

CAID

June 24, 2019

Contents

1 CAID	2
1.1 Dataset	2
1.2 Evaluation metrics	2
1.2.1 Balanced accuracy	3
1.2.2 F1-score	4
1.2.3 MCC	4
1.2.4 Per target accuracy	5
1.2.5 Target correlation matrix	6
1.2.6 ROC curve	7
1.2.7 PR curve	8
1.2.8 pROC/pPR scatter plot	8
1.2.9 Average overall ranking	9
1.2.10 Accuracy correlation between datasets	10
1.3 Consensus	11
1.3.1 Confusion matrix per threshold	11
1.3.2 Accuracy per threshold	12
1.3.3 Percentage of correct/incorrect classifications	13
1.3.4 clustermap of binary predictions correlation	14
1.4 Fully disordered targets	15
1.4.1 Correctly and incorrectly classified full IDPs	15
1.4.2 Full IDPs ROC	16

Chapter 1

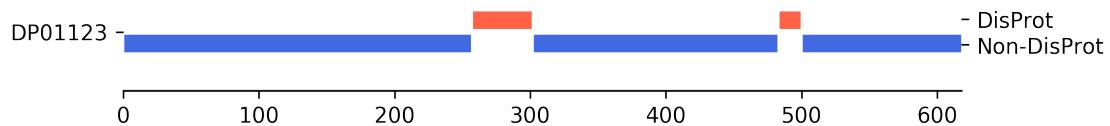
CAID

1.1 Dataset

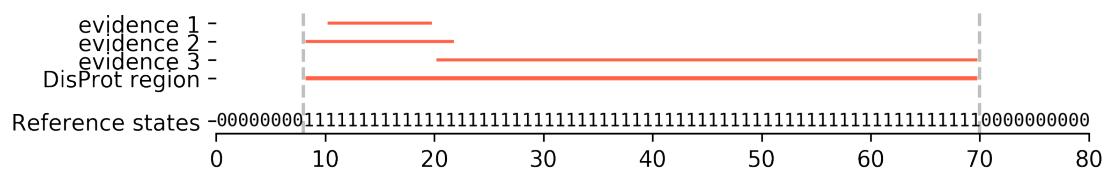
Critical Assessment of Intrinsic Disorder (CAID) is a continuous experiment where prediction methods for intrinsic disorder (ID) are blind tested on unpublished DisProt data.

```
Accordion(children=(RadioButtons(description='Reference:', index=1, options=('new-pdb-missing', 'new-di
```

Current analysis is performed on the **new-disprot-all** dataset with **simple** negative definition. This means that DisProt defines order for *all its new entries* and *the contrary of DisProt defines order*.



DisProt entries can have annotation covering the same sequence space. In these cases different evidences are merged in a unique continuous region. DisProt merged regions define positive cases (labeled as 1) in reference states. Remaining states are considered negatives.



1.2 Evaluation metrics

Metrics evaluating prediction scores are calculated applying **ROC** thresholds to prediction scores. Table is sorted by descending value of BAc column

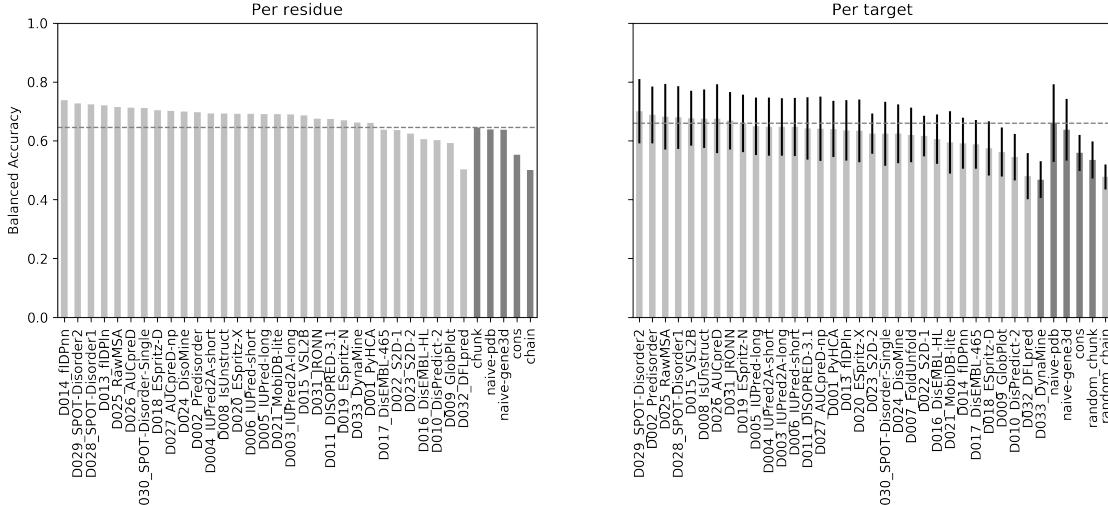
	FN	FP	TN	TP	BAc	F1s	MCC	Pre	Rec	Rec_n	AUC_PRC	AUC_ROC	npred	nref
D014_fIDPnn	11066	90800	191191	43452	0.738	0.460	0.357	0.324	0.797	0.678	0.475	0.814	645	646
D029_SPOT-Disorder2	8102	83325	138083	39649	0.727	0.464	0.348	0.322	0.830	0.624	0.340	0.760	610	646
D028_SPOT-Disorder1	8561	111175	170274	45732	0.724	0.433	0.330	0.291	0.842	0.605	0.268	0.744	644	646
D013_fIDPln	10876	101788	180203	43642	0.720	0.437	0.327	0.300	0.801	0.639	0.422	0.793	645	646
D025_RawMSA	14121	87752	194239	40483	0.715	0.443	0.327	0.316	0.741	0.689	0.414	0.780	646	646
D026_AUCpreD	10325	105752	168752	44230	0.713	0.432	0.318	0.295	0.811	0.615	0.479	0.757	644	646
D030_SPOT-Disorder-Single	11684	102523	179468	42920	0.711	0.429	0.314	0.295	0.786	0.636	0.318	0.757	646	646
D018_ESpritz-D	12566	102001	179918	41994	0.704	0.423	0.304	0.292	0.770	0.638	0.410	0.774	645	646
D027_AUCpreD-np	13471	99301	182690	41133	0.701	0.422	0.300	0.293	0.753	0.648	0.428	0.751	646	646
D024_DisoMine	13437	100089	181902	41167	0.699	0.420	0.298	0.291	0.754	0.645	0.388	0.765	646	646
D002_Predisorder	13600	95575	172625	40897	0.697	0.428	0.299	0.300	0.750	0.644	0.325	0.747	642	646
D008_IsUnstruct	13083	105743	176248	41521	0.693	0.411	0.286	0.282	0.760	0.625	0.323	0.744	646	646
D004_IUPred2A-short	14500	98375	183616	40104	0.693	0.415	0.289	0.290	0.734	0.651	0.313	0.741	646	646
D006_IUPred-short	13330	105000	176919	41230	0.692	0.411	0.285	0.282	0.756	0.628	0.311	0.739	645	646
D020_ESpritz-X	12969	106802	175117	41591	0.692	0.410	0.285	0.280	0.762	0.621	0.304	0.740	645	646
D021_MobiDB-lite	13044	107630	174289	41516	0.690	0.408	0.281	0.278	0.761	0.618	0.366	0.737	645	646
D005_IUPred-long	14874	97662	184257	39686	0.690	0.414	0.286	0.289	0.727	0.654	0.298	0.737	645	646
D003_IUPred2A-long	14491	100327	181664	40113	0.689	0.411	0.283	0.286	0.735	0.644	0.298	0.735	646	646
D015_VSL2B	13496	106734	174715	40797	0.686	0.404	0.276	0.277	0.751	0.621	0.301	0.732	644	646
D031_JRONN	15103	104987	176932	39457	0.675	0.397	0.261	0.273	0.723	0.628	0.302	0.724	645	646
D011_DISOPRED-3.1	12924	117034	164957	41680	0.674	0.391	0.257	0.263	0.763	0.585	0.290	0.701	646	646
D019_ESpritz-N	16357	101266	180653	38203	0.670	0.394	0.255	0.274	0.700	0.641	0.296	0.714	645	646
D033_DynaMine	14313	116663	165256	40247	0.662	0.381	0.239	0.256	0.738	0.586	0.271	0.707	645	646
D001_PyHCA	16402	106493	175498	38202	0.661	0.383	0.240	0.264	0.700	0.622	0.277	0.706	646	646
chunk	32511	32511	249479	22092	0.645	0.405	0.289	0.405	0.405	0.885	NaN	NaN	100	100
naive-pdb	6072	171438	109201	48119	0.639	0.352	0.215	0.219	0.888	0.389	0.528	0.634	630	646
D017_DisEMBL-465	20238	98679	182770	34055	0.638	0.364	0.208	0.257	0.627	0.649	0.283	0.685	644	646
naive-gene3d	6767	168792	112552	47544	0.638	0.351	0.212	0.220	0.875	0.400	0.547	0.643	639	646
D022_S2D-1	18180	110396	171053	36113	0.636	0.360	0.203	0.246	0.665	0.608	0.253	0.672	644	646
D023_S2D-2	16152	127731	153718	38141	0.624	0.346	0.183	0.230	0.703	0.546	0.229	0.654	644	646
D016_DisEMBL-HL	24236	96597	184852	30057	0.605	0.332	0.160	0.237	0.554	0.657	0.274	0.654	644	646
D010_DisPredict-2	21924	111501	170490	32680	0.602	0.329	0.151	0.227	0.598	0.605	0.250	0.637	646	646
D009_GlobPlot	21816	117085	164834	32744	0.592	0.320	0.137	0.219	0.600	0.585	0.231	0.624	645	646
cons	21503	141841	140150	33101	0.552	0.288	0.076	0.189	0.606	0.497	0.193	0.567	646	646
D032_DFLpred	53281	4983	277008	1323	0.503	0.043	0.018	0.210	0.024	0.982	0.142	0.410	646	646
chain	45733	45733	236257	8870	0.500	0.162	0.000	0.162	0.162	0.838	NaN	NaN	100	100

Where table column names mean:

label	meaning
BAc	balanced accuracy
F1s	F1-score
MCC	Matthew's Correlation Coefficient
Pre	Precision>Selectivity
Rec	Recall/Sensitivity
Rec_n	Specificity
AUC_ROC	Area under the ROC curve
AUC_PRC	Area under the PR curve
npred	number of predicted targets
nref	number of targets in reference

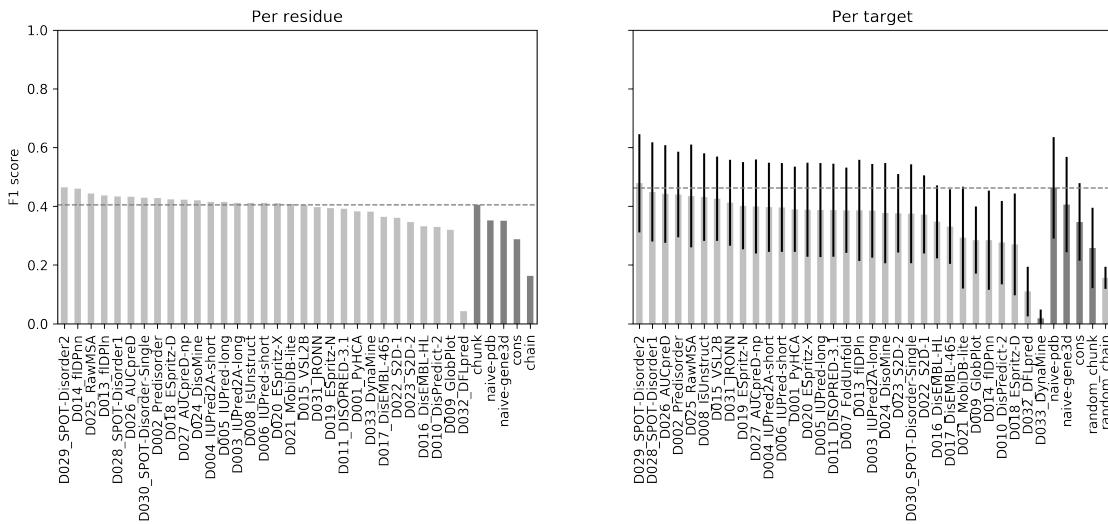
1.2.1 Balanced accuracy

Comparison of predictors and baselines performance by balanced accuracy.



1.2.2 F1-score

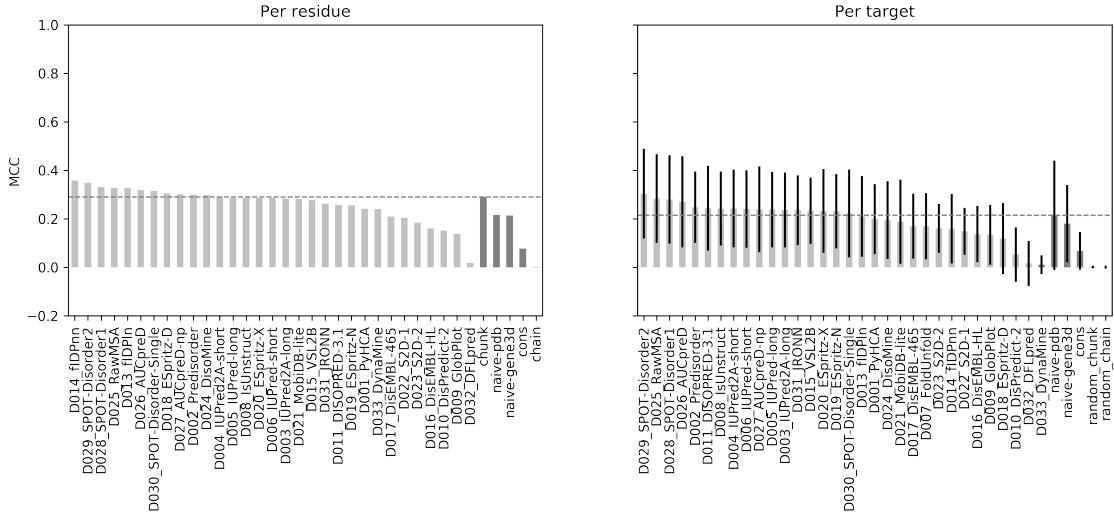
Comparison of predictors and baselines performance by F1-score.



Overall (left panel) and average per-target (right panel) F1-score. Light gray bars represent published prediction methods; dark gray bars represent baseline prediction methods. On the right panel standard deviation is shown as an error bar.

1.2.3 MCC

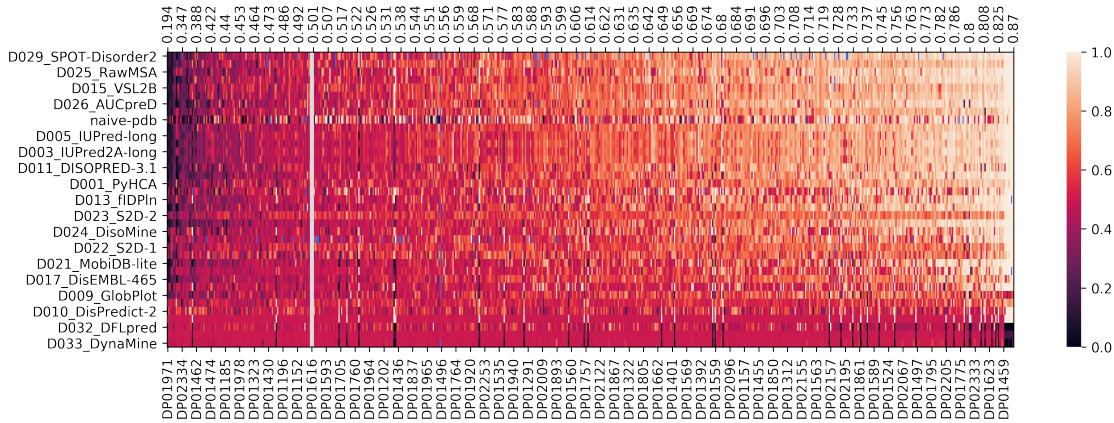
Comparison of predictors and baselines performance by Matthew's Correlation Coefficient.



Overall (left panel) and average per-target (right panel) MCC. Light gray bars represent published prediction methods; dark gray bars represent baseline prediction methods. On the right panel standard deviation is shown as an error bar.

1.2.4 Per target accuracy

Balanced accuracy score for each target for each prediction methods (including baselines)



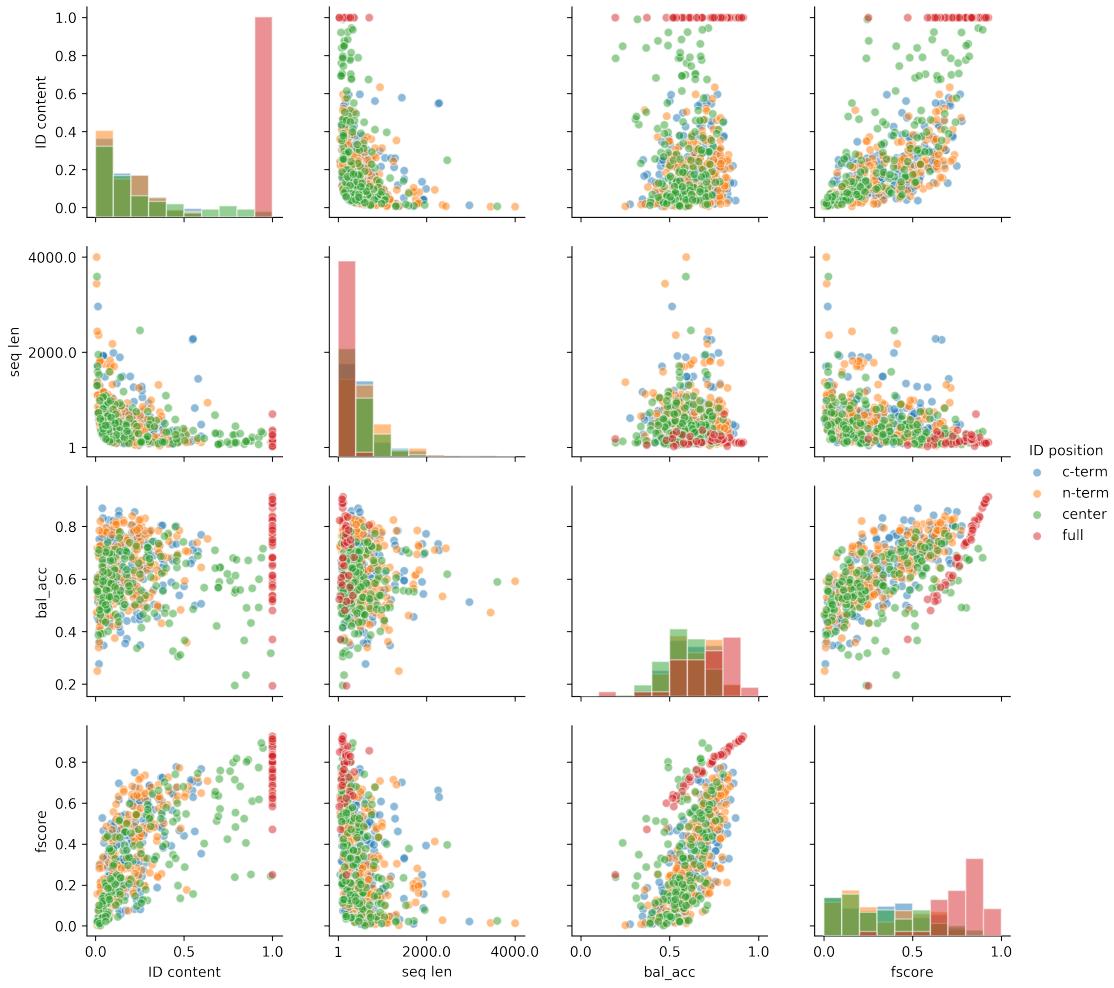
Heatmap of the predictors accuracy for each target. The higher the accuracy the lighter the color. Non-predicted targets are shown in blue. x and y axes are sorted by average accuracy over rows and columns respectively. A white semi-transparent vertical line marks the point where the average accuracy scores for a target is below (left) or above (right) 0.5. Accuracy score approaches 0.5 for a random classifier. Accuracy < 0.5 indicates anti-correlation between predicted and reference classes. Targets with an average accuracy score < 0.5 are:

DP01971	DP01870	DP02010	DP01898	DP01278	DP01281
DP01456	DP01432	DP01128	DP01427	DP01130	DP02334
DP01501	DP01584	DP01877	DP01248	DP01494	DP01145

DP01498	DP01512	DP01203	DP02149	DP01462	DP01366
DP01124	DP01141	DP01724	DP01907	DP01844	DP01883
DP01407	DP02231	DP01139	DP01474	DP01307	DP01590
DP02234	DP01316	DP01556	DP01285	DP01280	DP02328
DP01774	DP01925	DP01185	DP01794	DP01878	DP01772
DP02324	DP01500	DP01163	DP02073	DP01428	DP01477
DP01647	DP01978	DP01612	DP01499	DP01324	DP01505
DP01887	DP01504	DP01999	DP01434	DP01134	DP01503
DP01323	DP02168	DP01600	DP01355	DP01313	DP01193
DP02296	DP01172	DP02086	DP01551	DP01869	DP01430
DP01528	DP01309	DP02025	DP01252	DP01749	DP01140
DP01967	DP01150	DP02247	DP01396	DP01196	DP01279
DP01195	DP02169	DP01914	DP01115	DP01170	DP01473
DP01364	DP01854	DP02117	DP01152	DP01489	DP01339
DP02170	DP01110	DP01762	DP01177	DP01187	DP01120
DP01288					

1.2.5 Target correlation matrix

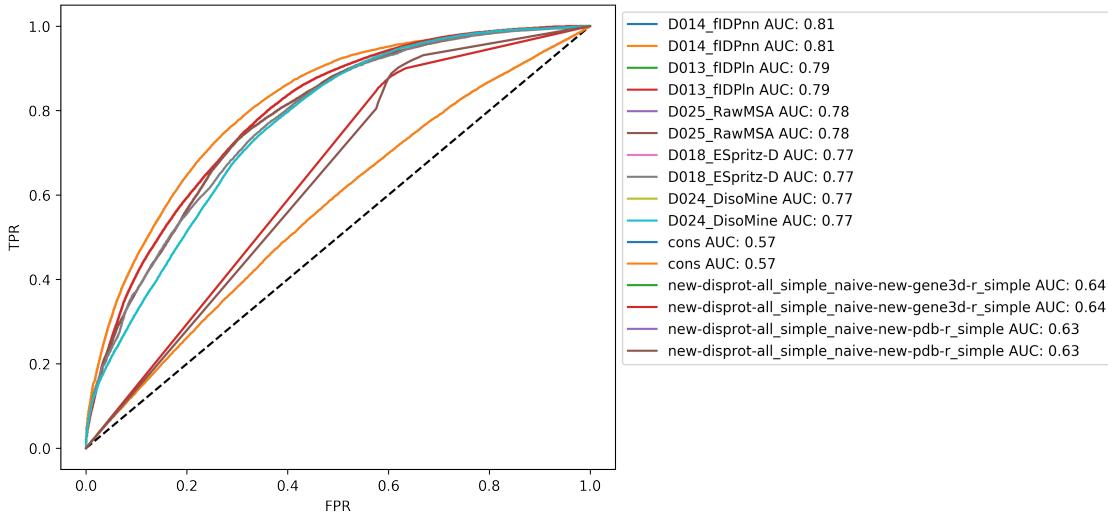
Commonly, experimental data has a bias for low disorder-content. DisProt targets have high disorder-content. Classifiers have been trained/engineered on low disorder-content. I expect difficult targets to have high disorder content. To verify if there is any correlation between target features I'm plotting 4 selected features against each other (Balanced accuracy, F1-Score, Sequence length and ID content). A fifth feature (ID position) divides the datasets in subsets. ID position is calculated as the average of the indexes of disordered residues along the sequence. A correlation is observed in a subset if its points gather around a diagonal.



Correlation matrix of Balanced accuracy, F1-Score, Sequence length and ID content. Average position of disorder is color-coded. Figure matrix is symmetrical. Plots along diagonal axis display single variables distributions. No meaningful correlation is observed.

1.2.6 ROC curve

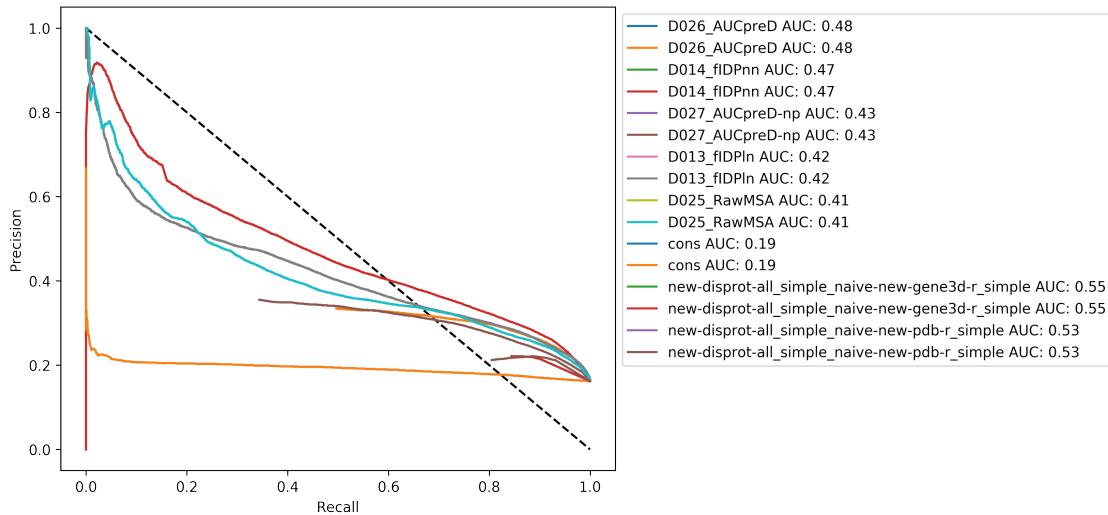
Receiver Operator Characteristic plot for predictors and baselines



False Positive Rate (FPR) on x axis, True Positive Rate (TPR) on y axis. Methods are sorted by their Area Under the Curve (AUC). Only first ten methods plus baselines are shown.

1.2.7 PR curve

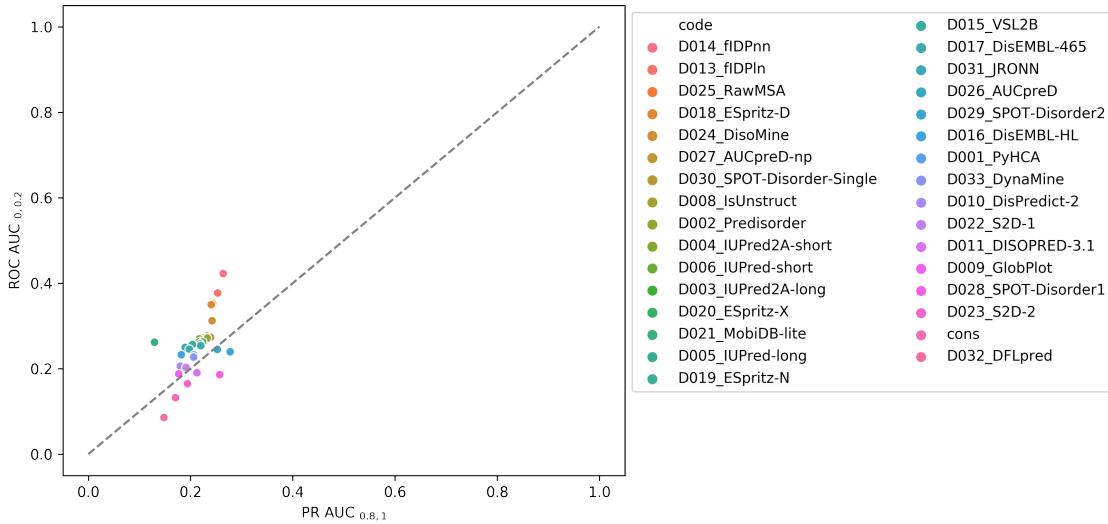
Precision Recall curve plot for predictors and baselines



Recall/Sensitivity on x axis, Precision/Selectivity on y axis. Methods are sorted by their Area Under the Curve (AUC). Only first ten methods plus baselines are shown.

1.2.8 pROC/pPR scatter plot

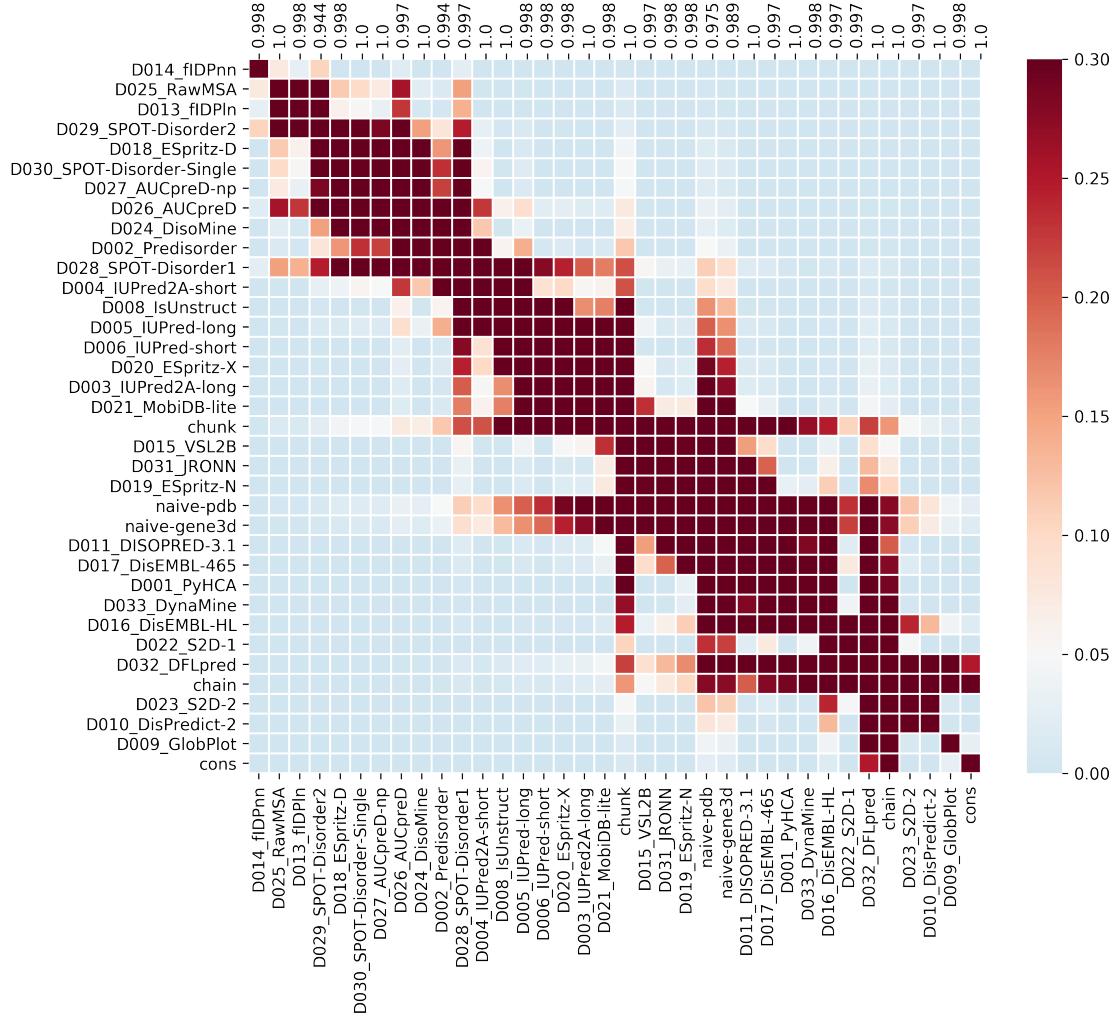
Plot of the AUCs from the ROC curve and PR curve



ROC AUC on the x axis, Precision-Recall (PR) AUC on the y axis. ROC AUC is calculated including ROC curve points with x values (FPR) between 0 and 0.2. PR AUC is calculated including PR curve points with x values (Recall) between 0.8 and 1. Both AUCs are then rescaled to the $[0, 1]$ range.

1.2.9 Average overall ranking

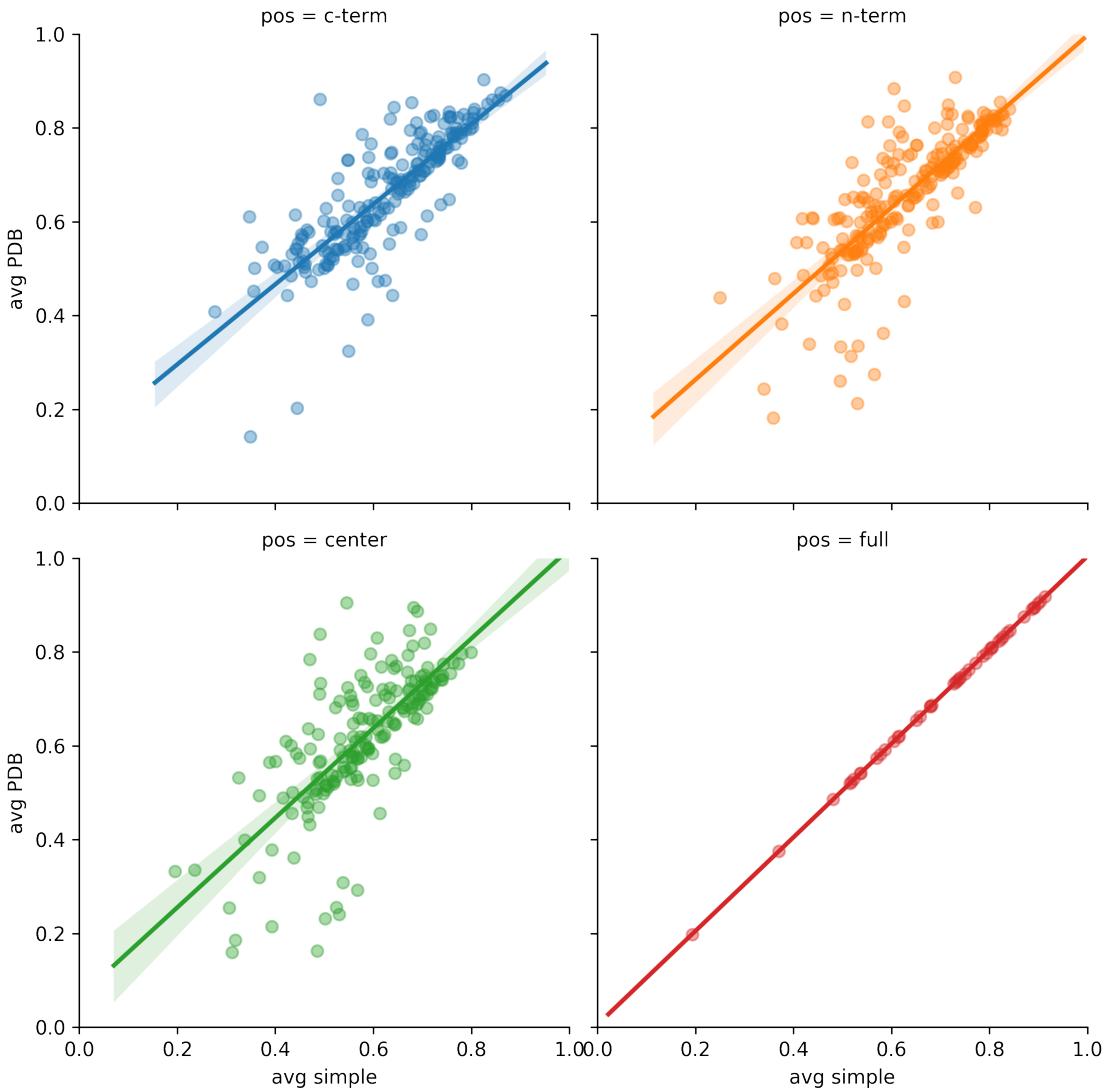
Predictor ranking and ranking statistical significance. Predictors are ranked on average rank from metrics scores: Balanced Accuracy, MCC, Precision, Recall, F1-score, F1-scores on negatives, Precision on negatives, Specificity, ROC AUC, PR AUC.



Heatmap of the p-value associated to the statistical significance of the difference between ranking distributions. Colorormap is centered on 0.05 so that any pvalue above 0.05 is red-ish. Red color indicates that the ranking difference between two predictors is not statistically significant. Top tick labels of x axis display prediction coverage for each predictor.

1.2.10 Accuracy correlation between datasets

Per target average balanced accuracy correlation between *simple* and *pdb* negative definition. Datasets is divided by average disorder position in targets.



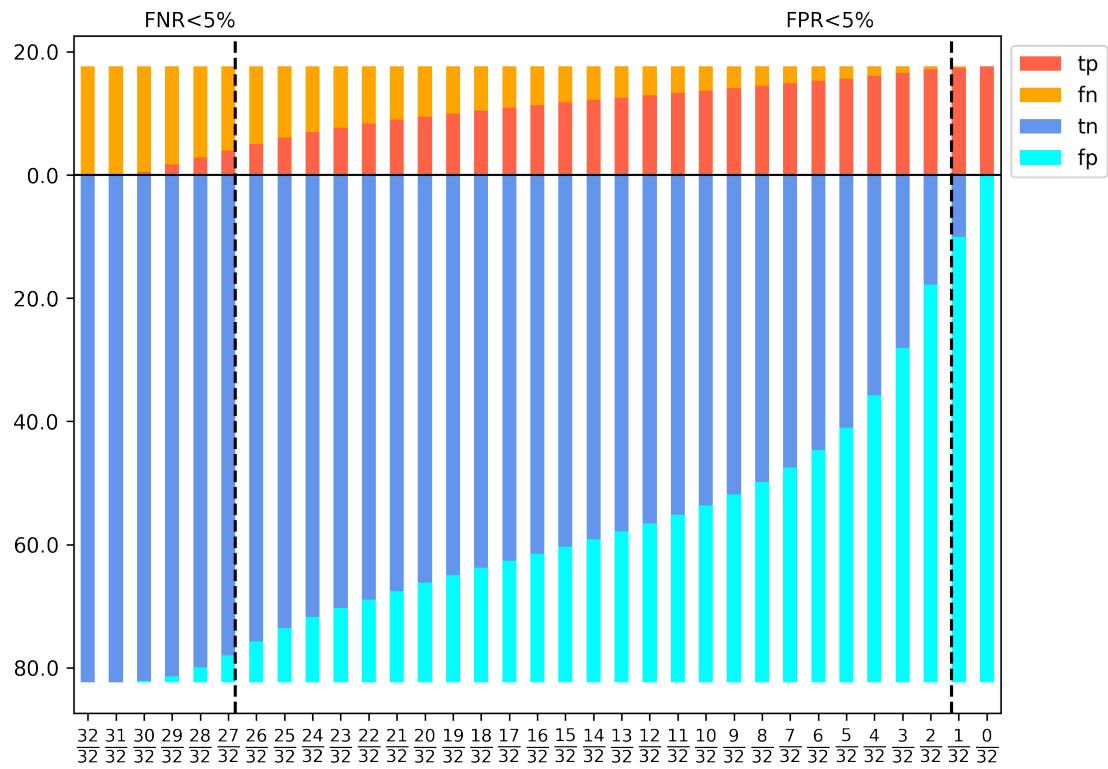
Average balanced accuracy for targets with reference negative defined by the *simple* rule on x axis. Average balanced accuracy for targets with reference negative defined by the *pdb* rule on y axis. Each panel includes only targets with a specific average disorder position (C-terminal, N-Terminal, central, full-disorder)

1.3 Consensus

Consensus among all prediction methods was calculated as the fraction of positive predictions per residue.

1.3.1 Confusion matrix per threshold

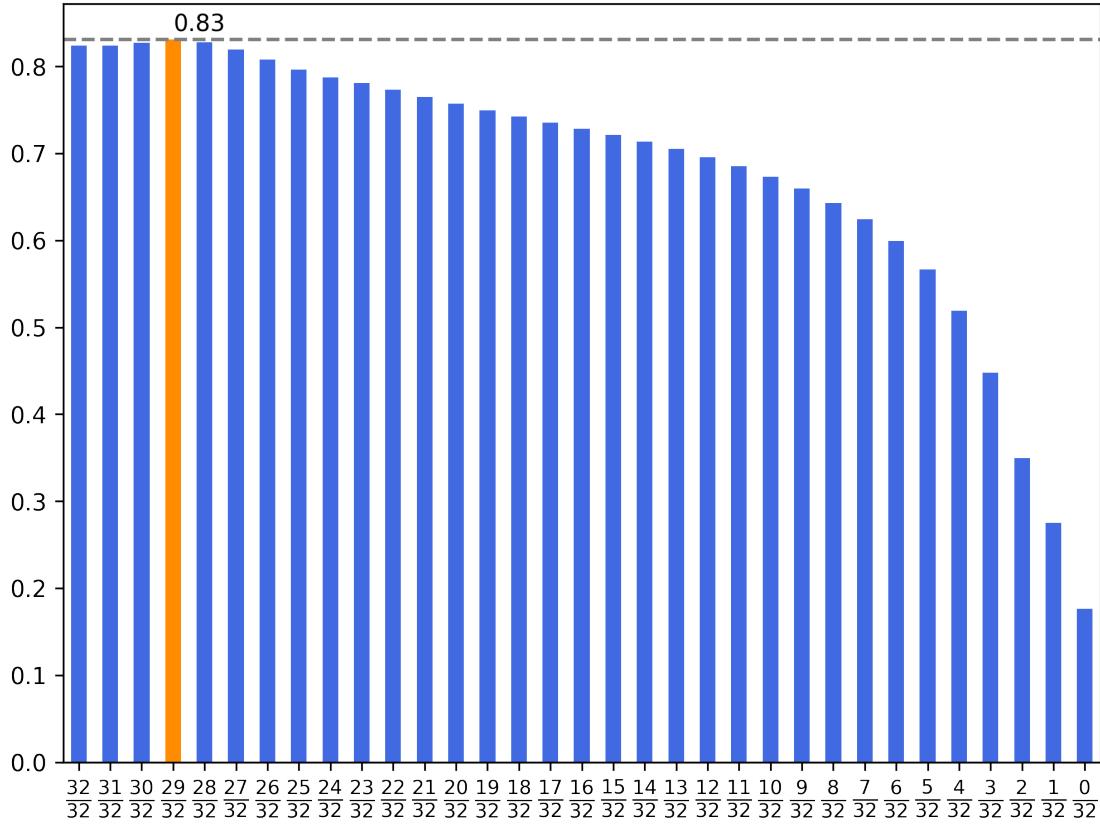
Predicted and actual positive and negatives for each threshold on the consensus score.



Percentage of correct and wrong assignment of positives (above 0) and negatives (below 0) for each threshold of the consensus.

1.3.2 Accuracy per threshold

Balanced accuracy score for each threshold of the consensus.



Accuracy distribution for each consensus threshold. Bar of max threshold is highlighted in orange.

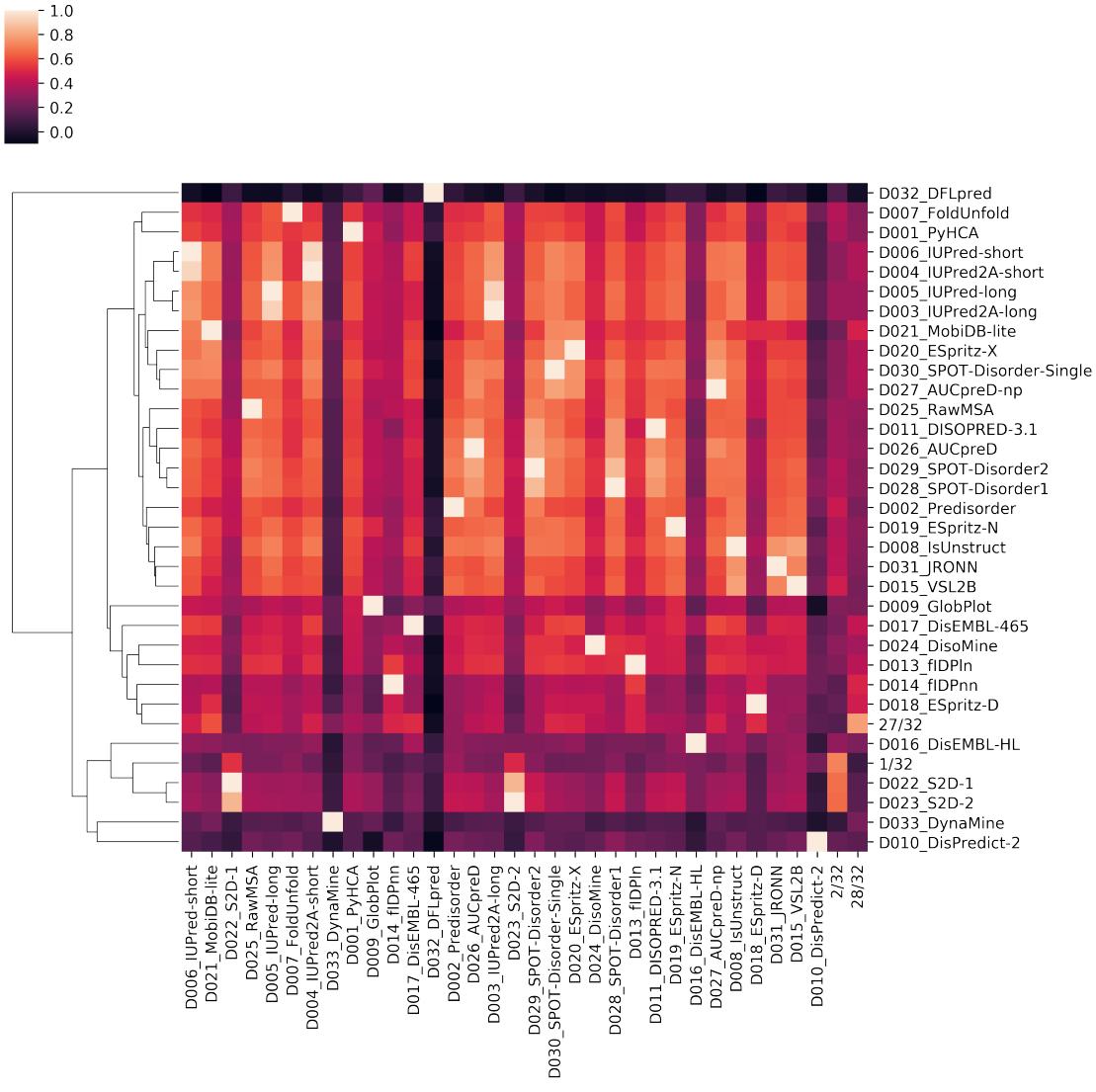
1.3.3 Percentage of correct/incorrect classifications

Percentage of correct and incorrect classifications for positives (defined by DisProt), negatives (defined by PDB) and undefined residues for each predictor.

	DisProt		PDB		Undefined		
	TP	FN	TN	FP	TN	FP	
D006_IUPred-short	56.2	43.8	94.7	5.3	66.2	33.8	
D021_MobiDB-lite	41.1	58.9	98.6	1.4	77.2	22.8	
D022_S2D-1	86.7	13.3	47.3	52.7	22.3	77.7	
D025_RawMSA	68.2	31.8	93.1	6.9	60.6	39.4	
D005_IUPred-long	64.5	35.5	92.5	7.5	58.9	41.1	
D007_FoldUnfold	66.6	33.4	82.5	17.5	48.8	51.2	
D004_IUPred2A-short	56.3	43.7	94.9	5.1	66.3	33.7	
D033_DynaMine	1.7	98.3	100.0	0.0	97.9	2.1	
D001_PyHCA	65.8	34.2	84.8	15.2	53.7	46.3	
D009_GlobPlot	38.3	61.7	90.0	10.0	70.0	30.0	
D014_fIDPnn	30.0	70.0	98.7	1.3	93.0	7.0	
D017_DisEMBL-465	38.7	61.3	95.2	4.8	76.1	23.9	
D032_DFLpred	9.4	90.6	89.0	11.0	89.4	10.6	
D002_Predisorder	80.7	19.3	82.4	17.6	41.8	58.2	
D026_AUCpreD	68.7	31.3	95.5	4.5	54.0	46.0	
D003_IUPred2A-long	63.4	36.6	92.8	7.2	59.6	40.4	
D023_S2D-2	85.8	14.2	50.4	49.6	24.7	75.3	
D029_SPOT-Disorder2	75.9	24.1	95.1	4.9	45.8	54.2	
D030_SPOT-Disorder-Single	55.6	44.4	97.7	2.3	65.3	34.7	
D020_ESpritz-X	53.2	46.8	95.6	4.4	67.5	32.5	
D024_DisoMine	57.4	42.6	91.0	9.0	67.3	32.7	
D028_SPOT-Disorder1	74.8	25.2	94.2	5.8	48.8	51.2	
D013_fIDPln	50.5	49.5	94.6	5.4	79.3	20.7	
D011_DISOPRED-3.1	64.5	35.5	93.9	6.1	49.9	50.1	
D019_ESpritz-N	68.7	31.3	86.6	13.4	51.6	48.4	
D016_DisEMBL-HL	53.0	47.0	74.4	25.6	63.8	36.2	
D027_AUCpreD-np	57.3	42.7	96.5	3.5	65.1	34.9	
D008_IsUnstruct	74.8	25.2	86.0	14.0	49.3	50.7	
D018_ESpritz-D	35.2	64.8	95.6	4.4	88.4	11.6	
D031_JRONN	74.1	25.9	81.7	18.3	47.3	52.7	
D015_VSL2B	81.5	18.5	77.2	22.8	40.0	60.0	
D010_DisPredict-2	41.6	58.4	81.6	18.4	72.5	27.5	

1.3.4 clustermap of binary predictions correlation

Correlation of binary states between predictors.



Heatmap of the correlation of binary prediction states for each couple of predictors. Pearson R is calculated between all predictions. Clustering is based on Euclidean distance calculated over an array (column) of R correlation coefficients.

1.4 Fully disordered targets

Statistics calculated for the subset of targets that are reported as completely disordered in DisProt.

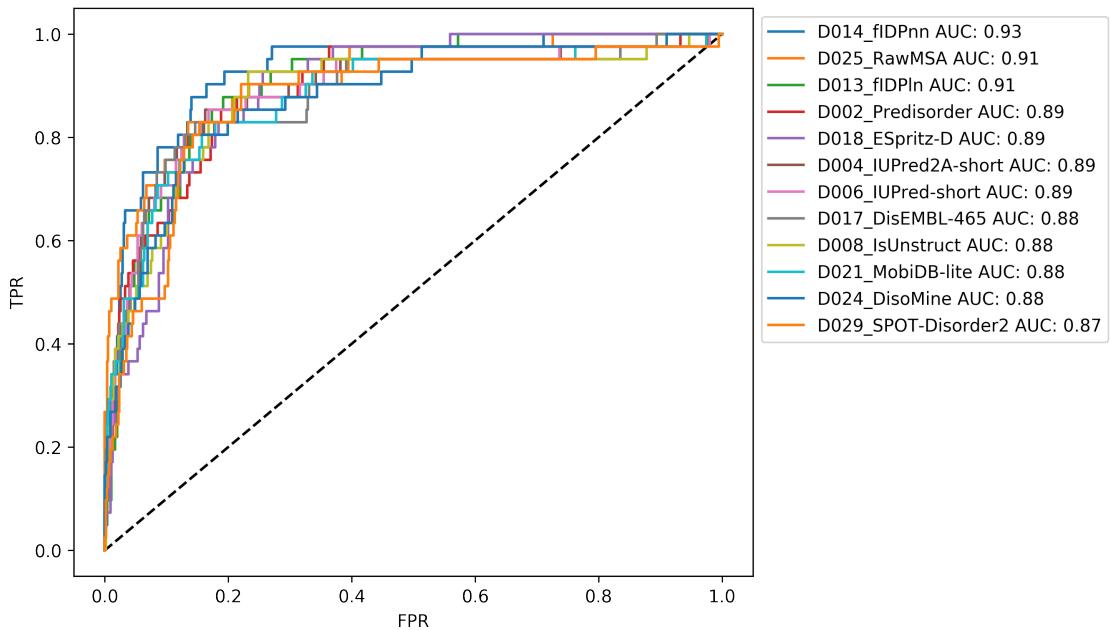
1.4.1 Correctly and incorrectly classified full IDPs

Number of correctly and incorrectly classified full IDPs with a prediction tolerance of 5%.

Actual Predicted	Positives		Negatives	
	TP	FN	FP	TN
D009_GlobPlot	44	0	0	602
D016_DisEMBL-HL	44	0	0	602
D017_DisEMBL-465	44	0	0	602
random_chain	44	0	0	602
D006_IUPred-short	44	0	1	601
random_chunk	44	0	1	601
D004_IUPred2A-short	44	0	2	600
D019_ESpritz-N	44	0	4	598
D001_PyHCA	44	0	5	597
D011_DISOPRED-3.1	44	0	6	596
D020_ESpritz-X	44	0	6	596
D030_SPOT-Disorder-Single	44	0	7	595
D027_AUCpreD-np	44	0	11	591
D002_Predisorder	44	0	13	589
D008_IsUnstruct	44	0	14	588
D026_AUCpreD	44	0	15	587
D015_VSL2B	44	0	24	578
D029_SPOT-Disorder2	44	0	28	574
D028_SPOT-Disorder1	44	0	31	571
D023_S2D-2	44	0	33	569
D024_DisoMine	44	0	55	547
D022_S2D-1	44	0	57	545
cons	44	0	160	442
D010_DisPredict-2	43	1	18	584
D025_RawMSA	43	1	20	582
D013_fIDPIn	43	1	41	561
naive-pdb	43	1	138	464
D003_IUPred2A-long	42	2	6	596
D005_IUPred-long	42	2	6	596
D031_IRONN	42	2	6	596
D014_fIDPnn	42	2	16	586
D018_ESpritz-D	42	2	52	550
naive-gene3d	42	2	159	443
D007_FoldUnfold	41	3	156	446
D021_MobiDB-lite	37	7	2	600
D032_DFLpred	13	31	0	602
D033_DynaMine	13	31	0	602

1.4.2 Full IDPs ROC

ROC for the classification power of Full IDPs. Average disorder scores for each target is compared to full IDPs (positives) and partial IDPs (negatives). 5% prediction tolerance is applied.



FPR on the x axis, TPR on the y axis. Methods are sorted by their AUC. Only first 12 methods are shown.