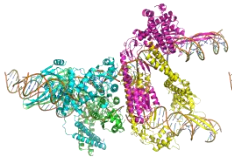
T304*
M1282



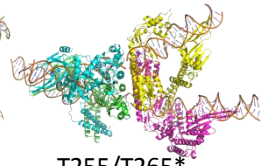
T306*
M1276



T308*
M1287

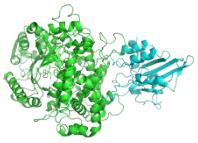


T254/T264*
M1228v1
M1239v1

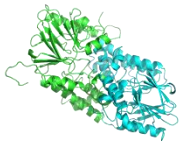


T255/T265*
M1228v2
M1239v2

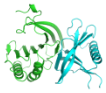
Hetero-oligomers



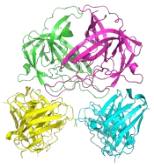
T276
H1230



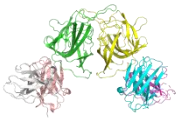
T244
H1208



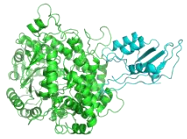
T296
H1245



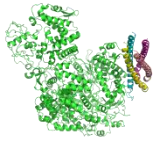
T278
H1232



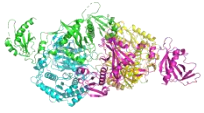
T280
H1233



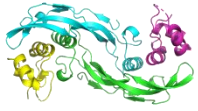
T274
H1229



T262
H1220

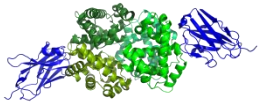


T300
H1267

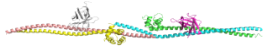


T238
H1202

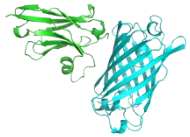
Antibodies and nanobodies



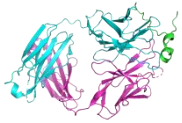
T240
H1204



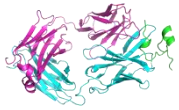
T294
H1244



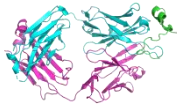
T248
H1215



T266
H1222

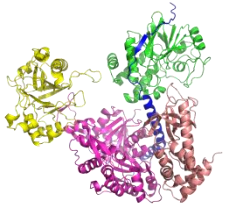


T268
H1223

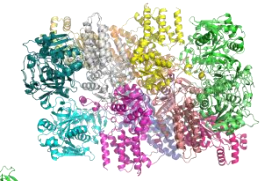


T270
H1225

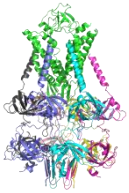
Large assemblies



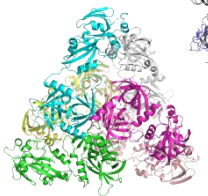
T256
H1213



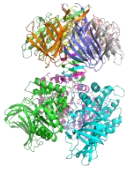
T258
H1217



T272
H1227



T302
T1270



T288/T290/T292
T1234/T1235
H1236

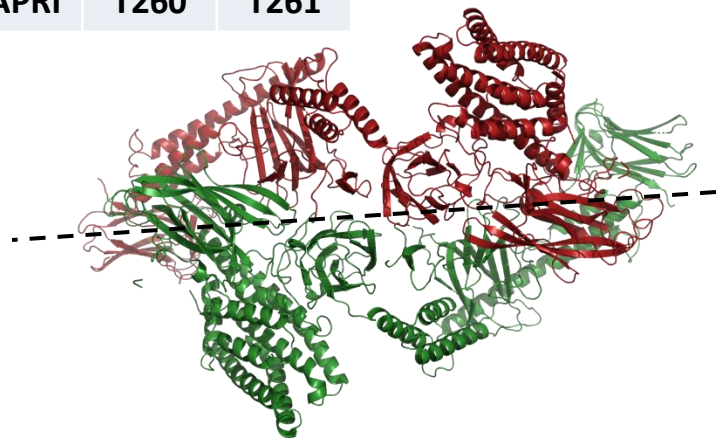
EXAMPLES

X-ray	2.9	A2

	Stage1	Stage2
CASP	T1218	T2218
CAPRI	T260	T261

#Contacts	Interface	Chains	Area
492	1	A:A’	2160

INT1 – “homo”, “dimer”



A difficult target that was not so difficult after all

DIFFICULT

AlphaFold ranked_0	
rms	51.05 Å
ipTM	0.515

Underlined and + means “and their servers”, i.e.

Cheng	MULTICOM
Kozakov	CLUSPRO
Huang	HDOCK
Kihara	LZERD
Yang	YANG-MULTIMER

Group stage1	Model	Fnat	L-rms	i-rms	Classification
Yang+	1	0.68	3.53	2.17	Medium
Chang, Cheng+, Kozakov+, **DEEPFOLD**, PEZYFoldings, FTBiot0119					Medium

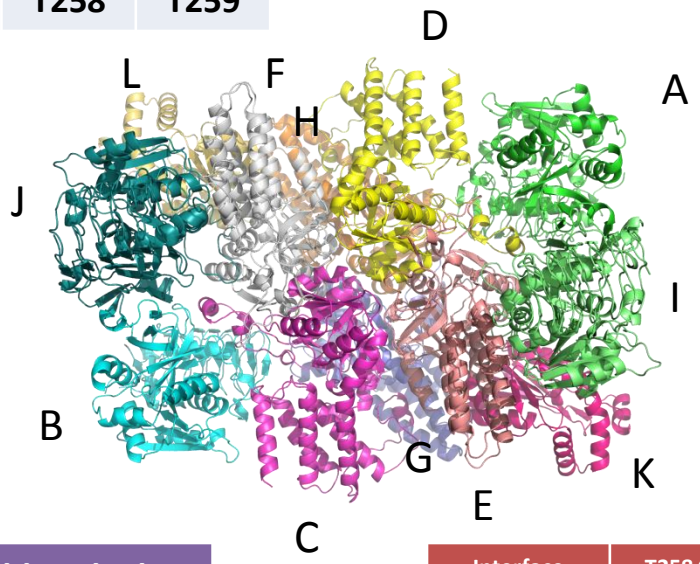
MassiveFold	First high quality model	Best quality model	Classification
0	-	-	Incorrect

Group stage2	Model	Fnat	L-rms	i-rms	Classification
Yang+	5	0.68	3.53	2.17	Medium
Huang+, Chang, Kihara, Kozakov+, **NKRNA-S**, **MIENSEMBLES**, **ZHENG**, FTBiot0119, Cheng+					Medium

EM	-	A2B2C2D2E2F2

	Stage1	Stage2
CASP	H1217	H2217
CAPRI	T258	T259

DIFFICULT



A=B
C=D
E=F
G=H
I=J
K=L

#Contacts	Interface	Chains	Area
227	1	C:F	2100
187	2 =	G:H	1750
186	3	F:J	1500
166	4	A:D	1250
155	5	C:G	1050
110	6	B:J	1000
99	7	H:L	720
113	8	C:E	700
107	9	E:K	600

average_of 1,2,3,4,5,6,7,8,9 – “large”

AlphaFold ranked_0	
rms	x Å
ipTM	0.663

Another target thought to be difficult but turned out easy

Top-1

Interface	T258 CAPRI	T258 CASP	T258 Scorers	T259 CAPRI	T259 CASP	MassiveFold*	
1	20/19***/1**	66/64***/2**	12***	15***	57/56***/1**	146***	High
2	13/12***/1**	35/31***/4**	9***	14***	40/35***/5**	137***	High
3	16/12***/4**	58/39***/17**	12/5***/7**	14/9***/4**	53/41***/8**	52***	High
4	19/17***/2**	64/61***/2**	12/10***/2**	15***	56/55***	139***	High
5	20/15***/4**	65/46***/17**	12/9***/3**	15/8***/7**	57/32***/24**	98***	High
6	17/16***/1**	59/54***/5**	12***	14/13***	49/46***/4**	138***	High
7	1	7/2**	5/3**	5/3**	10/4**	0	Incorrect
8	15/10***/2**	50/29***/12**	10/4***/5**	15/9***/4**	49/32***/7**	92***	High
9	0	6/2**	0	1	8/3**	0	Incorrect

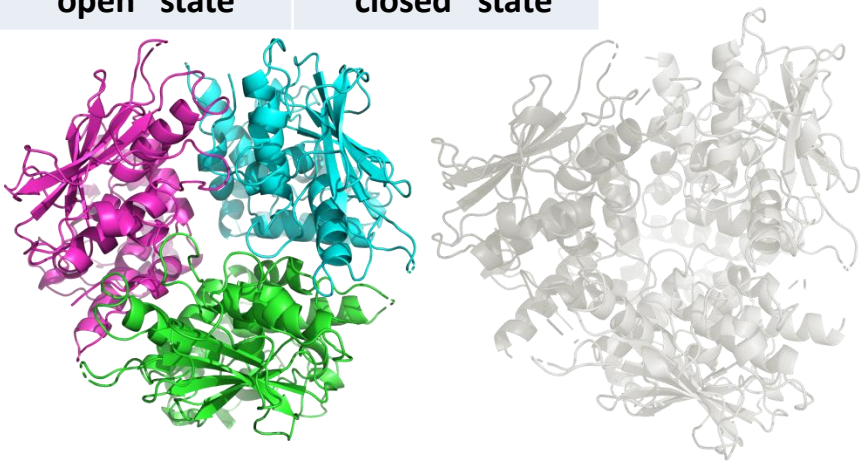
* Reduced set of 395 models

EM	-	A3	

	Stage1	Stage2	Stage1	Stage2
CASP	T1249v1	T2249v1	T1249v2	T1249v2
CAPRI	T250	T251	T252	T253
	"open" state		"closed" state	

#Contacts	Interface	Chains	Area
513	T250	A:B	1110
517	T252	A:B	1040

INT1 – "homo", "trimer", "conformer"



"open" state

AlphaFold ranked_0	
rms	1.14 Å
ipTM	0.702

EASY

DIFFICULT

Group stage1		Classification
Giulini, Cool-PSP, LCDD-team, MRAFold, LupengKong, PEZYFoldings, Wallner, Bhattacharya, GHZ-Man, **LZERD**, **YANG-MULTIMER**, *Cheng, Giulini*		Medium

MassiveFold	Medium quality model	Best quality model	Classification
147/1**	#164	#164	Medium

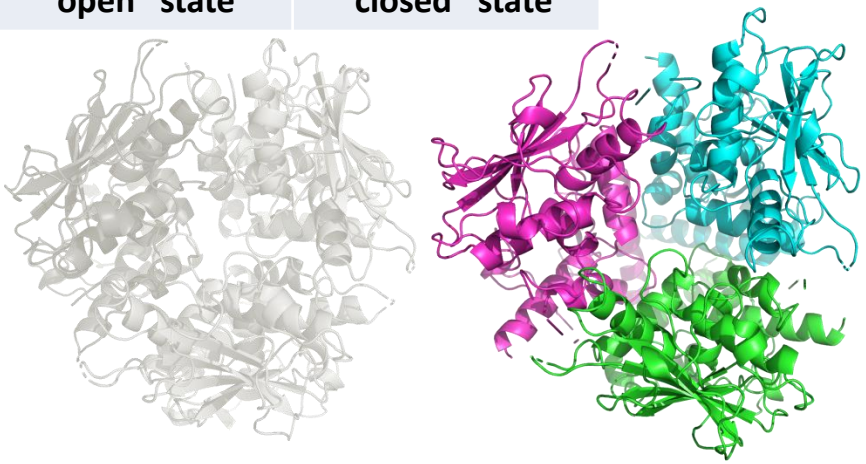
Group stage2		Classification
Cool-PSP, LCDD-team, MRAFold, LupengKong, FTBiot0119, RAGfold-Prot1, ShanghaiTech-human, **DEEPFOLD-SERVER**, **YANG-MULTIMER**		Medium

EM	-	A3	

	Stage1	Stage2	Stage1	Stage2
CASP	T1249v1	T2249v1	T1249v2	T1249v2
CAPRI	T250	T251	T252	T253
	"open" state		"closed" state	

#Contacts	Interface	Chains	Area
513	T250	A:B	1110
517	T252	A:B	1040

INT1 – "homo", "trimer", "conformer"



The "closed" state was difficult to predict, and not caught at all by the MassiveFold data

Giulini was the *only* predictor who found both states!

"closed" state

AlphaFold ranked_0	
rms	1.14 Å
ipTM	0.702

EASY

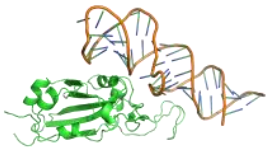
DIFFICULT

Group stage1		Classification
Vakser, Giulini, Huang, Pierce, plmfold, GuijunLab-QA, Yang-Server, Elofsson, **MDOCKPP**, **HDOCK**, **MQA-SERVER**, **GHZ-ISM**, **UNICORN**, **PTQ**		Acceptable

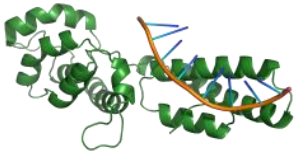
MassiveFold	Medium quality model	Best quality model	Classification
0	-	-	Incorrect

Group stage2		Classification
Giulini, Huang, Kihara, GuijunLab-QA, Yang-Server, Elofsson, **MDOCKPP**, **HDOCK**, **UNICORN**, **GHZ-ISM**, **PTQ**, **MILLISECONDS**		Acceptable

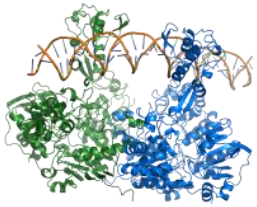
DNA and RNA binding



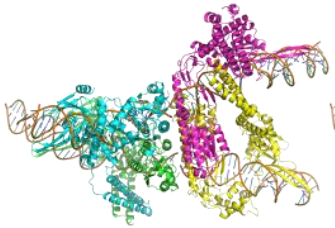
T304*
M1282



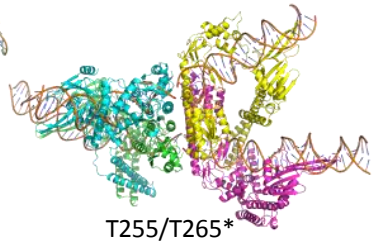
T306*
M1276



T308*
M1287



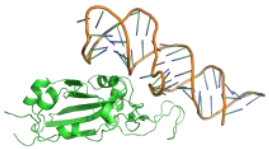
T254/T264*
M1228v1
M1239v1



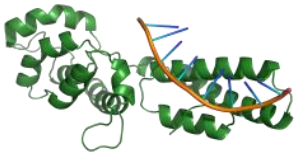
T255/T265*
M1228v2
M1239v2

DNA AND RNA BINDING

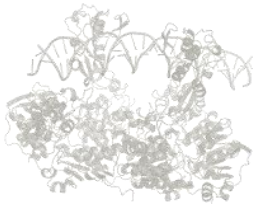
DNA and RNA binding



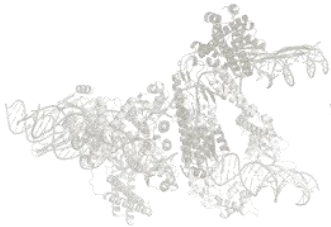
T304*
M1282



T306*
M1276



T308*
M1287



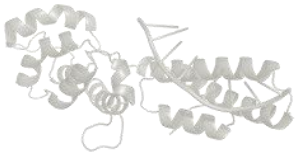
T254/T264*
M1228v1
M1239v1

T255/T265*
M1228v2
M1239v2

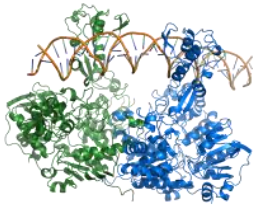
T304	M1282	No acceptable solutions	Highest DockQ	0.0544
T306	M1276	No acceptable solutions	Highest DockQ	0.0314

DNA and RNA binding

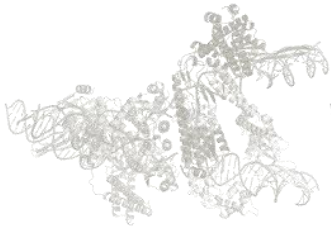
T304*
M1282



T306*
M1276



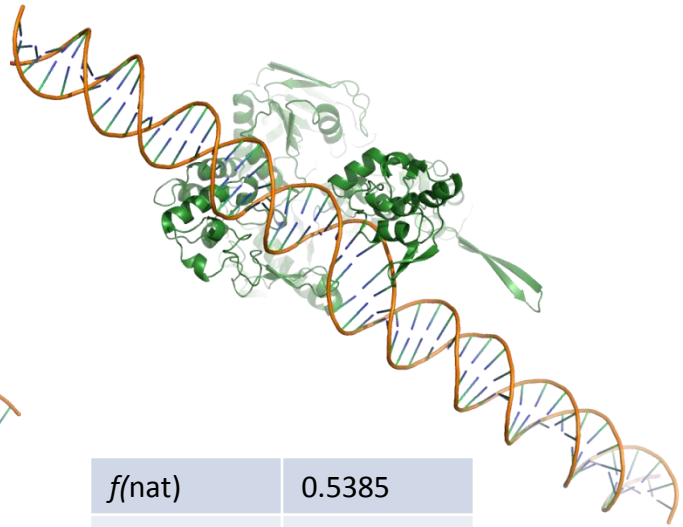
T308*
M1287



T254/T264*
M1228v1
M1239v1

T255/T265*
M1228v2
M1239v2

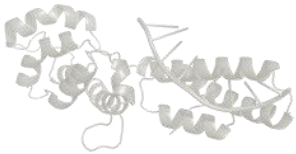
Predictors
Bhattacharya
Fernandez-Recio
ALPHAFOLD3-SERVER
B-LAB
GeneSilico
Diff
Scorers
Fernandez-Recio
Oliva
Kihara / ***LZERD***



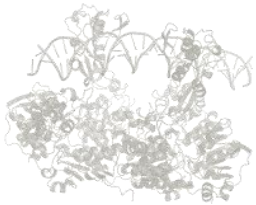
f(nat)	0.5385
f(nonnat)	0.8454
i-rms	3.8529

DNA and RNA binding

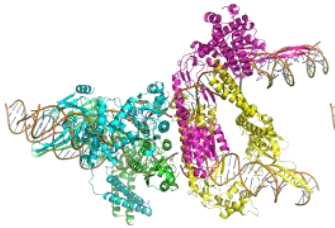
T304*
M1282



T306*
M1276



T308*
M1287



T254/T264*
M1228v1
M1239v1

T255/T265*
M1228v2
M1239v2

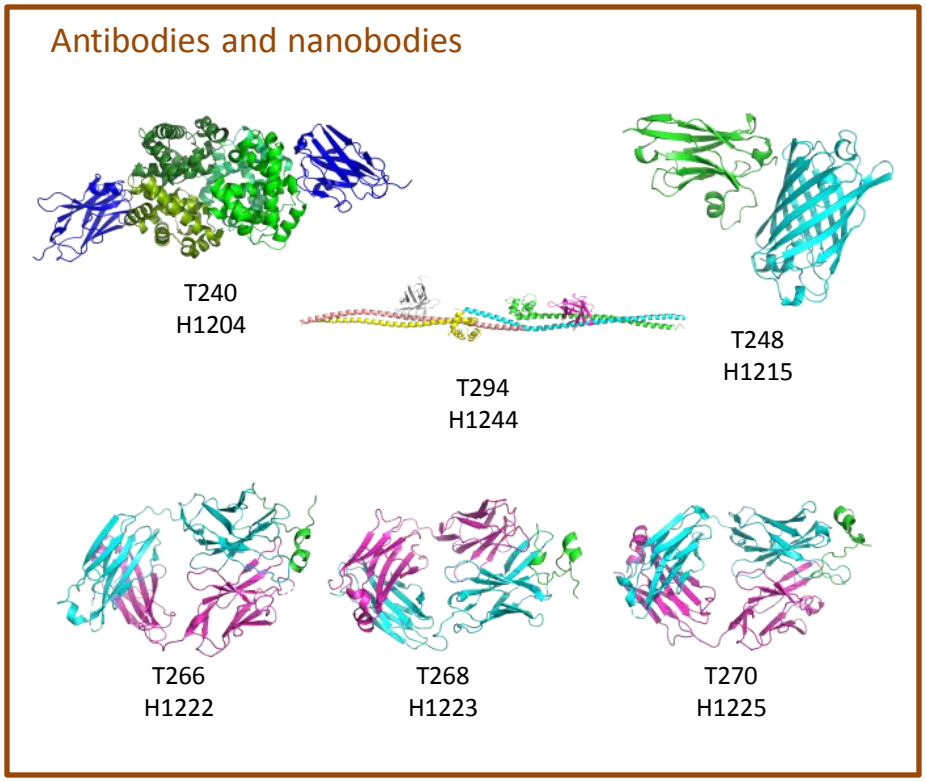
Predictors
CLUSPRO
Cool-PSP
Scorers
Zou
Oliva

Predictors
*Acceptable solutions for **many** Predictors, Scorers and Servers*

*The acceptable solutions are mostly due to medium-quality solutions for **T265***

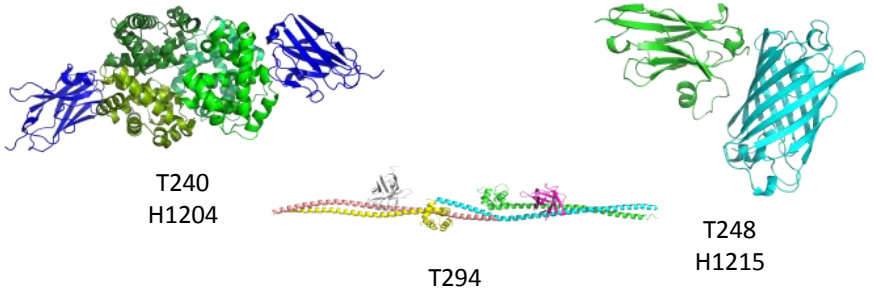
Interface 1	Protein-DNA
Interface 2	Protein-DNA, alternate conformation
Interface 3	Protein-protein alternate conformation

No acceptable solutions for interface 1
Medium-quality for interfaces 2 and 3



ANTIBODIES AND NANOBODIES

Antibodies and nanobodies



T240
H1204

T294
H1244

T248
H1215

T266
H1222

T268
H1223

T270
H1225

High

Kozakov

Acceptable

Cheng, Pierce, Zou

Fernandez-Recio

HYU-MLLab

LupengKong

MRAFold

MULTICOM (all variants)

OmniFold

YANG-MULTIMER, Yang, Yang-Server

MQA-SERVER

CSSB-Faker

FALCON2

Zou

No acceptable solutions for T294/H1244

High

Kozakov, **CLUSPRO**

Huang, **HDOCK**

Pierce, Brysbaert

Cheng, Cool-PSP

MENSEMBLES

Wallner, FTBiot0119

Zheng, **ZHENG-MM, NKRNA-S**

MULTICOM (all variants)

*Chang, Huang, **HDOCK, MDOCKPP***

Fernandez-Recio, Zou, Kihara

OpenComplex, elofsson, **OPENCOMPLEX**

ALPHAFOLD3-SERVER, CSSB-experimental

Zou, Kihara

X-ray	-	AB

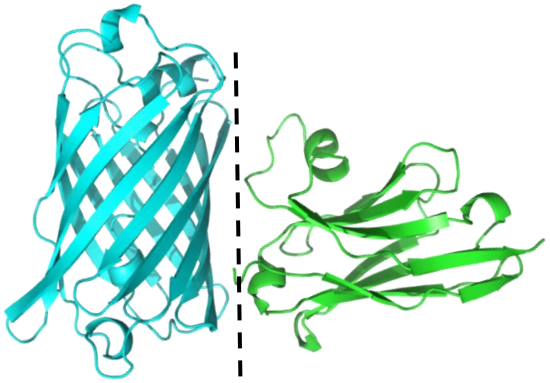
	Stage1	Stage2
CASP	H1215	T2215
CAPRI	T248	T249

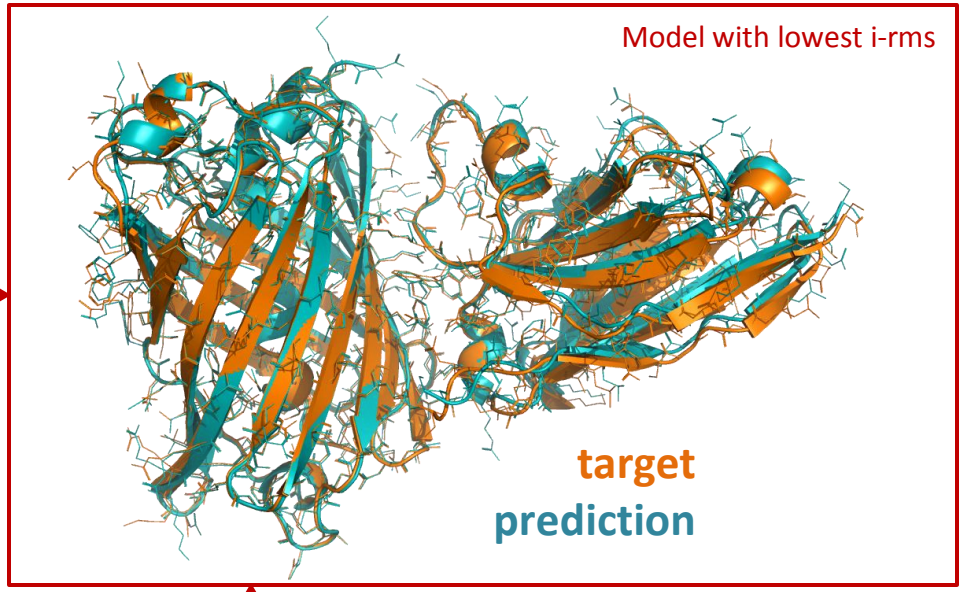
#Contacts	Interface	Chains	Area
97	1	A:B	750

INT1 – “nanobody”

DIFFICULT

A target thought to be difficult but turned out easy





AlphaFold ranked_0	
rms	14.31 Å
ipTM	0.799

Group stage1	Model	Fnat	L-rms	i-rms	Classification
Brysbaert	5	0.90	1.71	0.35	High
Pierce, Cheng+, Huang+, Kozakov+, Zheng+, Wallner, +others, *+some but not all Scorers*					High

MassiveFold	First high quality model	Best quality model	Classification
204/29***/16**	#2	#5	High

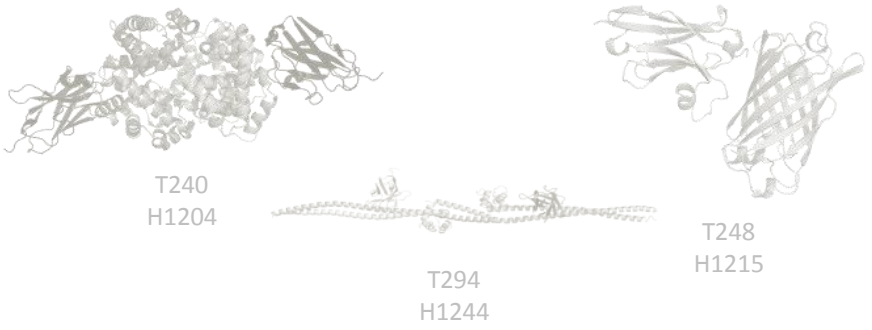
Group stage2	Model	Fnat	L-rms	i-rms	Classification
Bates	4	0.86	1.43	0.33	High
Bates, Fernandez-Recio, Kihara+, Kozakov+, Chang, Zheng, Yang+, +others					High

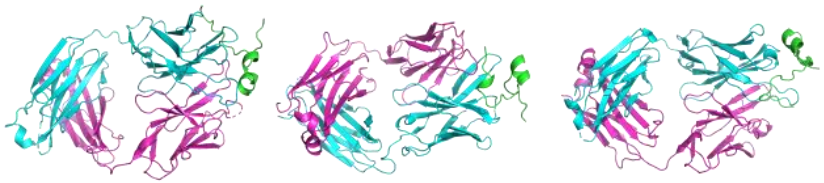
Underlined and + means “and their servers”, i.e.

Cheng	MULTICOM
Kozakov	CLUSPRO
Huang	HDOCK
Kihara	LZERD
Zheng	ZHENG-MULTIMER
Yang	YANG-MULTIMER

Medium
Chang, Cheng, Gray, Kihara
Zou, **MDOCKPP**, Yang
Huang, **HDOCK**, Czaplewski
Kozakov, **CLUSPRO**, Elofsson
ALPHAFOLD3-SERVER
Chattacharya, PEZYFoldings
CSSB-Faker, CSSB-human
DEEPFOLD, DeepFold-refine
FALCON2, **GHZ-ISM**
GUIJNLAB (all variants)
LCDD-team, LinYang
MILLISECONDS, pimfold
MQA-SERVER, McGuffin
MULTICOM (all variants)
PTQ, **UNICORN**, smg-laval
XGroup, **XGROUP**
YANG-MM, Yang-Server
Giulini, Kihara, ***LZERD***
Olechnovic, Zou, Chang
Huang, ***HDOCK****, Shirali*
Fernandez-Recio

Antibodies and nanobodies





T266 H1222 | T268 H1223 | T270 H1225

No acceptable solutions for T270/H1225

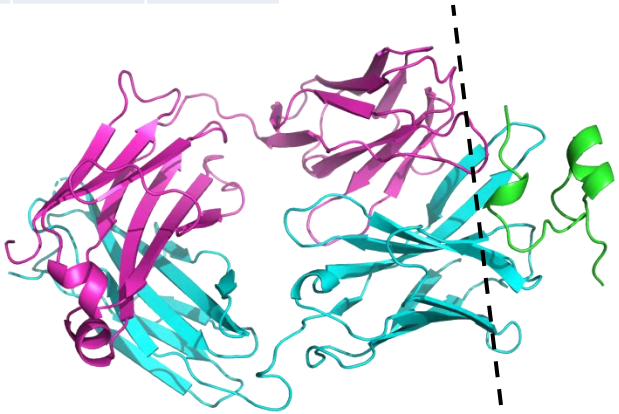
High
Kozakov, **CLUSPRO**, DeepFold-refine, **DEEPFOLD-SERVER**, LCDD-team, PEZYFoldings
Giulini, Olechnovic, ***LZERD***
Acceptable
Huang, **HDOCK**, Chang, GromihaLab, **OPENCOMPLEX**, OpenComplex
Elofsson, RAGfold-Prot1, Bhattacharya, Mialab-prediction, FTBiot0119
Kihara, ***MDOCKPP***

X-ray	-	A:HL

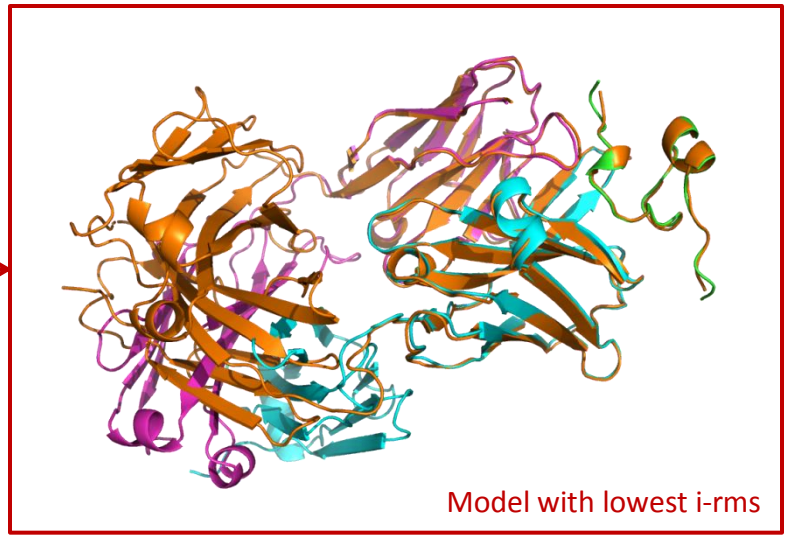
	Stage1	Stage2
CASP	H1223	H2223
CAPRI	T268	T269

#Contacts	Interface	Chains	Area
341	1	A:HL	930

INT1 – “homo”, “dimer”



DIFFICULT



AlphaFold ranked_0	
rms	x Å
ipTM	crashed

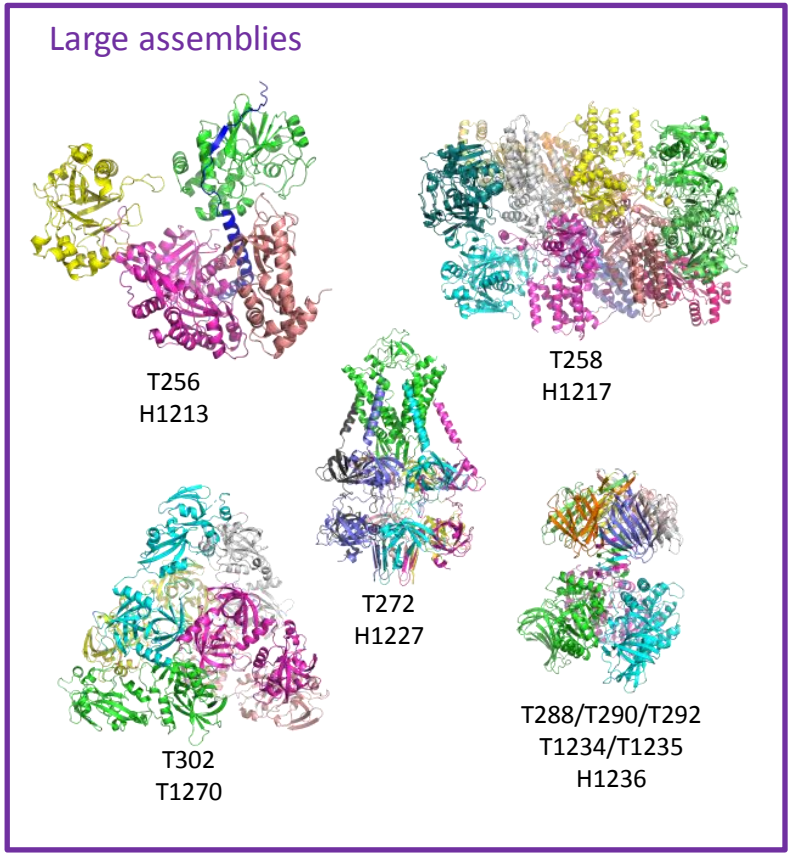
Group stage1	Model	Fnat	L-rms	i-rms	Classification
CLUSPRO	1	0.90	13.03	0.56	High
Kozakov, LCDD-team, DeepFold+, PEZYFoldings, *Olechnovic, Giulini,* ***LZERD***					High

MassiveFold	Medium quality model	Best quality model	Classification
108/1**	#7707	#7707	medium

Group stage2	Model	Fnat	L-rms	i-rms	Classification
LZERD	2	0.92	0.88	0.85	High
Cheng+, Kihara, Kozakov+, LCDD-team, DeepFold+, PEZYFoldings, Wallner					High

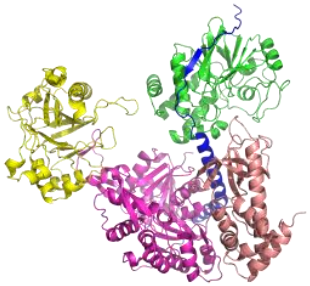
Underlined and + means “and their servers”, i.e.

Cheng	MULTICOM
Kozakov	CLUSPRO
DeepFold-refine	DEEPFOLD

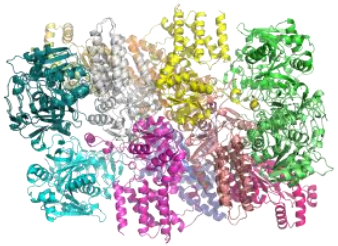


LARGE ASSEMBLIES

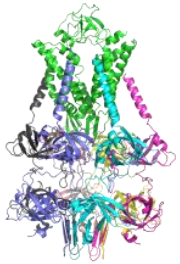
Large assemblies



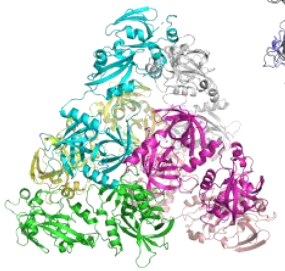
T256
H1213



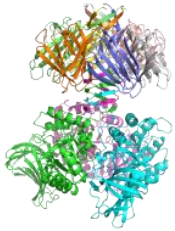
T258
H1217



T272
H1227



T302
T1270



T288/T290/T292
T1234/T1235
H1236

Medium quality for many predictors

CSSB-experimental

Chang, Fernandez-Recio, Giulini, HYU-MLLab, **YANG-MM**, **MILLISECONDS**, GromihaLab, **MULTICOM-{LLM,GATE}**, Wallner, **OPENCOMPLEX**
Giulini, Fernandez-Recio

High quality for some predictors, medium for most

Cheng, Giulini, **MDOCKPP**, GromihaLab, **COLABFOLD**, **MULTICOM** (all variants), Bhattacharya, **MULTIFOLD2**

High quality for the primary interfaces, no acceptable solutions for the weak interface

The large majority of groups

Medium quality for many predictors

Gray, Vakser

Kihara, Chang, Cheng, Czaplewski, Pierce, Fernandez-Recio, Huang, **HDOCK**, Zou, **MDOCKPP**, Schneidman, Brysbaert

Acceptable to medium quality for most predictors

Brysbaert, *Fernandez-Recio*

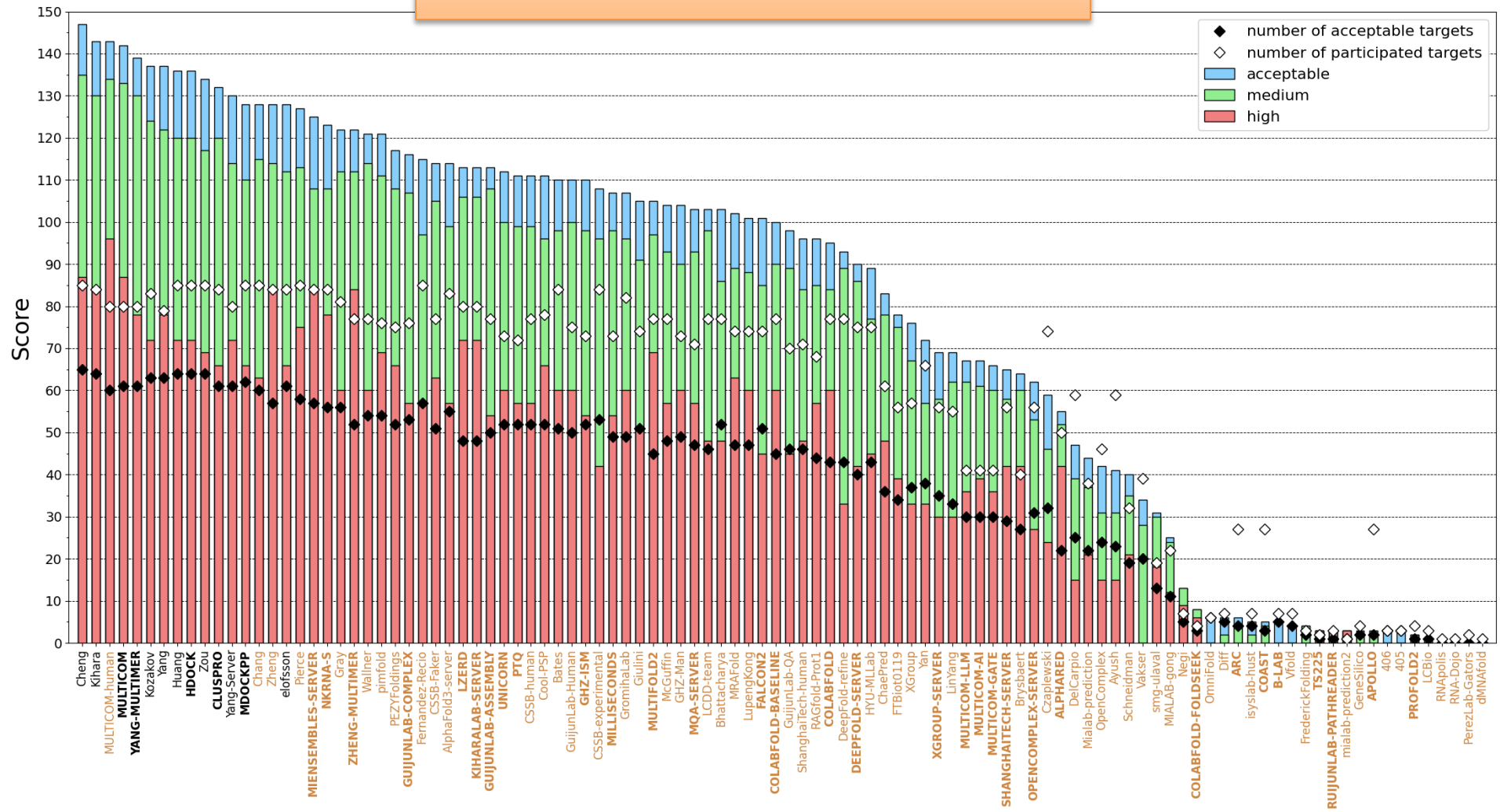
Kihara, **LZERD**, Zou, Chang, plmfold, MRAFold, LupengKong
Giulini, Zou, Kihara

$$\text{Score} = \omega_1 \cdot N_{ACC} + \omega_2 \cdot N_{MED} + \omega_3 \cdot N_{HIGH}$$

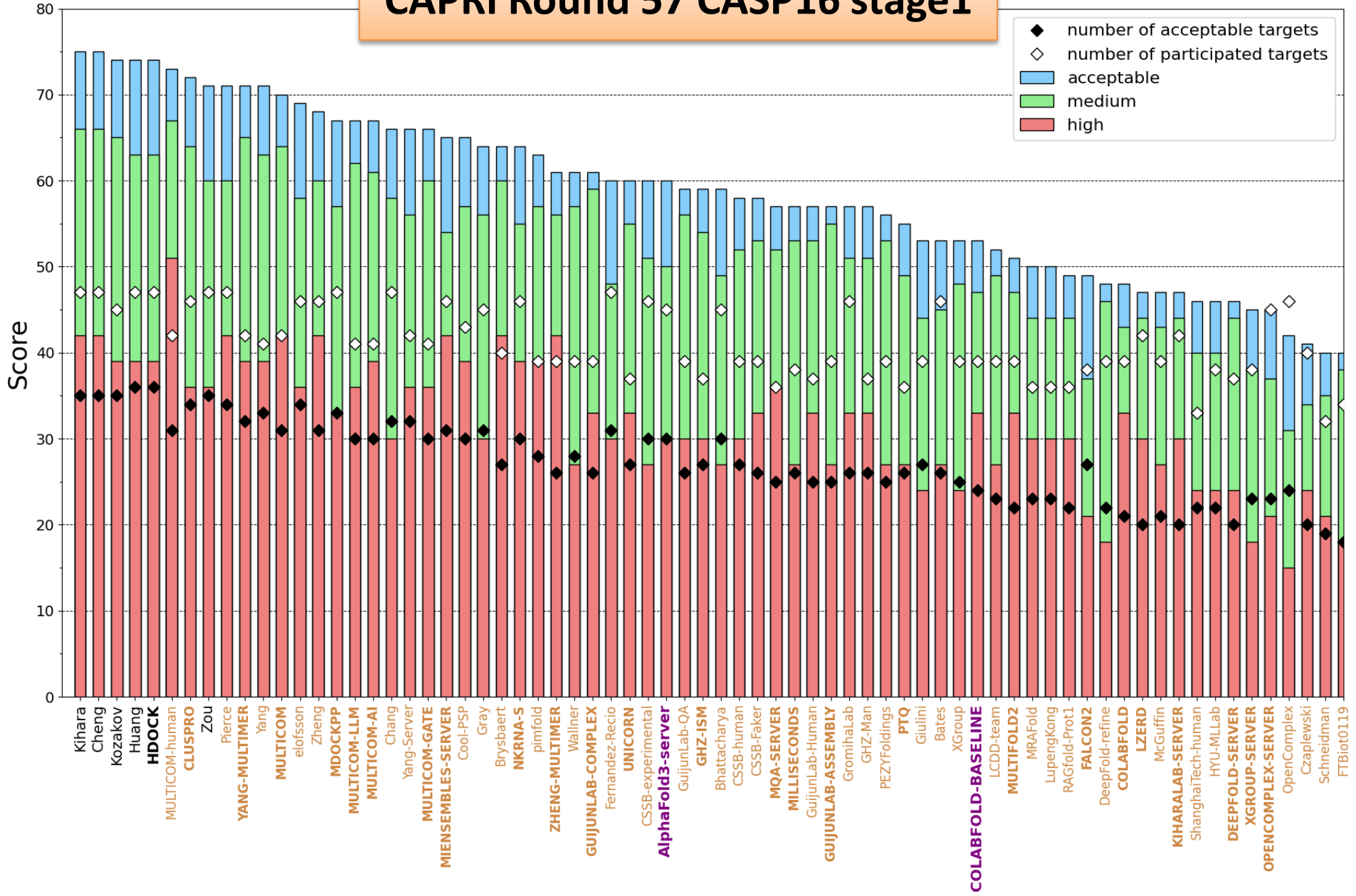
$\omega_1 = 1$; $\omega_2 = 2$; $\omega_3 = 3$

RANKING

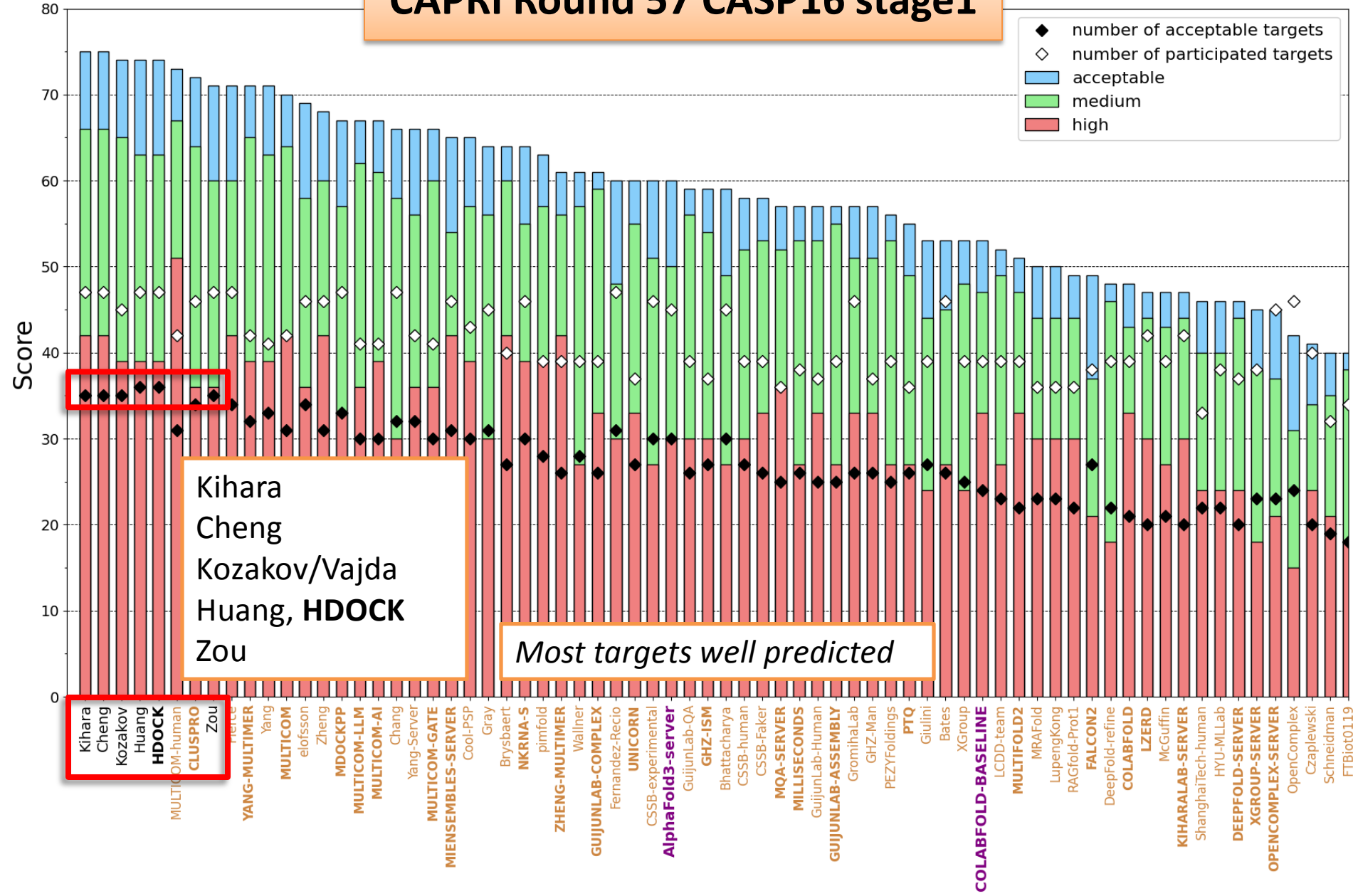
CAPRI Rounds 57 & 58
CASP16 stage1 & stage2



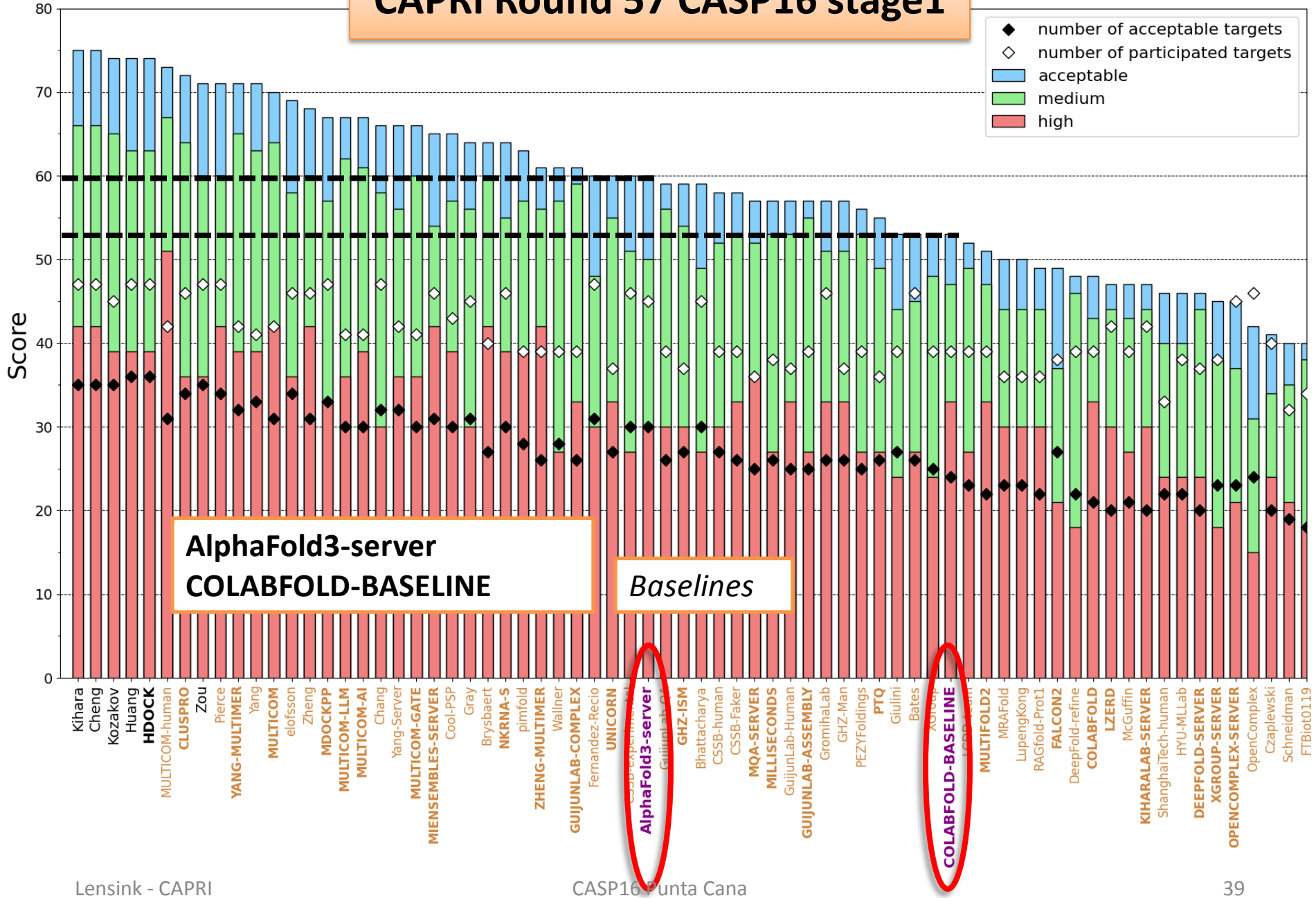
CAPRI Round 57 CASP16 stage1

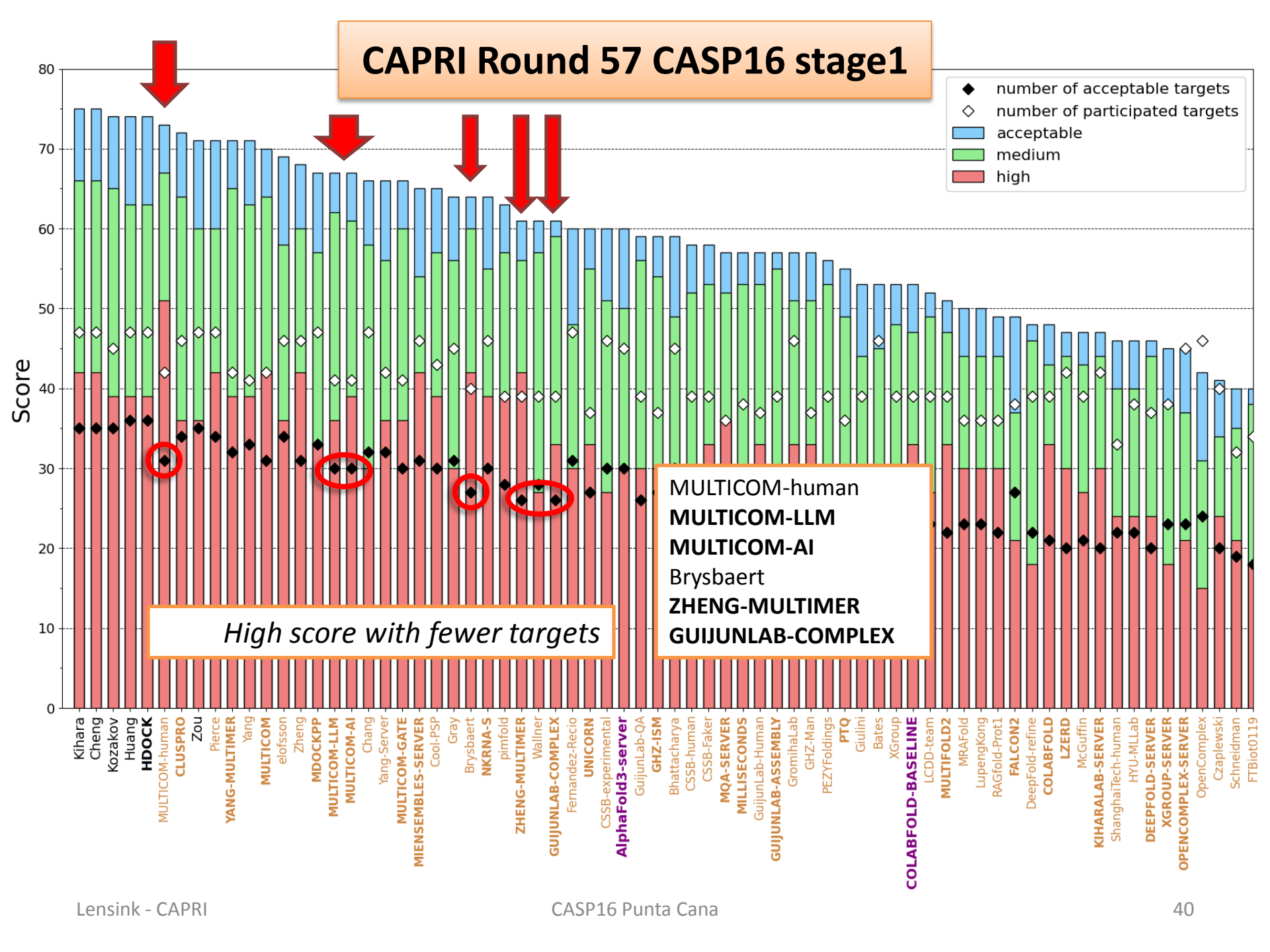


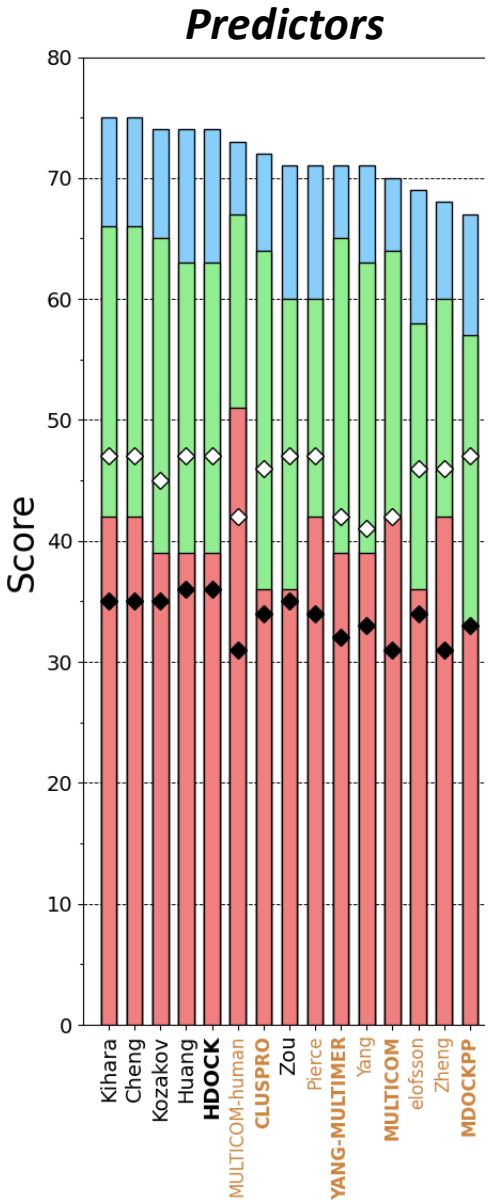
CAPRI Round 57 CASP16 stage1

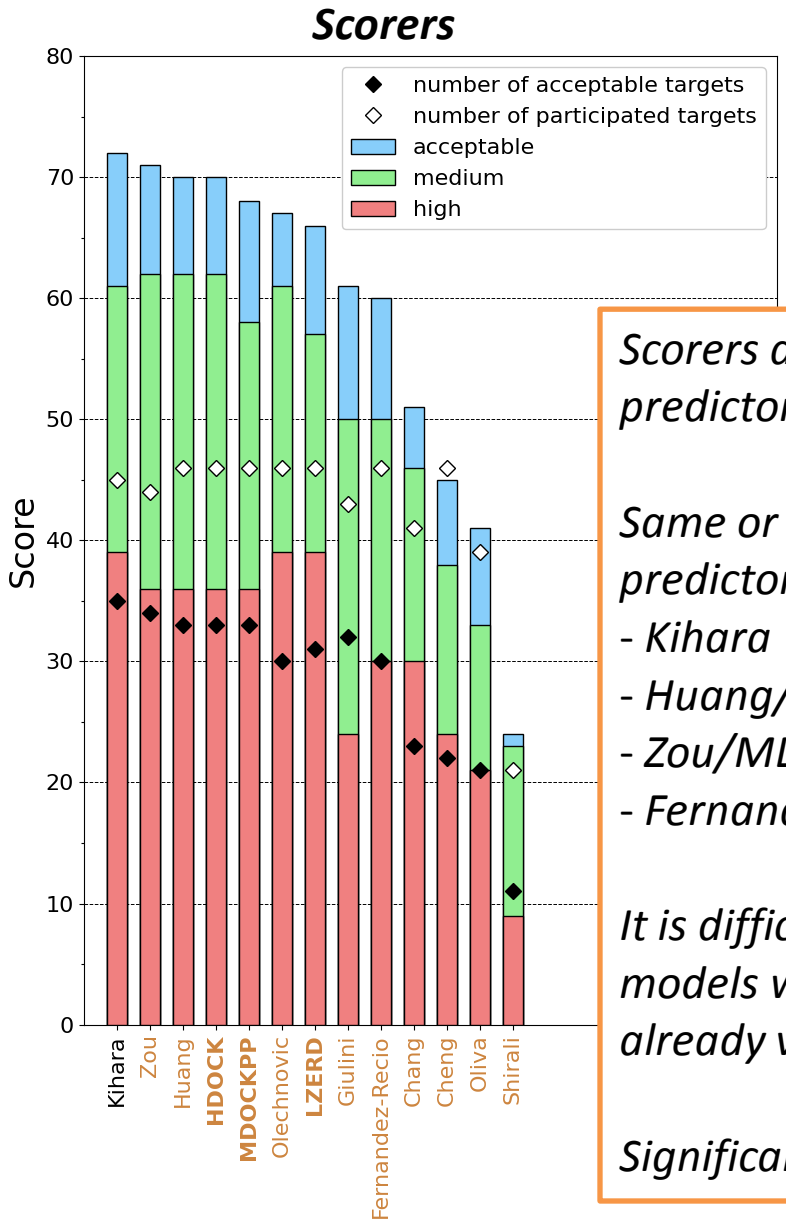


CAPRI Round 57 CASP16 stage1




CAPRI Round 57 CASP16 stage1
number of acceptable targets
number of participated targets
acceptable
medium
high
Score
80
70
60
50
40
30
20
10
0
MULTICOM-human
MULTICOM-LLM
MULTICOM-AI
Brysbaert
ZHENG-MULTIMER
GUIJUNLAB-COMPLEX
High score with fewer targets
Kihara
Cheng
Kozakov
Huang
HDOCK
MULTICOM-human
CLUSPRO
Zou
Pierce
YANG-MULTIMER
Yang
MULTICOM
elofsson
Zheng
MDOCKPP
MULTICOM-LLM
MULTICOM-AI
Chang
Yang-Server
MULTICOM-GATE
MIENSEMBLES-SERVER
Cool-PSP
Gray
Brysbaert
NKRNA-S
pimfold
ZHENG-MULTIMER
Wallner
GUIJUNLAB-COMPLEX
Fernandez-Recio
UNICORN
CSSB-experimental
AlphaFold3-server
GuijunLab-QA
GHZ-ISM
Bhattacharya
CSSB-human
CSSB-Faker
MQA-SERVER
MILLISECONDS
GuijunLab-Human
GUIJUNLAB-ASSEMBLY
GromihaLab
GHZ-Man
PEZYFoldings
PTQ
Giulini
Bates
XGroup
COLABFOLD-BASELINE
LCDD-team
MULTIFOLD2
MRAFold
LupengKong
RAGfold-Prot1
FALCON2
DeepFold-refine
COLABFOLD
LZERD
McGuffin
KIHARALAB-SERVER
ShanghaiTech-human
HYU-MLLab
DEEPFOLD-SERVER
XGROUP-SERVER
OPENCOMPLEX-SERVER
OpenComplex
Czaplewski
Schneidman
FTBiot0119



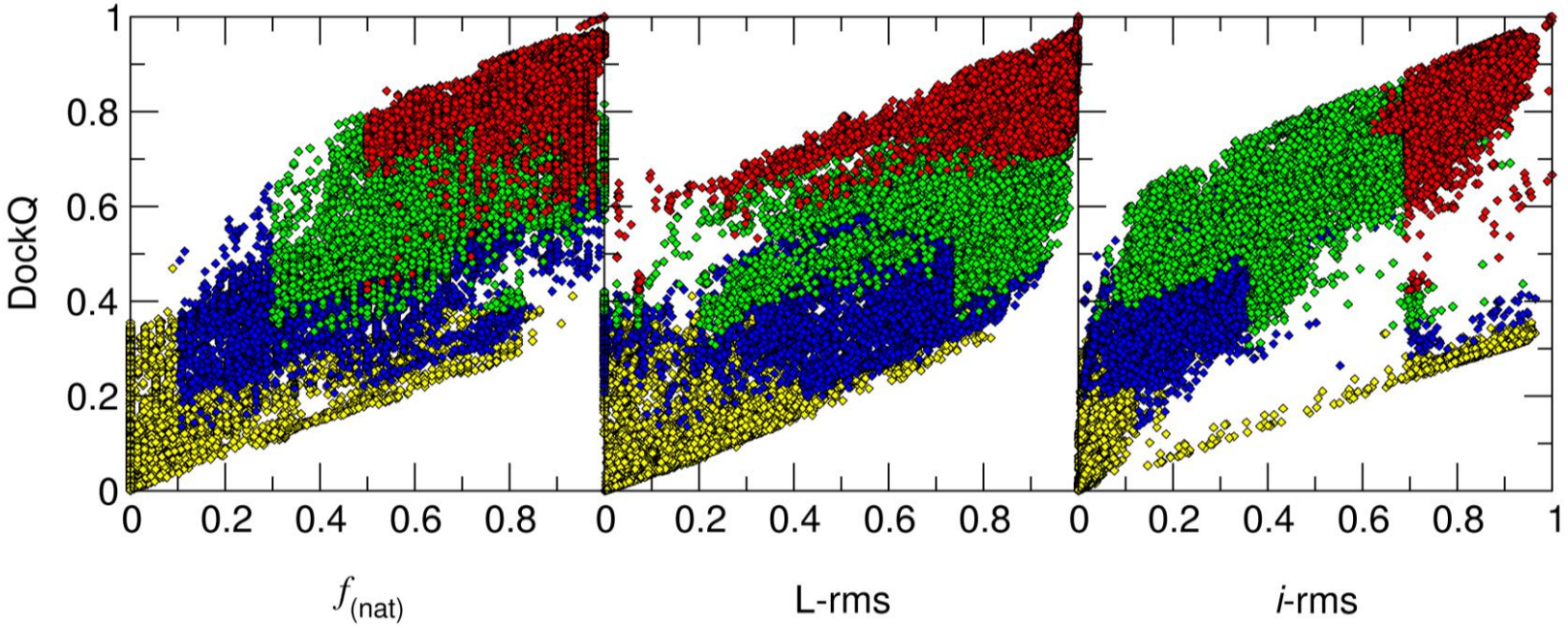


Scorers do not do a better job than predictors

Same or similar scores for predictor/scorer teams:
- *Kihara*
- *Huang/HDOCK*
- *Zou/MDOCKPP*
- *Fernandez-Recio*

It is difficult to identify the best models when most other are already very good ones

*Significant improvement for **LZERD***



DockQ = ⅓ F(nat) + ⅓ L-rms + ⅓ i-rms

DOCKQ

```
function rms_scaled(rms, d) {
  r = rms / d;
  r = 1.0 / (1.0 + r*r);
  return(r);
}
BEGIN { d1 = 8.5; d2 = 1.5; }
{ q = ($1 + rms_scaled($2, d1) + rms_scaled($3, d2)) / 3.0;
  printf "%6.4f\n", q;
}
```

- Extract DockQ values for all participants' best top-5 model
- Apply assessment units rules for multi-interface targets
- Remove exact duplicates
- Calculate μ and σ
- Express DockQ in σ (Z-score), retain only positives, cap at +2
- Sum

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- Apply assessment units rules for multi-interface targets
- Remove exact duplicates
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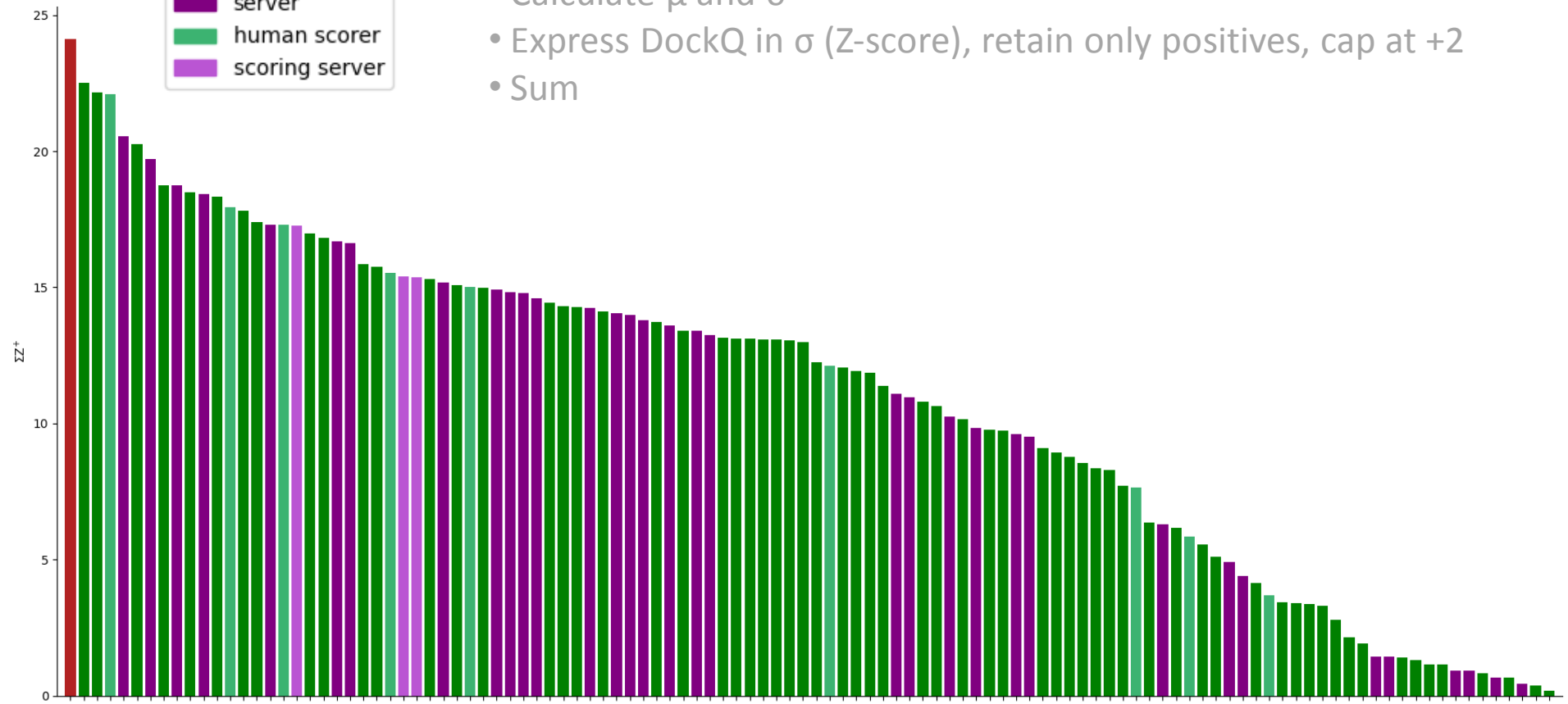

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- Calculate μ and σ
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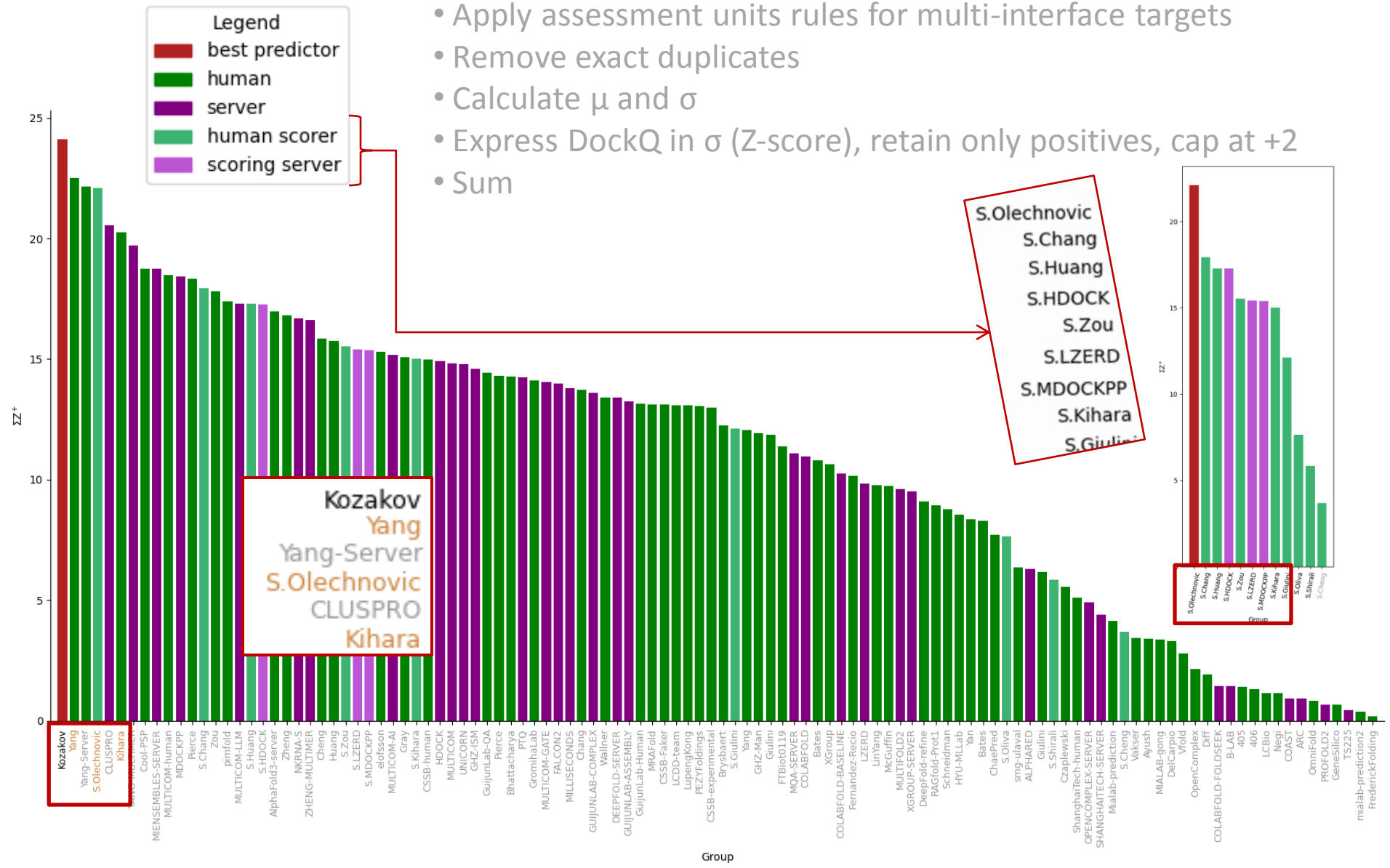
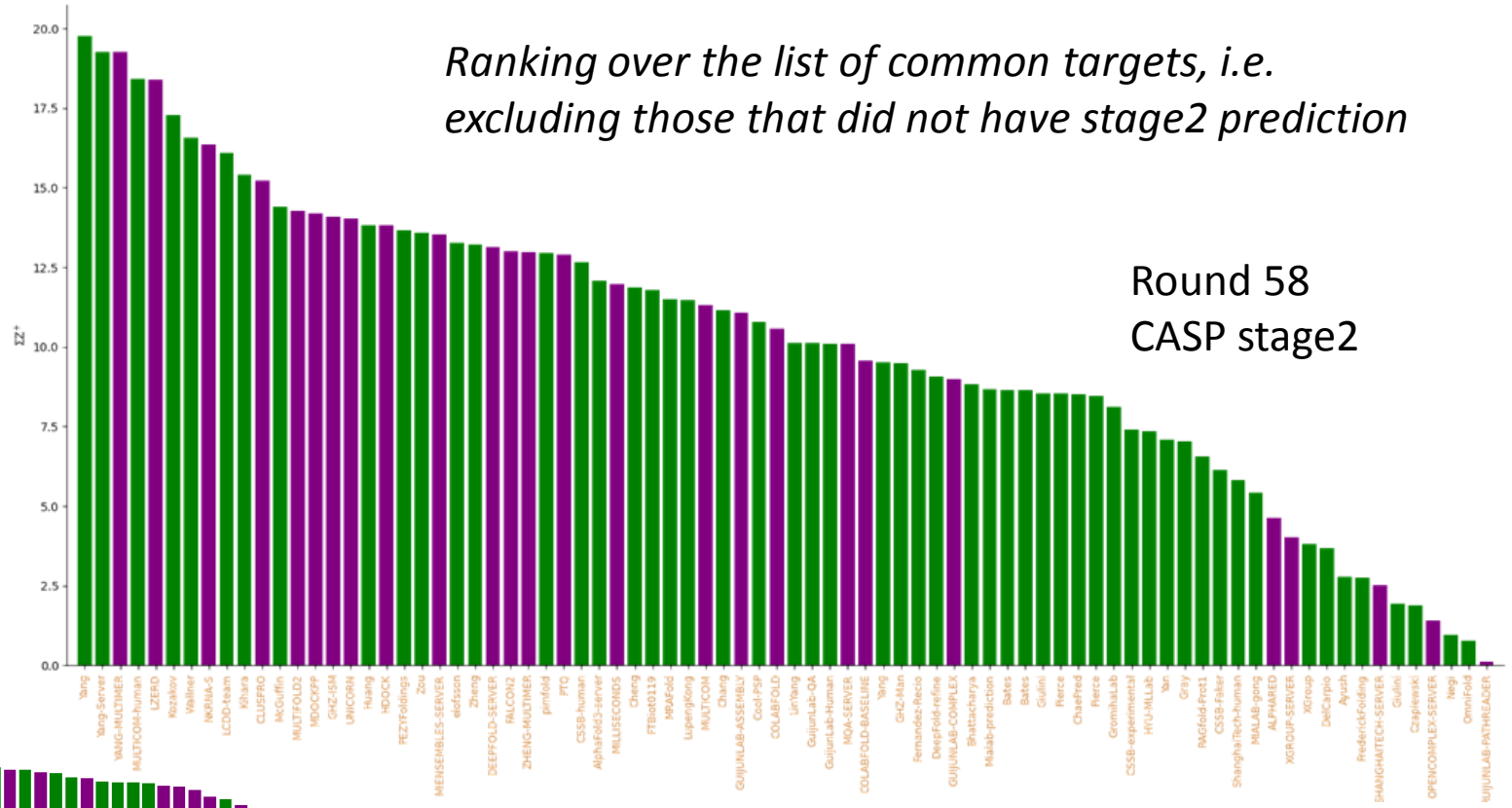
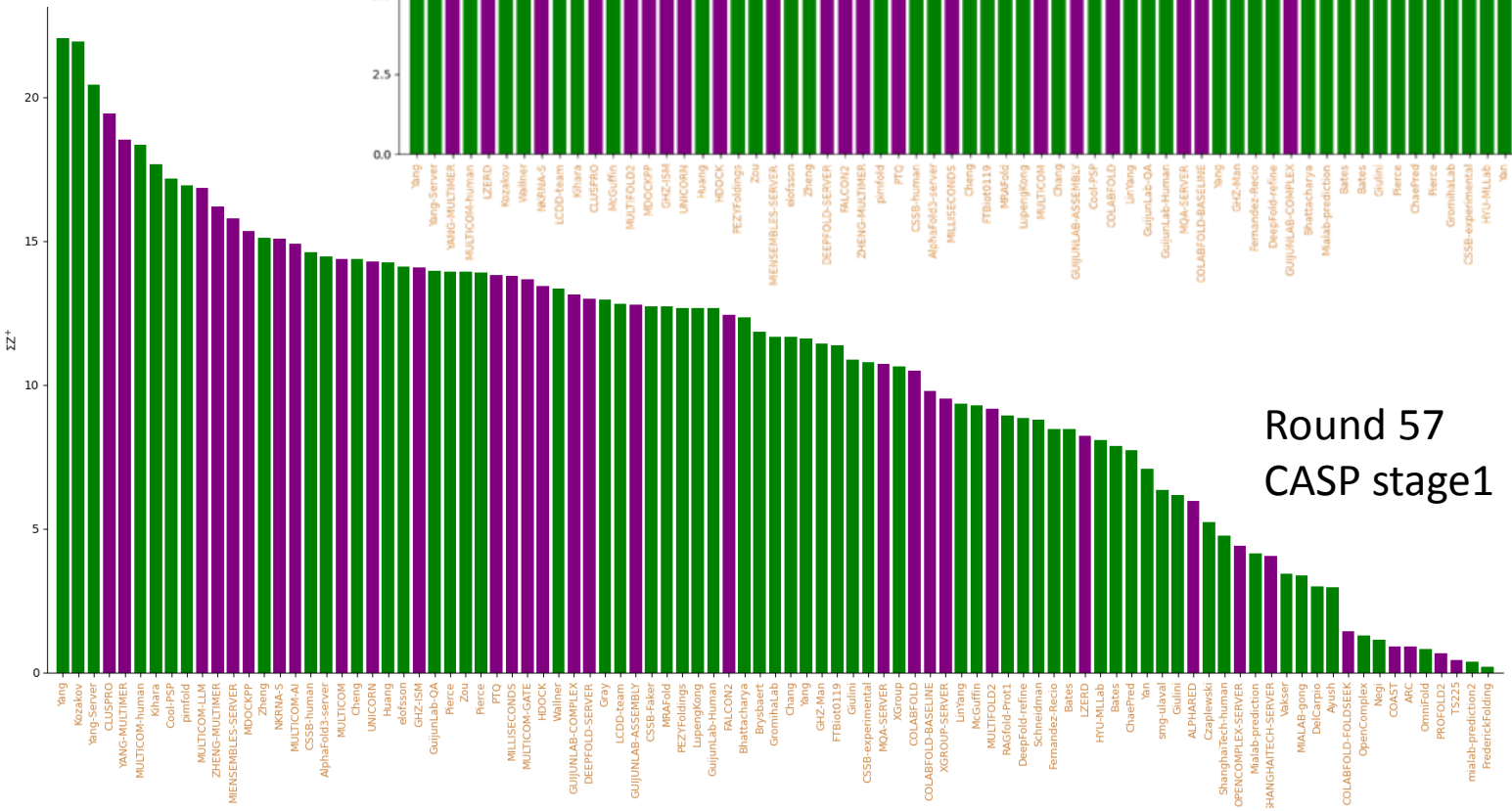
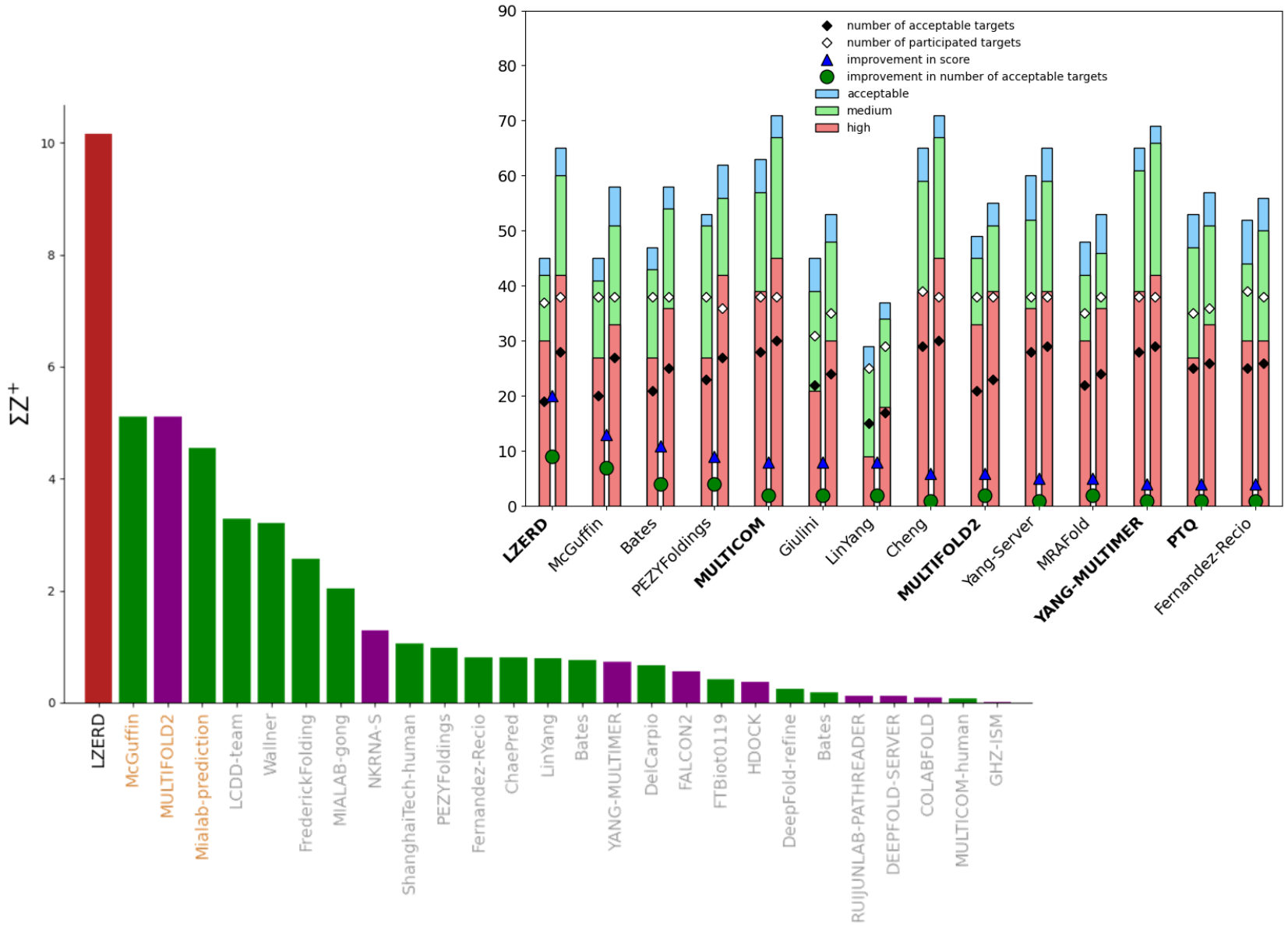


Ranking over the list of common targets, i.e. excluding those that did not have stage2 prediction



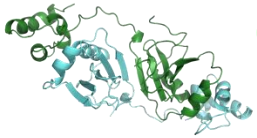


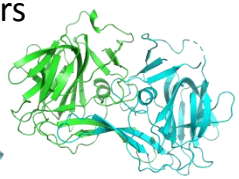
Ordered on improvement in score
Minimum 20 targets participated
Difference in participation R58 vs R57 no more than 4 targets

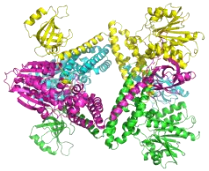


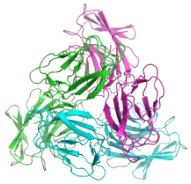
TARGETS THAT FAILED

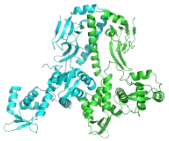
Homo-oligomers

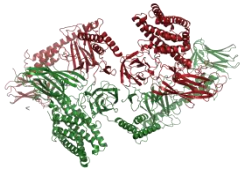

T236
T1201

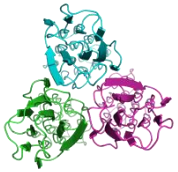

T242
T1206


T282
T1237


T286
T1240

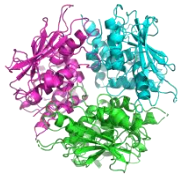

T309*
T1298

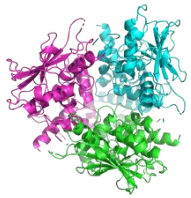

T260
T1218


T298
T1259

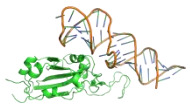
* No MassiveFold

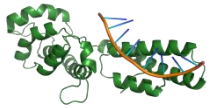
Conformers

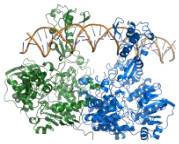

T250
T1249v1

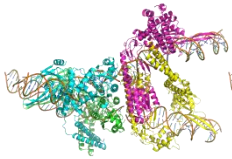

T252
T1249v2

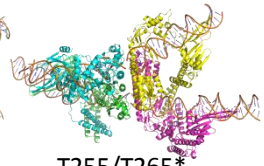
DNA and RNA binding


T304*
M1282

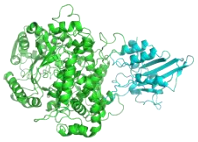

T306*
M1276

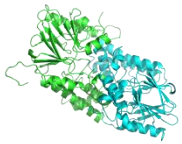

T308*
M1287

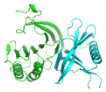

T254/T264*
M1228v1
M1239v1

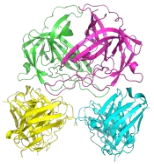

T255/T265*
M1228v2
M1239v2

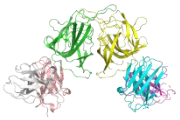
Hetero-oligomers

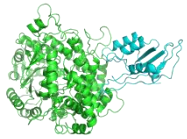

T276
H1230

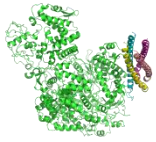

T244
H1208

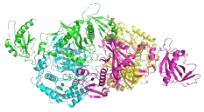

T296
H1245

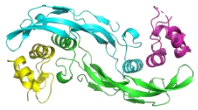

T278
H1232


T280
H1233

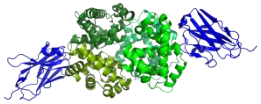

T274
H1229

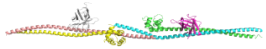

T262
H1220

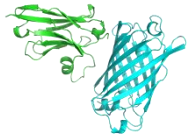

T300
H1267

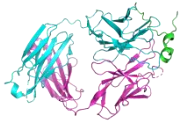

T238
H1202

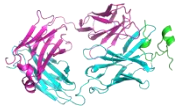
Antibodies and nanobodies

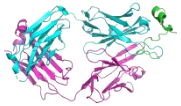

T240
H1204


T294
H1244

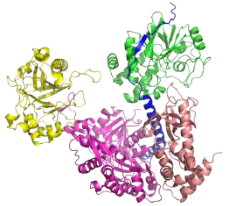

T248
H1215

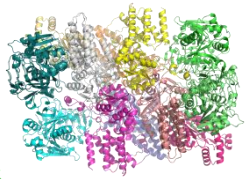

T266
H1222

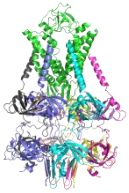

T268
H1223

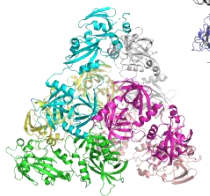

T270
H1225

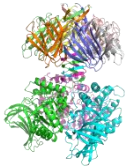
Large assemblies


T256
H1213

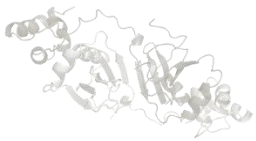

T258
H1217

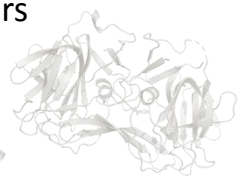

T272
H1227

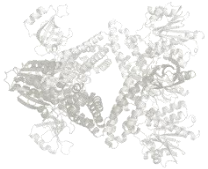

T302
T1270

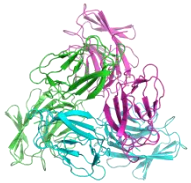

T288/T290/T292
T1234/T1235
H1236

Homo-oligomers


T236
T1201

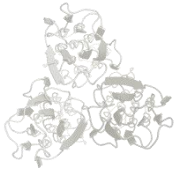

T242
T1206


T282
T1237


T286
T1240

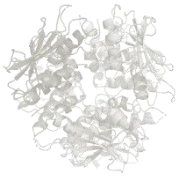

T309*
T1298

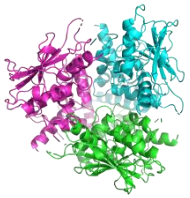

T260
T1218


T298
T1259

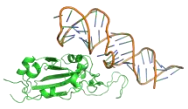
* No MassiveFold

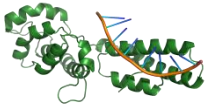
Conformers

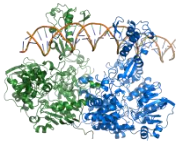

T250
T1249v1

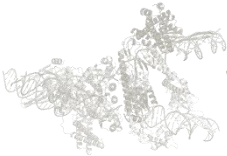

T252
T1249v2

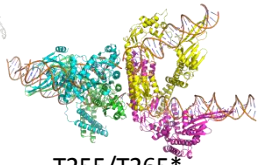
DNA and RNA binding


T304*
M1282

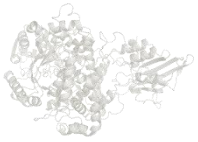

T306*
M1276


T308*
M1287


T254/T264*
M1228v1
M1239v1

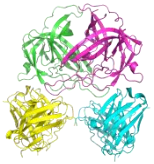

T255/T265*
M1228v2
M1239v2

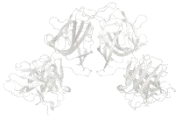
Hetero-oligomers

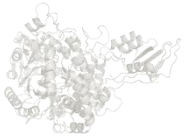

T276
H1230

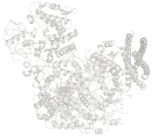

T244
H1208

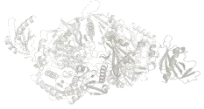

T296
H1245


T278
H1232


T280
H1233

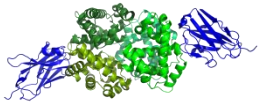

T274
H1229

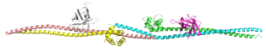

T262
H1220


T300
H1267

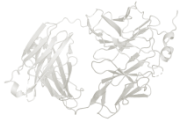

T238
H1202

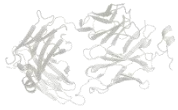
Antibodies and nanobodies

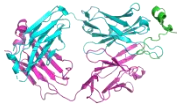

T240
H1204


T294
H1244

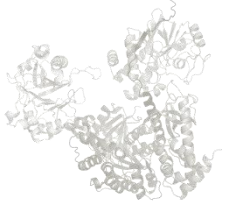

T248
H1215

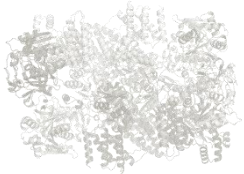

T266
H1222

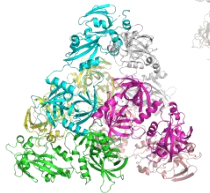

T268
H1223


T270
H1225

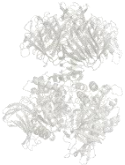
Large assemblies


T256
H1213

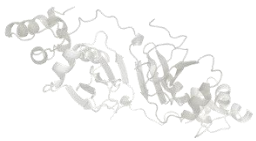

T258
H1217


T302
T1270

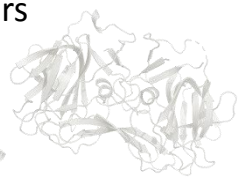

T272
H1227


T288/T290/T292
T1234/T1235
H1236

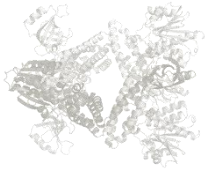
Homo-oligomers



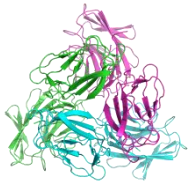
T236
T1201



T242
T1206



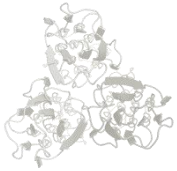
T282
T1237



T286
T1240

T309*
T1298

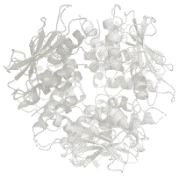
T260
T1218



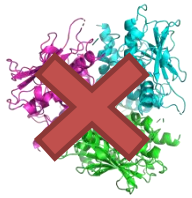
T298
T1259

* No MassiveFold

Conformers



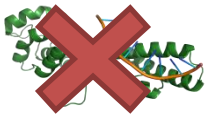
T250
T1249v1



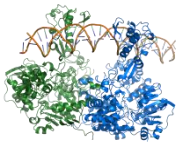
T252
T1249v2

DNA and RNA binding

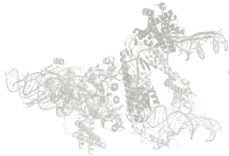
T304*
M1282



T306*
M1276



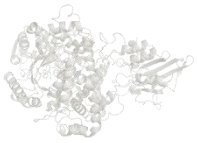
T308*
M1287



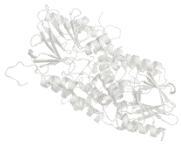
T254/T264*
M1228v1
M1239v1

T255/T265*
M1228v2
M1239v2

Hetero-oligomers

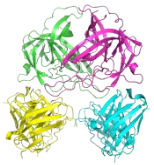


T276
H1230

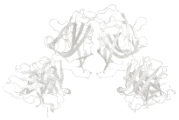


T244
H1208

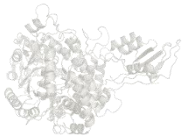
T296
H1245



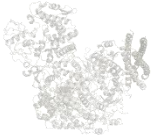
T278
H1232



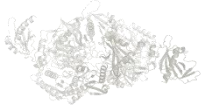
T280
H1233



T274
H1229



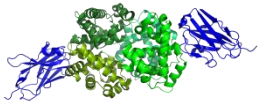
T262
H1220



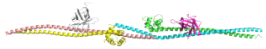
T300
H1267

T238
H1202

Antibodies and nanobodies

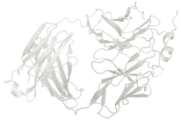


T240
H1204

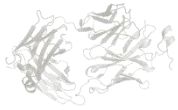


T294
H1244

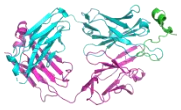
T248
H1215



T266
H1222

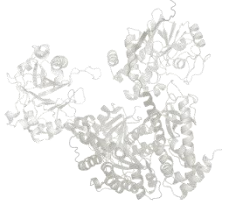


T268
H1223

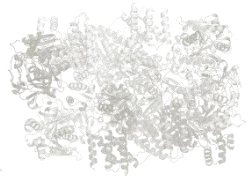


T270
H1225

Large assemblies



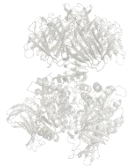
T256
H1213



T258
H1217

T272
H1227

T302
T1270



T288/T290/T292
T1234/T1235
H1236

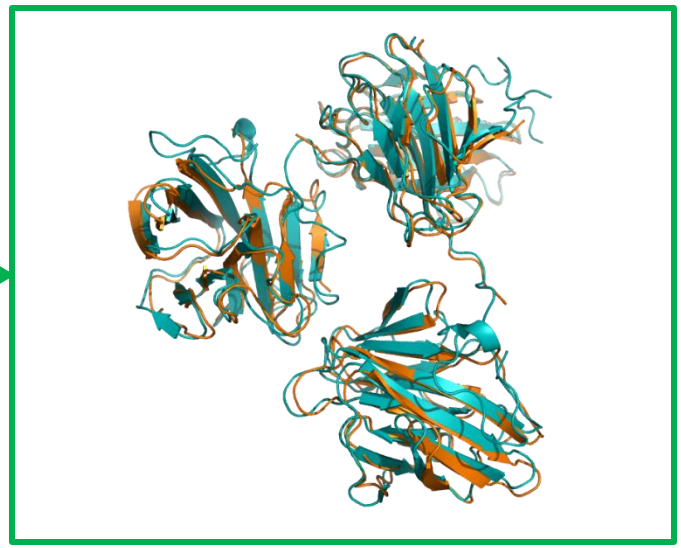
(weak interface)

X-ray	-	A3

	Stage1	Stage2
CASP	T1240	T2240
CAPRI	T286	T287

#Contacts	Interface	Chains	Area
135	1	A:B	900

INT1 – “homo”



DIFFICULT

AlphaFold ranked_0	
rms	7.85 Å
ipTM	0.477

These are the *only* acceptable+ models

Group stage1	Model	Fnat	L-rms	i-rms	Classification
Wallner	1	0.88	1.53	1.04	Medium
S.Fernandez-Recio	9	0.79	7.72	2.54	Acceptable

MassiveFold	First acceptable model	Best quality model	Classification
16	#474	#512	Acceptable

Group stage2	Model	Fnat	L-rms	i-rms	Classification
Wallner	3	0.80	1.15	1.03	Medium
Fernandez-Recio	9	0.79	7.72	2.54	Acceptable

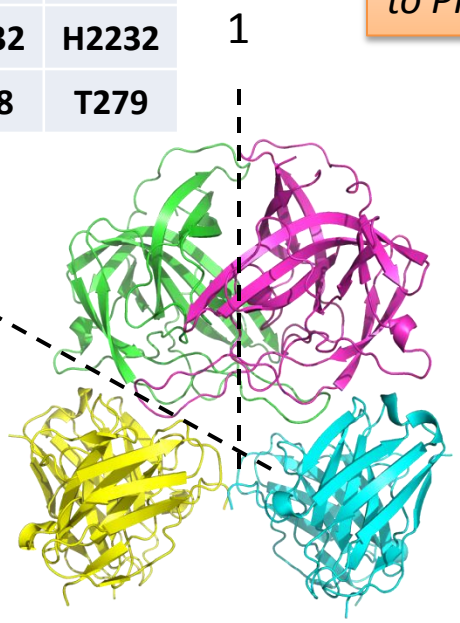
X-ray	-	A2B2

	Stage1	Stage2
CASP	H1232	H2232
CAPRI	T278	T279

Only A2 stable in solution, according to PISA

#Contacts	Interface	Chains	Area
200	1	A:B	1285
334	2	AB:C	450

INT1 – "homo", "dimer"
INT2 – "hetero"



EASY

Top-1

T278/H1232	CAPRI (20)	CASP (72)	Scorers (13)
Interface 1	20/18***/2**	67/60***/7**	10/9***/1**
Interface 2	0	1	0

T279/H2232	CAPRI (18)	CASP (58)	MassiveFold	
Interface 1	18/17***	57/52***	4619***	high
Interface 2	0	1	66	incorrect

AlphaFold ranked_0	
rms	x Å
ipTM	0.781

Group stage1	Model	Fnat	L-rms	i-rms	Classification
Smg-ulaval	2	0.51	6.35	1.13	Medium
Gray, Kihara, Zou, **MDOCKPP**, Pierce, **FALCON2**					Acceptable

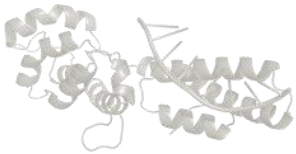
MassiveFold	First acceptable model	Best quality model	Classification
66	#2509	#3531	Acceptable

Group stage2	Model	Fnat	L-rms	i-rms	Classification
Plmfold	4	0.39	14.84	1.94	Medium
FALCON2, plmfold, Zou, **MILLISECONDS**					Acceptable

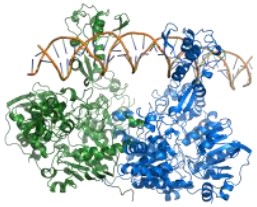
These are the *only* acceptable+ models

DNA and RNA binding

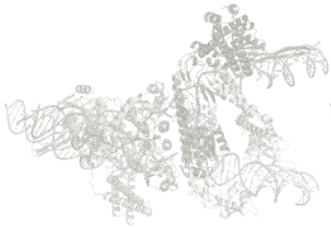
T304*
M1282



T306*
M1276



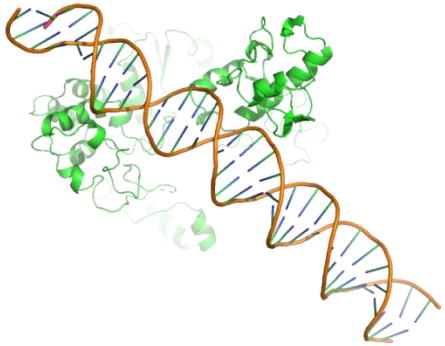
T308*
M1287

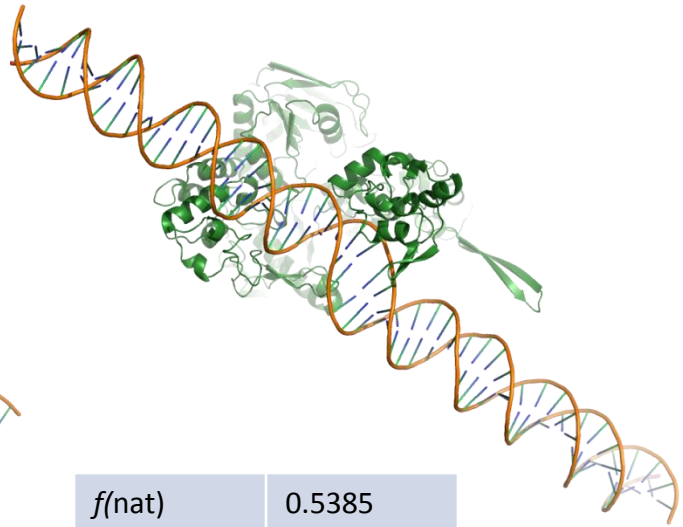


T254/T264*
M1228v1
M1239v1

T255/T265*
M1228v2
M1239v2

Predictors
Bhattacharya
Fernandez-Recio
ALPHAFOLD3-SERVER
B-LAB
GeneSilico
Diff
Scorers
Fernandez-Recio
Oliva
Kihara / ***LZERD***





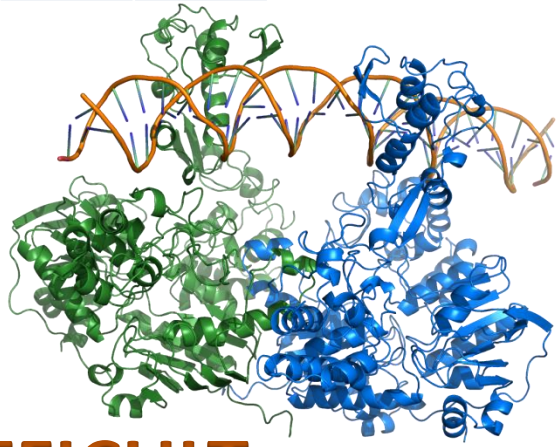
f(nat)	0.5385
f(nonnat)	0.8454
i-rms	3.8529

EM		

	Stage1	Stage2
CASP	M1287	-
CAPRI	T308	-

#Contacts	Interface	Chains	Area
227	1	A:C	1565
164	2	A:DNA	420

INT1 – “homo”, “dimer”
INT2 – “DNA/RNA”

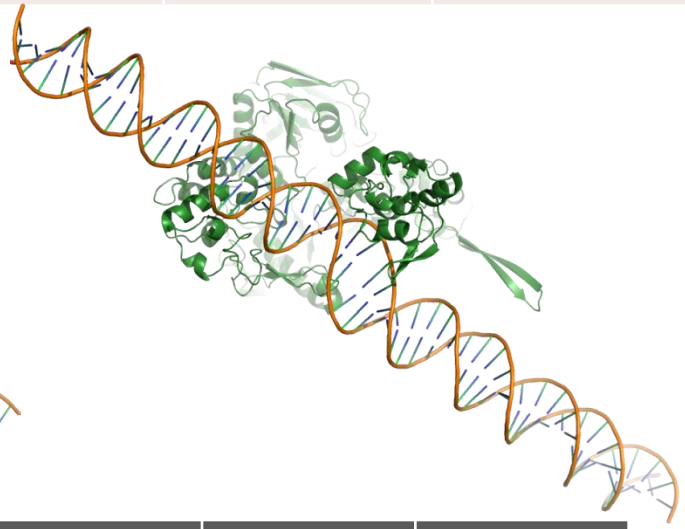


DIFFICULT

AlphaFold ranked_0	
rms	x Å
ipTM	NA

Top-1

T308/M1287	CAPRI (16)	CASP (29,28)	Scorers (12,11)
Interface 1	14/2**	19/3**	12
Interface 2	0	1	0



Group stage1	Model	Fnat	L-rms	i-rms	Classification
Bhattacharya	5	0.54	16.55	3.85	Acceptable
Diff, Fernandez-Recio, **B-LAB**, GeneSilico, **AlphaFold3-server**					Acceptable
*S.Fernandez-Recio, S.Kihara, **S.LZERD**, S.Oliva*					Acceptable

102 acceptable in the MassiveFold set
First: #120
Best: #173

High

Kozakov/Vajda

Acceptable

Cheng, Pierce, Zou

Fernandez-Recio

HYU-MLLab

LupengKong

MRAFold

MULTICOM (all variants)

OmniFold

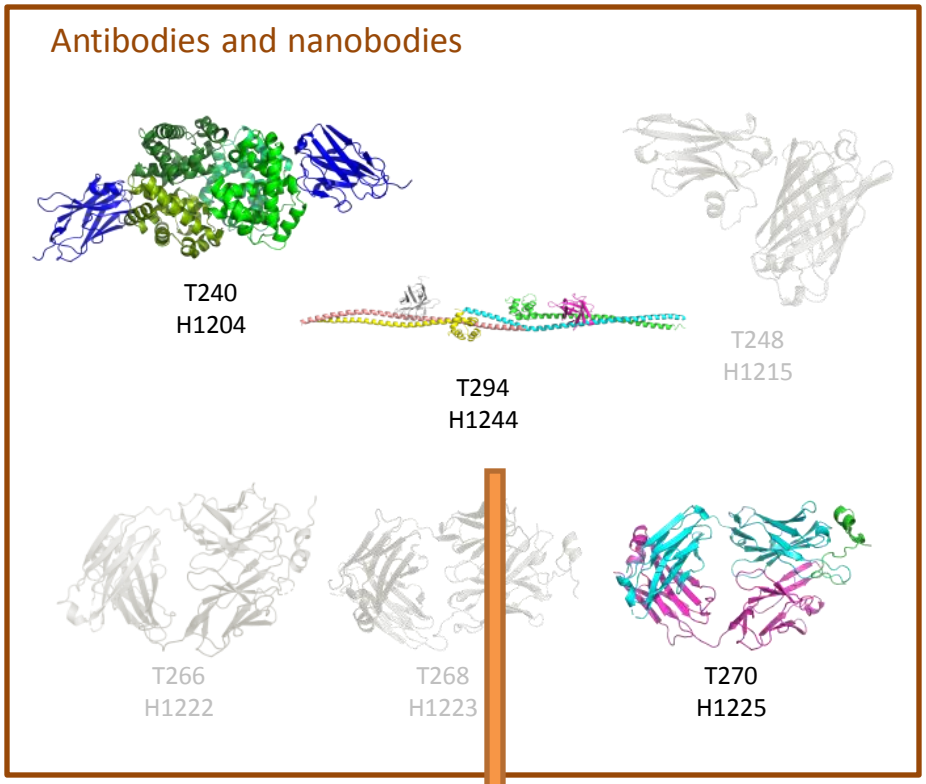
YANG-MULTIMER, Yang, Yang-Server

MQA-SERVER

CSSB-Faker

FALCON2

Zou



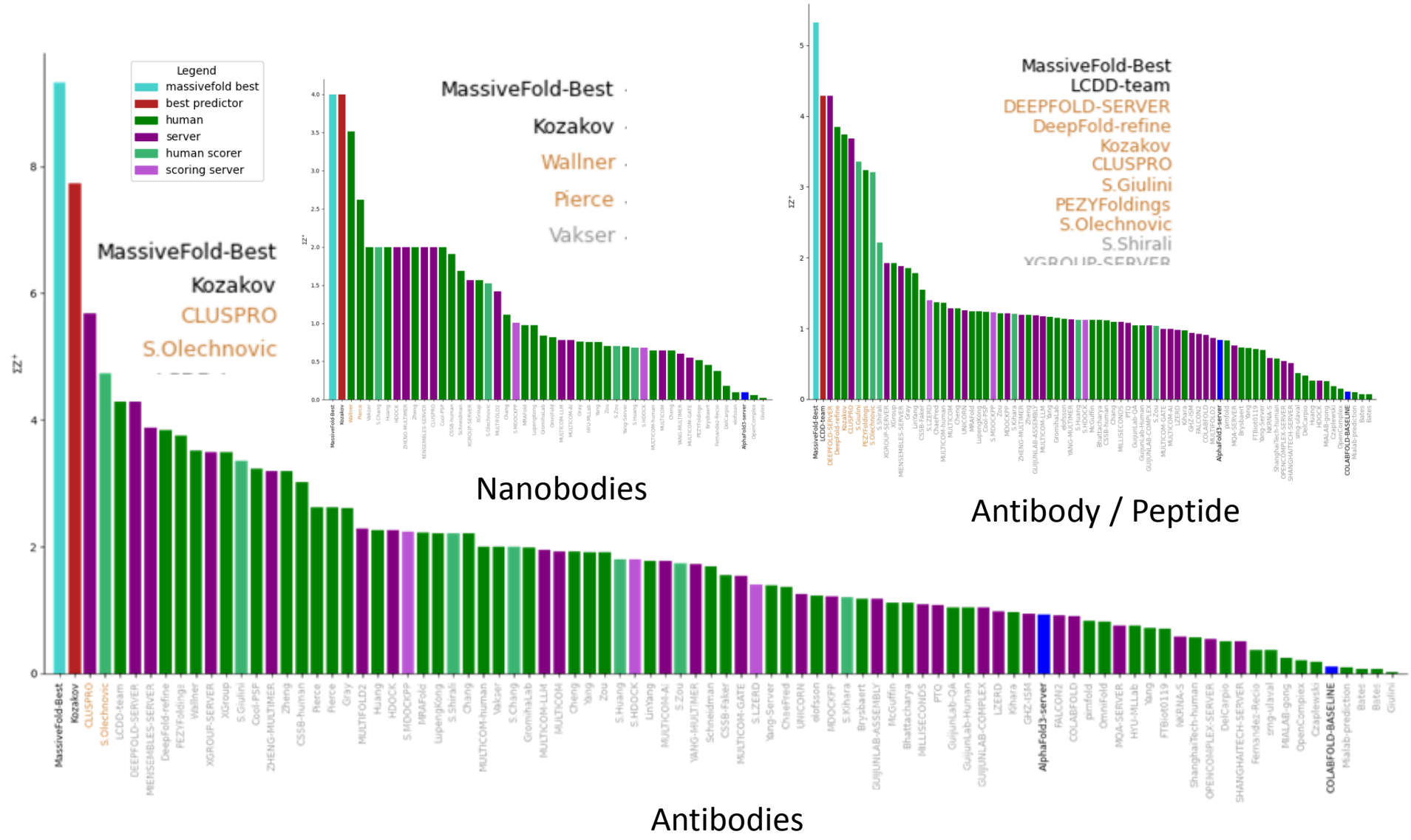
No acceptable solutions for T270/H1225

25 acceptable in the MassiveFold set
First: #249
Best: #4902

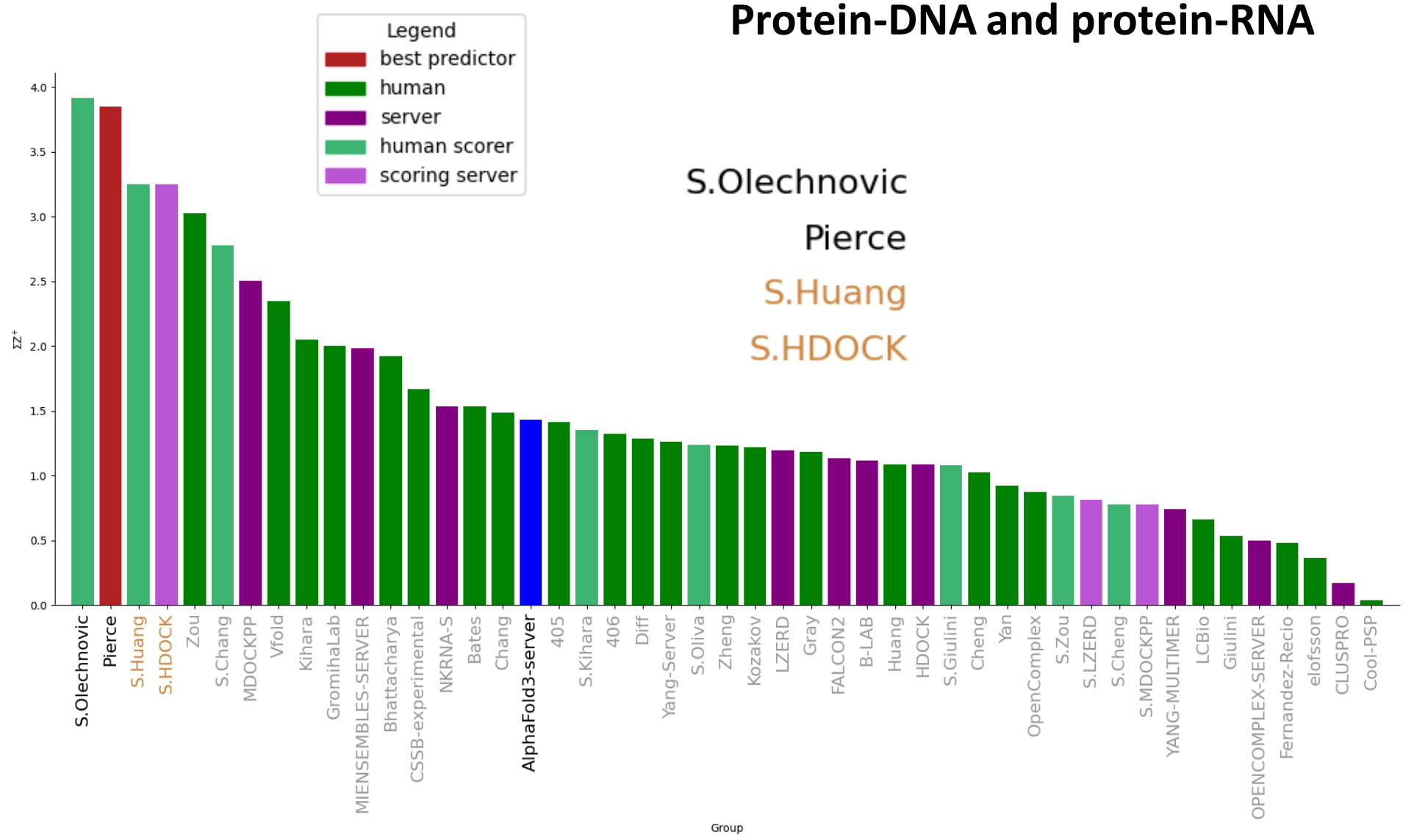
No acceptable solutions for T294/H1244

No good models in the MassiveFold set

PERFORMANCE IN CATEGORIES

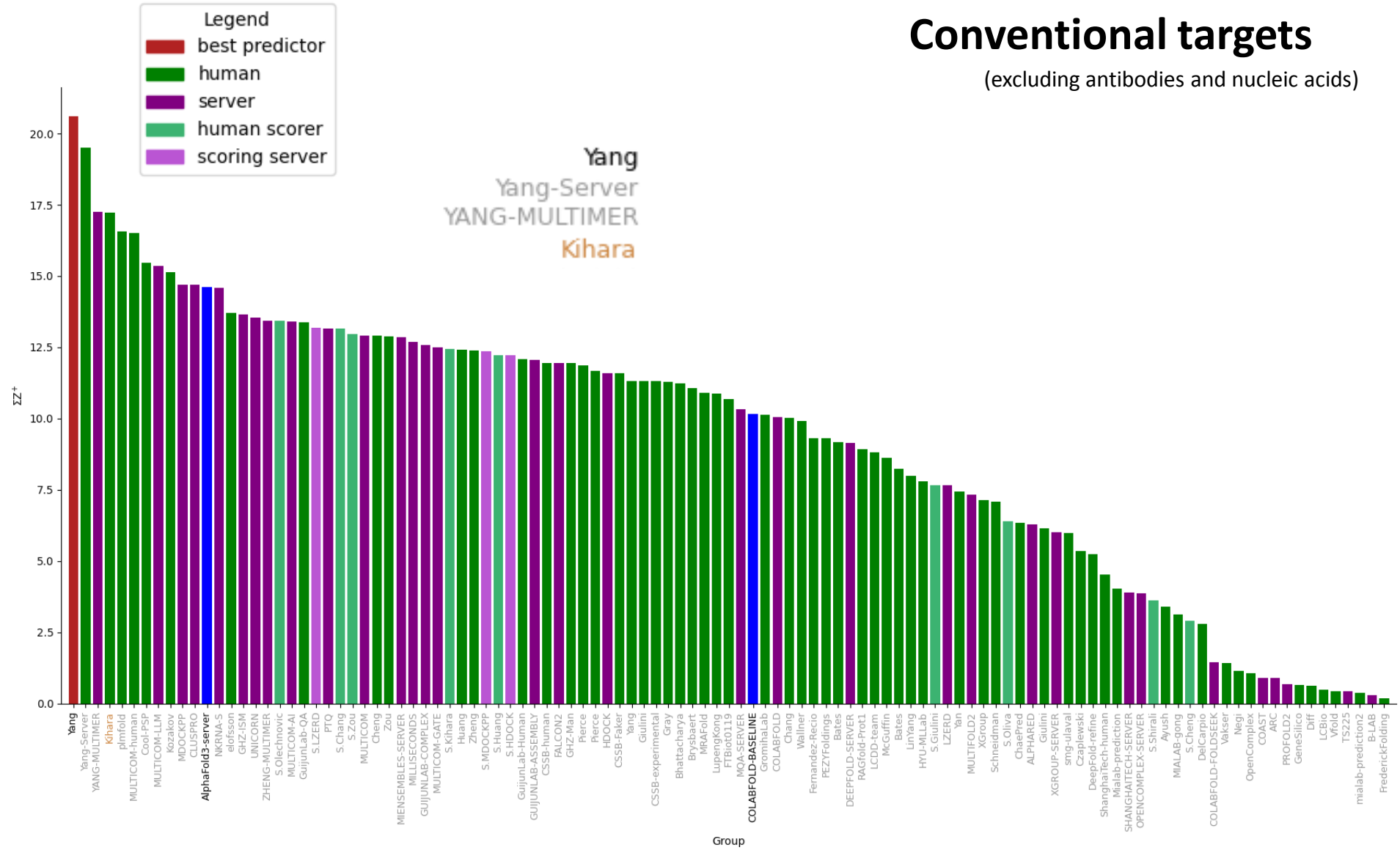

Legend
massivefold best
best predictor
human
server
human scorer
scoring server
MassiveFold-Best
Kozakov
CLUSPRO
S.Olechnovic
MassiveFold-Best
Kozakov
Wallner
Pierce
Vakser
MassiveFold-Best
LCDD-team
DEEPFOLD-SERVER
DeepFold-refine
Kozakov
CLUSPRO
S.Giulini
PEZYFoldings
S.Olechnovic
S.Shirali
Nanobodies
Antibody / Peptide
Antibodies

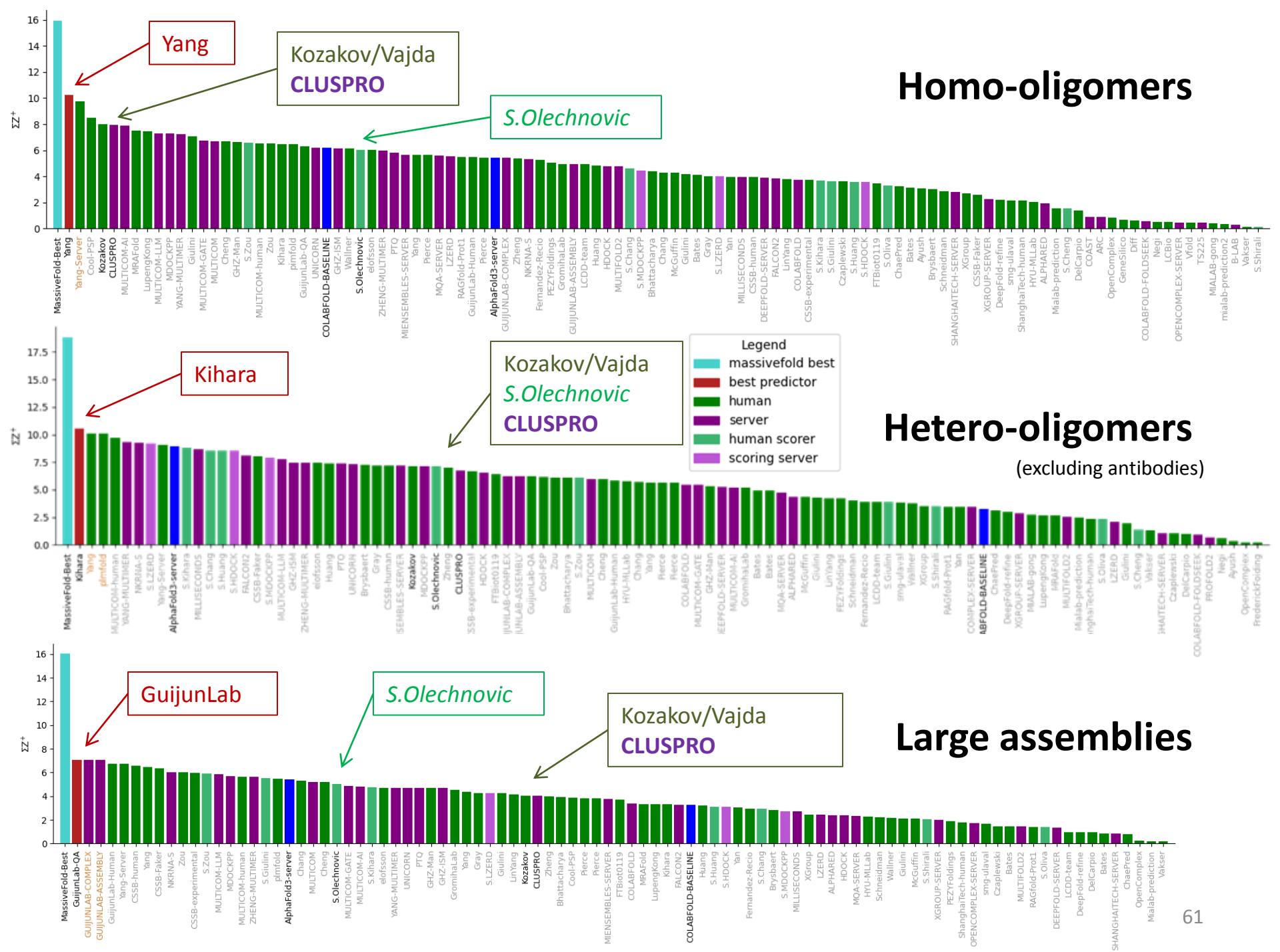
Protein-DNA and protein-RNA

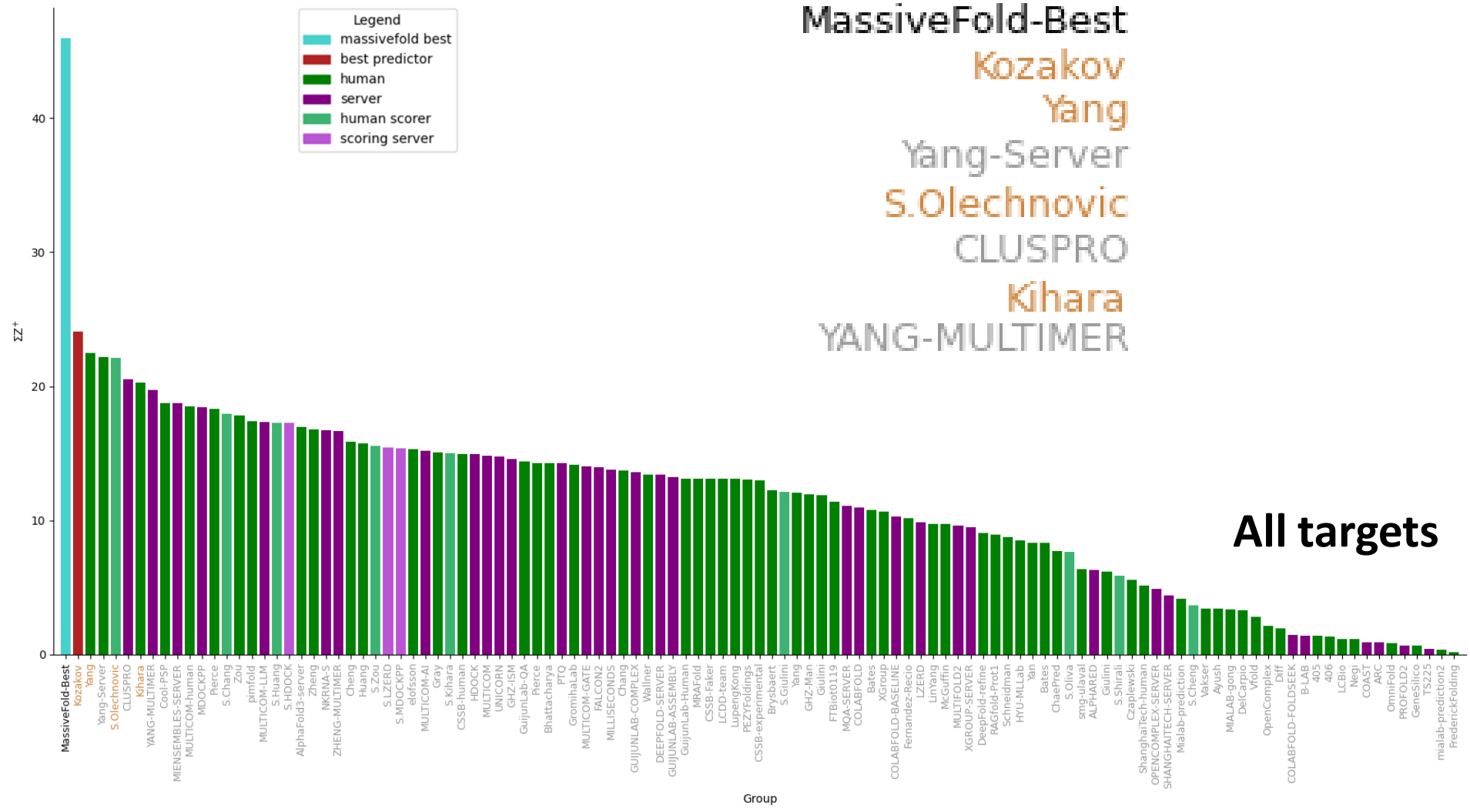


Conventional targets

(excluding antibodies and nucleic acids)




Yang
Kozakov/Vajda
CLUSPRO
S.Olechnovic
Homo-oligomers
Kihara
Kozakov/Vajda
S.Olechnovic
CLUSPRO
Legend
massivefold best
best predictor
human
server
human scorer
scoring server
Hetero-oligomers
(excluding antibodies)
GuijunLab
S.Olechnovic
Kozakov/Vajda
CLUSPRO
Large assemblies

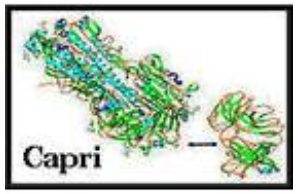

Legend
massivefold best
best predictor
human
server
human scorer
scoring server
MassiveFold-Best
Kozakov
Yang
Yang-Server
S.Olechnovic
CLUSPRO
Kihara
YANG-MULTIMER
All targets
ΣZ⁺
Group

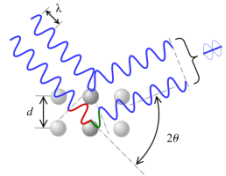
Conclusions

- PRO'S:
  - This year's session was a big success
    - Flat distribution of scores; many predictors producing good models
    - The best predictors find good models for 75% of targets
      - Kihara, Cheng, Kozakov/Vajda, Huang+, Zou
    - Fewer targets found but of better quality
      - MULTICOM, Zheng, Brysbaert, GuijunLab
  - Significant progress in the prediction of antibody and nanobody binding
    - Best performance by Kozakov/Vajda
  - In terms of relative prediction performance, some groups stand out:
    - **Kozakov/Vajda+**, **Yang+**, **Kihara**
    - scorer **Olechnovic**
    - LZERD for stage2 vs stage1, and for scoring
- CON'S:
  - Alternate conformers were ***not*** found
  - Nucleic acids remain problematic; DNA is easier than RNA
  - Scoring needs more development
    - MassiveFold "best" outperforms everybody, especially on "conventional" targets
  - Scorers recognize the *good* models, but not the *best* ones

Acknowledgements

- CAPRI community
- CASP community
- CASP organizers
- The MassiveFold team & IFB, IDRIS
- The experimentalists
- DeepMind





Computational Biology:
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- **Statistical physics of biomolecular interactions**
- **Structural biology of protein-carbohydrate interactions**
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- **The impact of evolution on protein-protein interaction and vice versa**