

Estimating the quality of 3D protein models using the ModFOLD7 server

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Estimating the Quality of 3D Protein Models
Using the ModFOLD7 Server

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Ali H. A. Maghrabi and Liam J. McGuffin

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Abstract

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Assessing the accuracy of 3D models has become a keystone in the protein structure prediction field. ModFOLD7 is our leading resource for Estimates of Model Accuracy (EMA), which has been upgraded by integrating a number of the pioneering pure-single- and quasi-single-model approaches. Such an integration has given our latest version the strengths to accurately score and rank predicted models, with higher consistency compared to older EMA methods. Additionally, the server provides three options for producing global score estimates, depending on the requirements of the user: (1) ModFOLD7_rank, which is optimized for ranking/selection, (2) ModFOLD7_cor, which is optimized for correlations of predicted and observed scores, and (3) ModFOLD7 global for balanced performance. ModFOLD7 has been ranked among the top few EMA methods according to independent blind testing by the CASP13 assessors. Another evaluation resource for ModFOLD7 is the CAMEO project, where the method is continuously automatically evaluated, showing a significant improvement compared to our previous versions. The ModFOLD7 server is freely available at <http://www.reading.ac.uk/bioinf/ModFOLD/>.

Key words

Estimates of model accuracy (EMA), Model quality assessment (MQA), Protein structure prediction, Protein modeling, Tertiary structure prediction, Critical assessment of techniques for protein structure prediction (CASP), Continuously evaluate the accuracy and reliability of predictions (CAMEO)

1 Introduction

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Since researchers from different fields of biological sciences started relying on the three-dimensional structural models of proteins, prediction programs have been improving rapidly. One of the major components of structure prediction pipelines is the evaluation or assessment of the predicted model accuracy. It is possible to generate many hundreds of alternative 3D models for any give protein target using many different algorithms. Often, the best modeling method is not always the most accurate for a given target, so it is problematic to choose rank and select the models that are most likely to be the closest to the native structure. Furthermore, local regions of models may differ in quality, and so it may help a

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biologist to know whether their specific regions of interest are accurately modeled, for example, predicted interface/interacting residues. Such problems have been recognized by the field of structural bioinformatics, and many developers have focused their attention toward improving methods for Model Quality Assessment (QA) that support their prediction pipelines. Such tools and servers are also currently referred to as the Estimates of Model Accuracy (EMA) methods.

The EMA (a.k.a. QA) methods and servers were included for evaluation as a category in two major worldwide organizations that are specialized in the protein structure prediction field. The first organization conducts independent blind testing with the Critical Assessment of Techniques for Protein Structure Prediction (CASP) [1] experiments, which are held every other year. The second organization is the continuously automatic model evaluation project called CAMEO [2]. Both organizations have highlighted the importance of the EMA development for the improvement of protein structure prediction and have helped to encourage progress in the field.

Modern methods of EMA can be classified into three broad categories. (1) The pure-single-model methods, which can score the data from the information of an individual model—they are featured by their rapid processing and their strong performance at model ranking and selection, but they often produce less consistent global scores. (2) The clustering/consensus approaches, which use multiple alternative models build for the same protein target—these types of methods have the opposite features of the single-model methods, and they have been far more accurate but are more computationally intensive and do not work when very few similar models are available. (3) The quasi-single-model methods, which can score an individual model against a pool of reference alternative models that are generated from the same target sequence. Quasi-single-model methods attempt to provide comparable accuracy to clustering methods, while addressing real-life needs of researchers with few/single models.

ModFOLD [3] is our EMA protocol, and various successive versions have been competing with the top-leading model quality assessment programs throughout the past 10 years. ModFOLD was built in the beginning as two separate methods. The original single-model method was called by its own original name, ModFOLD. Additionally, we developed a clustering-based method, called ModFOLDclust [4]. Over the years, both methods have been merged with the adoption of a number of other methods to develop a new ModFOLD program which was a pioneer of the quasi-single-model approach.

The quasi-single-model approach was firstly implemented with the third version of ModFOLD [5]. By using this approach, ModFOLD3 was able to generate reference sets of models from the

target sequence, using the IntFOLD-TS [6] method, which were used for comparison with the submitted model using ModFOLD-clust2 [4]. ModFOLD has since undergone a number of updates through versions 4 [7], 5 [8], and 6 [9], which have maintained the use of a quasi-single-model approach. Each successive version has been ranked among the top-performing EMA methods of the recent CASP experiments. The implementation of quasi-single method has helped our ModFOLD pipeline keep its competitiveness using the predictive power offered by clustering-based methods, as well as being capable of making predictions for a single model at a time. While we have made significant progress in performance over the years with our ModFOLD methods, there is still room for improvement in many aspects of EMA.

Here, we describe significant major updates to the ModFOLD server. The server has been popular with modelers around the world, having completed hundreds of thousands of EMA jobs for thousands of unique users over the past decade.

2 Methods

The latest version of our server, ModFOLD7, uses a new quality assessment technique which combines the strengths of multiple pure-single- and quasi-single-model methods for the improvement of prediction accuracy. The server comprises a single-model approach which combines ten scoring methods. Six of the methods are pure-single-model inputs methods, and they include the following: (1) Contact Distance Agreement (CDA) which uses MetaPSICOV [10] to relate to the agreement between the predicted residue contacts and the contacts in model; (2) Secondary Structure Agreement (SSA) which uses PSIPRED [11] to relate to the agreement between the predicted secondary structure of each residue and the secondary structure state of the residue in model according to Dictionary of Secondary Structures of Proteins (DSSP); (3) ProQ2 [12]; (4) ProQ2D [13]; (5) ProQ3D [13]; and (6) VoroMQA [14]. The remaining four methods are quasi-single-model input methods, and they are as follows: (1) ModFOLDclust_single (MFcs) which uses input model against the 130 IntFOLD5 reference models; (2) Disorder “B-factor” Agreement (DBA) which compares DISOPRED [15] scores against the MFcs score; (3) ModFOLDclustQ_single (MFcQs) [4] which uses input model against the IntFOLD5 reference models; and (4) ResQ [16] which estimates the residue-specific quality and B-factor, and it compares the input model against LOMETS [17] models. The combination of the component per-residue/local quality scores from each of the ten methods is processed using Neural Networks (NNs), resulting in a final consensus of per-residue quality scores for each model. A flowchart of the data and processes used in the ModFOLD7 server is shown in Fig. 1.

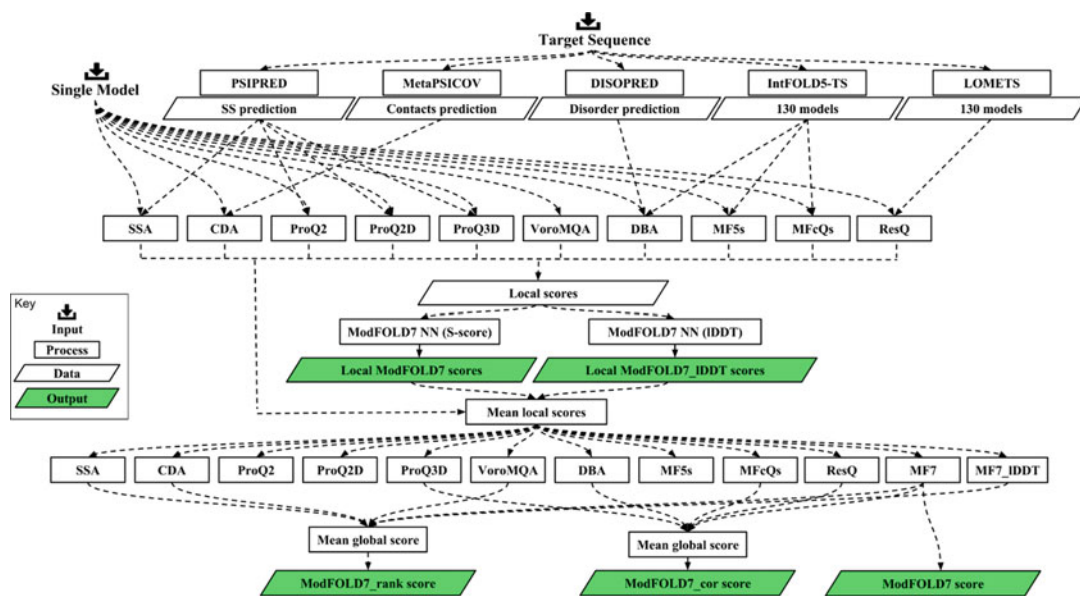


Fig. 1 Flow of data illustrating the local and global estimates of model accuracy in ModFOLD7. The method pipeline starts with two inputs, the target sequence and a single model. The target sequence is evaluated with five preprocessing methods. The resulting data from the preprocessing methods with the input single model then are evaluated with ten scoring methods resulting in local score input data. Next, the local scores are processed using two neural networks (NN) trained to two target functions, the *S*-score and the IDDT score, resulting in the final local score outputs. Lastly, the mean local scores from each method are used to form 12 global scores, which are then optimally combined in the different ways indicated to form the three variants of ModFOLD7

2.1 The ModFOLD7 Component Per-Residue/Local Quality Scoring Methods

The ModFOLD7 NNs were trained using two separate target functions for each residue in a model: the residue contact-based IDDT score and the superposition-based *S*-score which has been used in previous versions of ModFOLD. The RSNNs package for R was used to construct the NNs, which were trained using data derived from the evaluation of CASP11 and 12 server models versus native structures. The per-residue similarity scores were calculated using a simple multilayer perceptron (MLP). For the method trained using the IDDT score (ModFOLD7_res_lddt), the MLP input consisted of a sliding window (size = 5) of per-residue scores from all ten of the methods described above, and the output was a single quality score for each residue in the model (50 inputs, 25 hidden, 1 output). For the method trained using the *S*-score (ModFOLD7_res), this time only seven of the ten methods were used as inputs—all apart from the ProQ2, CDA, and SSA scores—with a sliding window (size = 5), therefore 35 inputs, 18 hidden, 1 output. For both of the per-residue scoring methods, the similarity scores, *s*, for each residue were converted back to distances, *d*, with $d = 3.5\sqrt{(1/s) - 1}$.

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2.2 The ModFOLD7 Global Scoring Methods

Global scores were calculated by taking the mean per-residue scores (the sum of the per-residue similarity scores divided by sequence lengths) for each of the ten individual component methods, described above, plus the NN output from ModFOLD7_res and ModFOLD7_res_lddt. Furthermore, three additional quasi-single global model quality scores were generated for each model based on the original ModFOLDclust, ModFOLDclustQ, and ModFOLDclust2 global scoring methods (in a similar vein to the ModFOLD4_single and ModFOLD5_single global scores, tested in CASP10 and CASP11, respectively). Thus, we ended up with 15 alternative global QA scores, which could be combined in various ways in order to optimize for the different facets of the quality estimation problem. For the CASP13 experiment, we registered three ModFOLD7 global scoring variants: (1) The ModFOLD7 global score, which used the mean per-residue NN output score from ModFOLD7_res—this score considered alone was found to have a good balance of performance both for correlations of predicted versus observed scores and rankings of the top models. (2) The ModFOLD7_cor global score variant $((MFcQs + DBA + ProQ3D + ResQ + ModFOLD7_res)/5)$ was found to be an optimal combination for producing good correlations with the observed scores, that is, the predicted global quality scores produced should produce closer to linear correlations with the observed global quality scores. (3) The ModFOLD7_rank global score variant $((CDA + SSA + VoroMQA + ModFOLD7_res + ModFOLD7_res_lddt)/5)$ was found to be an optimal combination for ranking, that is, the top-ranked models (top 1) should be closer to the highest accuracy, but the relationship between predicted and observed scores may not be linear. The local scores of the ModFOLD7 and ModFOLD_rank variants used the output from the ModFOLD7_res NN, whereas the ModFOLD_cor variant used the local scores from the ModFOLD7_res_lddt NN.

2.3 Server Inputs and Outputs

Like the previous versions, the ModFOLD7 server requires only the amino acid sequence for the protein target and a single 3D model (in PDB format) for evaluation. However, users can upload more than one PDB file in a compressed archive. Optionally, users can also give their target a name and also provide their e-mail address, so that they can receive a notification of the result (*see Notes 1–6*).

The results are provided in a clean and simple user interface so that it can be interpreted easily by nonexperts at a glance. Once the prediction process is complete, a results page is generated containing a single table summarizing the quality assessment scores for each submitted model. Each assessed model is represented in the table graphically, with thumbnail images of the local error plots and annotated 3D models. Images in the table are clickable for detailed

3D visualization using the JSmol/HTML5 framework. Conveniently, interactive 3D results can also be viewed on mobile devices without any plugin requirement. The results table shows a global score for each model, a p -value indicating the likelihood that the model is incorrectly folded and a plot of the local errors in the model in Ångströms. Users can also download the models annotated with the ModFOLD7 predicted local quality scores, which have been inserted into the B -factor column of the ATOM records for each submitted model. The raw machine-readable data files for each set of predictions, which comply with the CASP data standards, are also provided for developers and more advanced users. An overview of the ModFOLD7 interface is shown in Fig. 2 (see Notes 7–12).

2.4 Independent Benchmarking and Cross-Validation


The three alternative optimized scoring methods of the ModFOLD7 server have been benchmarked against their respective previous versions from the ModFOLD6 server (Fig. 3). For the cumulative GDT_TS of top-ranked model, ModFOLD6_rank method was giving a score below 44.5 as their highest, whereas ModFOLD7_rank was able to cross the 45 and go higher. For the Pearson correlation comparing the predicted score versus the observed score (GDT_TS), ModFOLD6_cor achieved a correlation 0.9250, while for ModFOLD7_cor, the correlation was found to be over 0.9300. For the evaluation of local model quality prediction accuracy using the area under the ROC curve (AUC) (where residues with IDDT scores $\leq 0.6 = 0$), ModFOLD6 could not reach an AUC score of 0.93, whereas ModFOLD7 was closer to 0.95. Such results indicate that our latest version, ModFOLD7, has demonstrated progress in performance compared to ModFOLD6, and according to many measures, the improvements are significant.

ModFOLD7 is also one of the EMA servers that are continuously independently benchmarked for local EMA performance by the evaluating organization, CAMEO. For the last year, the CAMEO public EMA data (<https://www.cameo3d.org/>) show that ModFOLD7 is one of the leading public EMA methods for producing local (per-residue) quality scores. The results from CAMEO also show that ModFOLD7 is performing significantly better than its previous versions, ModFOLD6 and ModFOLD4 [7, 9] (Table 1).

3 Case Study

In 2018, the ModFOLD7 servers participated in the latest worldwide Critical Assessment of Techniques for Protein Structure Prediction competition (CASP13). The goal of this competition was to help advance the methods which identify protein structure from

Input page



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Bioinformatics Web Servers

The ModFOLD Model Quality Assessment Server (Version 7.0)

This form allows you to predict the quality of 3D models for a given protein target. Further information and references can be found on the [ModFOLD home page](#). Before you submit a prediction please refer to the [help page](#). Click 'Help' in each section for detailed instructions.

Required - Input sequence of protein target (single letter code) [help](#)

Required - Upload model/models (either a single PDB file or a tarred and gzipped directory of PDB files) [help](#)
 No file chosen

Select global accuracy score optimisation preference [help](#)
☒ Ranking (the models with the highest global accuracy are ranked at the top)
☐ Balanced (good correlations and top model ranking)
☐ Correlation (the predicted accuracy scores correlate linearly with the observed accuracy scores)

Optional - E-mail address (you will be sent a link to graphical and machine readable results when the job is completed) [help](#)

Optional - Short name for protein target [help](#)

Please cite the following papers:

Maghrabi, A.H.A. & McGuffin, L.J. (2017) ModFOLD6: an accurate web server for the global and local quality estimation of 3D models of proteins. 45, W416-W421. Nucleic Acids Res. doi: 10.1093/nar/gkx332. [PubMed](#)

McGuffin, L.J., Shuld, A.M., Kempster, R., Maghrabi, A.H.A., Nealon, J.O., Salehe, B.R., Atkins, J.D. & Roche, D.B. (2017) Accurate Template Based Modelling in CASP12 using the INFOLD4-TS, ModFOLD6 and RefOLD methods. Proteins: Structure, Function, and Bioinformatics, 86 Suppl 1, 335-344. doi: 10.1002/prot.25360. [PubMed](#)

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Output page

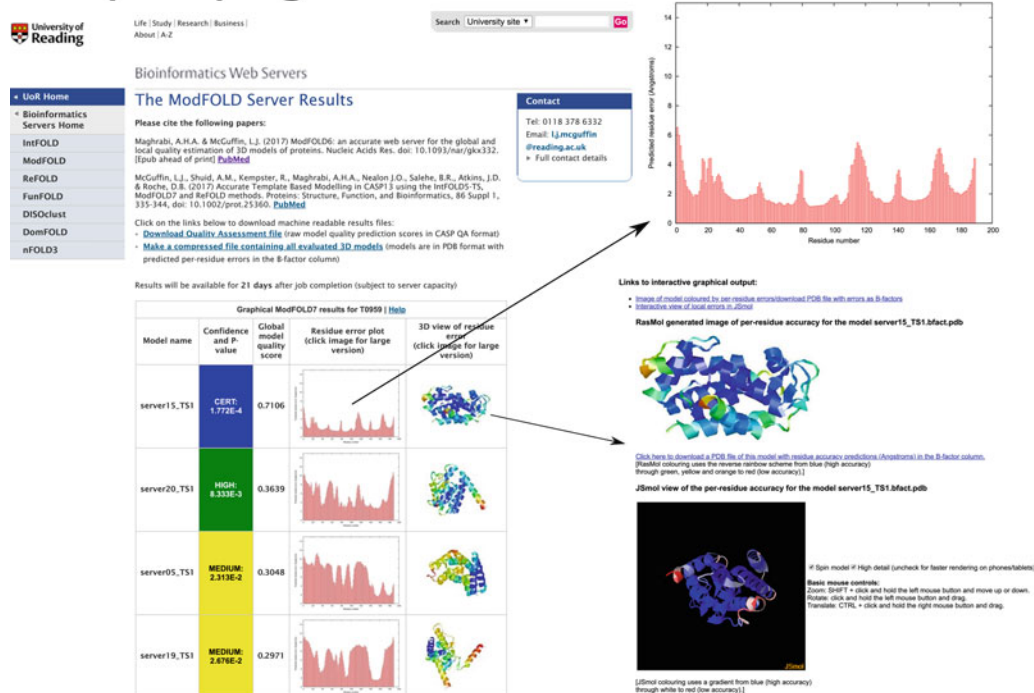


Fig. 2 ModFOLD7 server inputs and outputs pages. *Inputs page*: containing a text box to paste the amino acid sequence of protein target in single-letter code, a push button to upload model/models (either a single PDB file or a tarred and gzipped directory of PDB files) of the protein target, three options to select the global accuracy score optimization preference, and two optional text boxes to input the user e-mail address and to give a short name for protein target. *Outputs page*: showing the result page for models submitted to CASP13 generated for target T0959. The main output page is shown with summary tables of the results for each model. Results can also be visualized in more detail by clicking on the thumbnail images in the main table

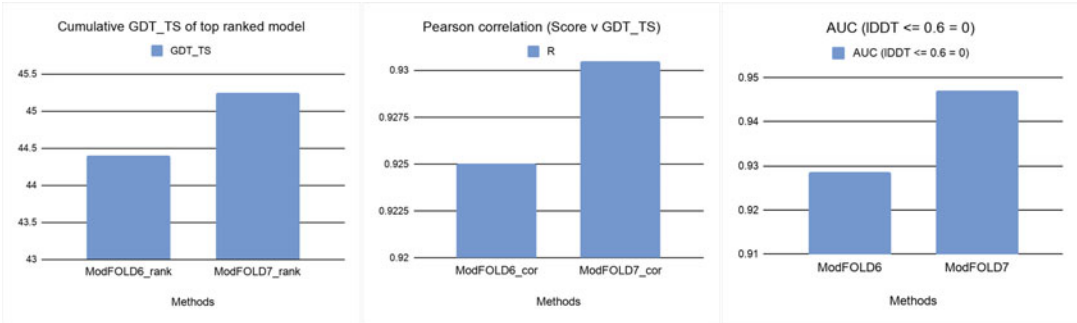


Fig. 3 Histograms showing a comparison between the three variants of ModFOLD6 and the respective variants of ModFOLD7 using three evaluation methods: the cumulative GDT_TS of top-ranked models, the Pearson correlations between predictive and observed scores, and the local accuracy as measured by the AUC score ($IDDT \leq 0.6 = 0$). Evaluation is based on cross-validated CASP11 data

Table 1
Top EMA methods in CAMEO

Server	Structural models			ROC		ROC normalized		PR		PR normalized	
	Submitted	Received	%	AUC		AUC		AUC		AUC	
				0,1	0,0.2	0,1	0,0.2	0,1	0,0.8,1	0,1	0,8,1
QMEANDisCo	9816	9041	92.1	0.93	0.77	0.86	0.71	0.9	0.66	0.83	0.61
ModFOLD7_IDDT	9816	8283	84.4	0.91	0.71	0.77	0.6	0.87	0.61	0.74	0.51
ModFOLD6	9816	6709	68.3	0.89	0.65	0.61	0.44	0.84	0.58	0.57	0.4
QMEAN	9816	9054	92.2	0.87	0.61	0.8	0.56	0.81	0.53	0.74	0.49
ProQ2	9816	9464	96.4	0.86	0.58	0.82	0.56	0.79	0.5	0.76	0.48
ModFOLD4	9816	7191	73.3	0.85	0.57	0.62	0.42	0.78	0.49	0.57	0.36

One year of data downloaded from <http://www.cameo3d.org/>. One year [2018-03-30–2019-03-23]—“All” dataset. The table is sorted by the ROC AUC score
ROC receiver operating characteristic, AUC area under the ROC curve, PR precision and recall

sequence by testing them objectively via the process of blind pre-
diction. The competition includes many subcategories, one of them
is the Estimate of Model Accuracy (EMA) where our ModFOLD7
methods are independently evaluated. The CASP assessors provide
sequences of proteins whose structures have never been observed
before. Participants use their prediction servers in order to generate
the 3D models of the target structures. Once server models have
been generated for a given target, they are then used for the EMA
category; participants use their model quality assessment methods
in order to estimate the accuracy of the predicted models for each
target.

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In CASP13, the assessors provide predictors with anonymous protein sequence (targets), and these targets are submitted by different biological research teams around the world who have a vested interest in determining their structures. An example of one of these protein targets is Endolysin KPP12 (CASP3 target T0962), a bacteriophage found to have a therapeutic effect in *Pseudomonas aeruginosa keratitis* [18]. The study shows that the morphological and DNA sequence analysis of KPP12 have led to identifying the family of that protein and the similarities with other viruses, and therefore, researchers are testing whether the protein is the same as its family members. Using KPP12 as a treatment can result in the suppression of neutrophil infiltration, and it also can greatly enhance bacterial clearance in the infected cornea.

The only available data for KPP12 were the sequence. Participants from different organizations and companies started to predict the structure of that protein by using their own methods. After structure prediction, the created models were assessed in terms of its quality and how close are these models to their protein native structures. The results showed that ModFOLD7 has given the best EMA score among all the other methods in all measurements such as LDDT with 0.660 and CAD with 1.990 (Table 2). Such information about model quality is invaluable in identifying: firstly, the very best 3D models of a protein that are the closest to the native

Table 2
The top ten EMA methods for Target T0962 (KPP12) in CASP13 in terms of absolute differences in score between the top selected model and the best model according to observed structure (smaller scores indicate higher performing methods)

Rank	Gr. Name	GDT_TS	LDDT	CAD(AA)	SG
1	SBROD-plus	0.000	0.660	1.990	0.000
2	ModFOLD7	0.000	0.660	1.990	0.000
3	ModFOLD7_cor	0.000	0.660	1.990	0.000
4	MASS2	10.170	2.110	3.991	8.475
5	Bhattacharya-Server	10.170	2.110	3.991	8.475
6	Pcons	6.215	2.660	3.121	10.452
7	VoroMQA-B	4.802	2.850	2.033	5.933
8	Kiharalab	4.802	2.850	2.033	5.933
9	ProQ4	4.802	2.850	2.033	5.933
10	MASS1	4.802	2.850	2.033	5.933

EMA methods are evaluated for target T0962 in CASP13. The evaluation was performed using GDT_TS, IDDT, CAD, and SG measuring scores. Only the top ten methods are shown, and the table is sorted using IDDT scores. The scores are calculated over all models for all targets (QA stage 2–best 150). The data are downloaded from http://predictioncenter.org/casp13/qa_diff2best.cgi

structures, secondly, the likelihood that models are of good or poor
quality overall, and finally, the magnitude of errors in specific local
regions of the protein and the regions that are likely to have the
fewest errors.

4 Notes

1. The ModFOLD server version 7.0 requires the amino acid
sequence of your target protein and either a single 3D model
file in PDB format or a tarball containing a directory of multi-
ple separate files in PDB format. To produce a tarball file for
your own 3D models, for Linux/OSX/other Unix users:
(a) Tar up the directory containing your PDB files, for example,
type the following at the command line: tar cvf my_models.tar
my_models/, (b) Gzip the tar file, for example, gzip my_mo-
dels.tar, (c) upload the gzipped tar file (e.g., my_models.tar.gz)
to the ModFOLD server; and for Windows users: (a) download
a file archiver application such as 7-zip, (b) select the directory
(folder) of model files to add to the .tar file, click "Add," select
the "tar" option as the "Archive format:," and save the file as
something memorable, for example, my_models.tar, (c) select
the tar file, click "Add," and then select the "GZip" option as
the "Archive format:"—the file should then be saved as
my_models.tar.gz, and (d) upload the gzipped tar file (e.g.,
my_models.tar.gz) to the ModFOLD server.
2. Providing the e-mail address will give the permission to send a
link with the graphical results and machine-readable results
directly after the predictions are completed. However, if the
user does not provide the e-mail address, then she/he must
bookmark the results page in order to view and refer to it when
it is available.
3. In the text box labeled "Input sequence of protein target,"
users should carefully paste in the full amino acid for the
interested target protein in single-letter format. An example
sequence (CASP13 target T0949) is inserted as
MAAKKGMTTVLVSAGVIGALQWEKAVALPNPSG
QVINGVHHYTIDFNYYYKPDRMTWHVGEKVELTIDN
RSQSAPPIAHQFSIGRTLVS RDNGFPKSQAIAVGWKDNF
FDGVPITSGGQTGPVPAFSVSLNKGQKYTFSEFVVPNKP
KWEYGCFLQTGQHFMNGMHGILDILPAQGS.
4. It is important that the user provides the full sequence that
corresponds to the sequence of residue coordinates in the
model file. If the model does not contain numbering which
corresponds directly to the order of residues in the sequence
file, then the server will attempt to renumber the residues in
the model files accordingly. However, submitting a model file

- p>with residues that are not contained in the provided sequence 320
-
- p>will not complete the prediction for that model. 321
5. Users must ensure that each PDB file contains the coordinates 322
for one model only. Please do not upload a single PDB file 323
containing the coordinates for multiple alternative NMR mod- 324
els. The coordinates for multiple models should always be 325
uploaded as a tarred and gzipped directory of separate files. 326
 6. Assigning a short memorable name to user's prediction jobs is 327
useful for identifying and distinguishing them, because Mod- 328
FOLD will not necessarily return the results in the order the 329
user submitted them. 330
 7. The results table is ranked according to decreasing global 331
model quality score. The global model quality scores range 332
between 0 and 1. In general, scores less than 0.2 indicate that 333
there may be incorrectly modeled domains, and scores greater 334
than 0.4 generally indicate more complete and confident mod- 335
els, which are highly similar to the native structure. If the global 336
model quality scores are low, then the per-residue scores can 337
give you an idea of specific domains or regions in your protein 338
that might be correctly modeled. 339
 8. From the global scores, the p -value which represents the prob- 340
ability that each model is incorrect can be calculated. In other 341
words, for a given predicted model quality score, the p -value is 342
the proportion of models with that score that do not share any 343
similarity with the native structure (TM-score < 0.2). Each 344
model is also assigned a color-coded confidence level depend- 345
ing on the p -value: $p < 0.001$ = blue = CERT = Less than a 346
1/1000 chance that the model is incorrect, 347
 $p < 0.01$ = green = HIGH = Less than a 1/100 chance that 348
the model is incorrect, $p < 0.05$ = yellow = MEDIUM = Less 349
than a 1/20 chance that the model is incorrect, 350
 $p < 0.1$ = orange = LOW = Less than a 1/10 chance that 351
the model is incorrect, $p > 0.1$ = red = POOR = Likely to be a 352
poor model with little or no similarity to the native structure. 353
 9. The per-residue scores indicate the predicted distance 354
(in Angstroms) between the CA atom of the residue in the 355
model and the CA atom of the equivalent residue in the native 356
structure. Thumbnail images of plots depicting the per-residue 357
error versus residue number are included in each row in the 358
results table. Each of the thumbnails links to a page that dis- 359
plays a larger view of the plot and contains a further link to 360
download a PostScript version. Each row in the table also dis- 361
plays a thumbnail of the 3D cartoon view of the model which is 362
color coded with the residue error according to the RasMol 363
temperature coloring scheme. Each small image also links to a 364
page that shows a larger image of the 3D view and contains a 365

link to download a PDB file of the model with residue accuracy
predictions (Angstroms) in the *B*-factor column. The model is
also loaded into JSmol for convenient interactive viewing of
per-residue errors within the browser.

10. The time taken for a prediction will depend on the length of
sequence, the number of models submitted, and the load on
the server. For a new run on single model, the user should
typically receive his/her results back within 24 h, once the job
is running. Large batches of models (several hundred) for a
single target may take several days to process. If the user has
already submitted a model for the same target sequence within
the same week, then the reference model library for that
sequence will already be available to the server (the results
will be cached) and so she/he will receive the results back
much more quickly (within a few hours).
11. For fair usage policy, the users are allowed to have one job
running at a time for each IP address, so please wait until your
previous job completes before submitting further data. If you
already have a job running, then you will be notified, and your
uploaded data will be deleted. Once your job has completed,
your IP address will be unlocked and you will be able to submit
new data.
12. Users should check the header of the machine-readable results
file (provided as a link at the top of the result page) for any
errors that may have occurred following file submission. Please
e-mail us for help if you encounter a persistent error.

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