

Supplementary Information:
Deep neural network for interpreting RNA binding protein
target preferences

Mahsa Ghanbari¹ and Uwe Ohler^{1,2,3}

¹The Berlin Institute for Medical Systems Biology, Max Delbrück Center for
Molecular Medicine, Hannoversche Str. 28, Berlin 10115, Germany

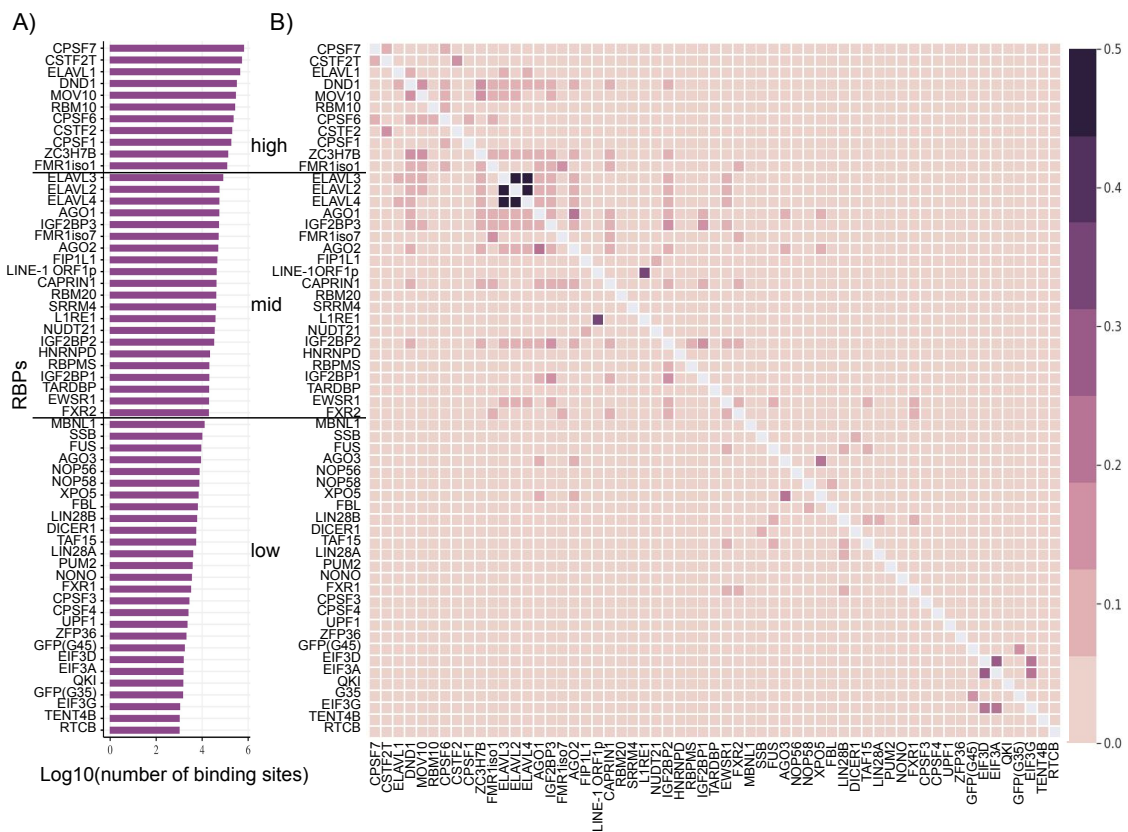
²Department of Biology, Humboldt Universität zu Berlin, Unter den Linden 6,
Berlin 10117, Germany

³Department of Computer Science, Humboldt Universität zu Berlin, Unter den
Linden 6, Berlin 10117, Germany

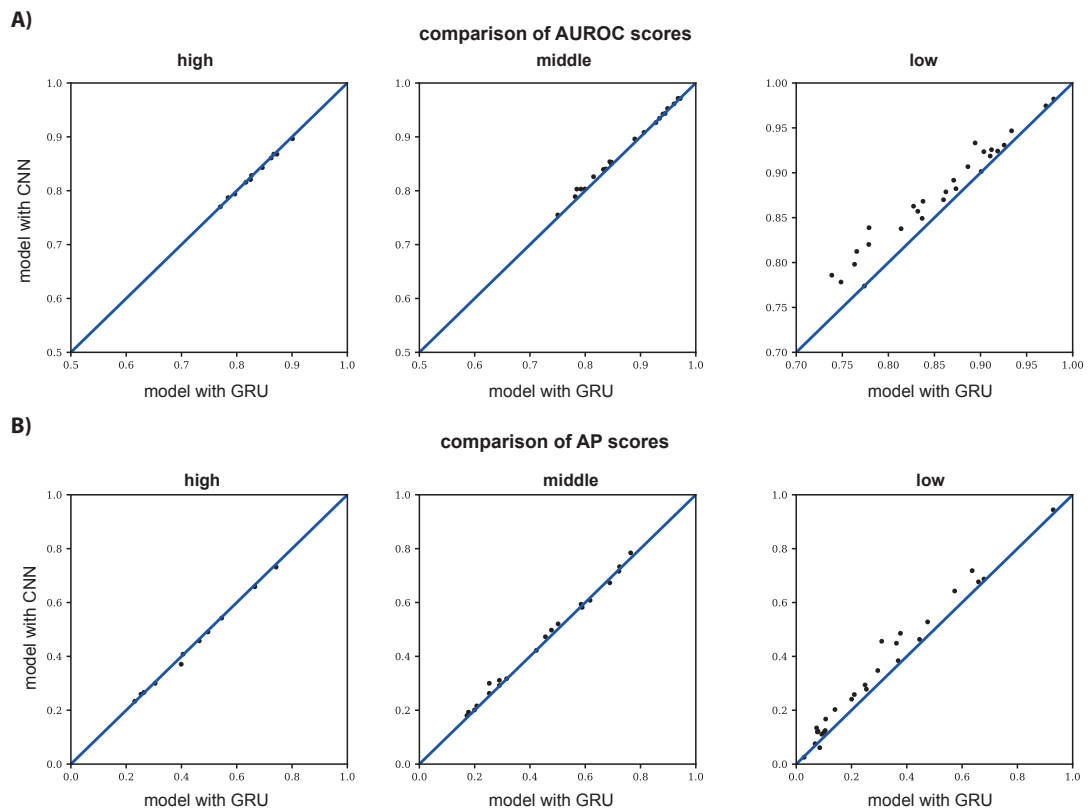
Supplemental information includes Supplemental Table S1 and Supplemental Figures S1-13.

RBP	AUROC	AP	RBP	AUROC	AP
AGO1	0.789076	0.317035	HNRNPD	0.942418	0.47266
AGO2	0.853832	0.49748	IGF2BP1	0.826114	0.192926
AGO3	0.868226	0.485672	IGF2BP2	0.839561	0.291862
CAPRIN1	0.755036	0.216009	IGF2BP3	0.840454	0.422296
CPSF1	0.770088	0.233365	L1RE1	0.961325	0.589827
CPSF3	0.798064	0.118253	LIN28A	0.785889	0.167328
CPSF4	0.778281	0.0757451	LIN28B	0.923507	0.448803
CPSF6	0.787158	0.259414	MBNL1	0.982158	0.944225
CPSF7	0.793916	0.542165	MOV10	0.828301	0.408187
CSTF2	0.815647	0.3	NOP56	0.924164	0.687188
CSTF2T	0.842871	0.658515	NOP58	0.930788	0.676819
DICER1	0.857085	0.241041	NUDT21	0.850143	0.26264
DND1	0.820734	0.457522	LINE-1 ORF1p	0.971041	0.673126
EIF3A	0.882287	0.202734	NONO	0.925687	0.383958
EIF3D	0.869932	0.124661	TENT4B(PAPD5)	0.8492	0.121876
EIF3G	0.891675	0.134418	PUM2	0.946767	0.718361
ELAVL1	0.896556	0.731773	QKI	0.97455	0.642795
ELAVL2	0.926606	0.60828	RBM10	0.860757	0.490855
ELAVL3	0.943415	0.716039	RBM20	0.908388	0.5935
ELAVL4	0.934444	0.581832	RBPMS	0.971549	0.784266
EWSR1	0.852801	0.201107	RTCB	0.773793	0.0252931
FBL	0.906787	0.347475	SRRM4	0.803274	0.311076
FIP1L1	0.803026	0.300094	SSB	0.918654	0.52801
FMR1iso1	0.867917	0.26645	TAF15	0.878692	0.278177
FMR1iso7	0.896127	0.520597	TARDBP	0.952737	0.733116
FUS	0.901412	0.463117	UPF1	0.812371	0.119511
FXR1	0.862783	0.2582	XPO5	0.837698	0.293879
FXR2	0.803092	0.180022	ZC3H7B	0.867818	0.370814
GFP(G35)	0.820182	0.0609622	ZFP36	0.933268	0.456097
GFP(G45)	0.838807	0.111121			

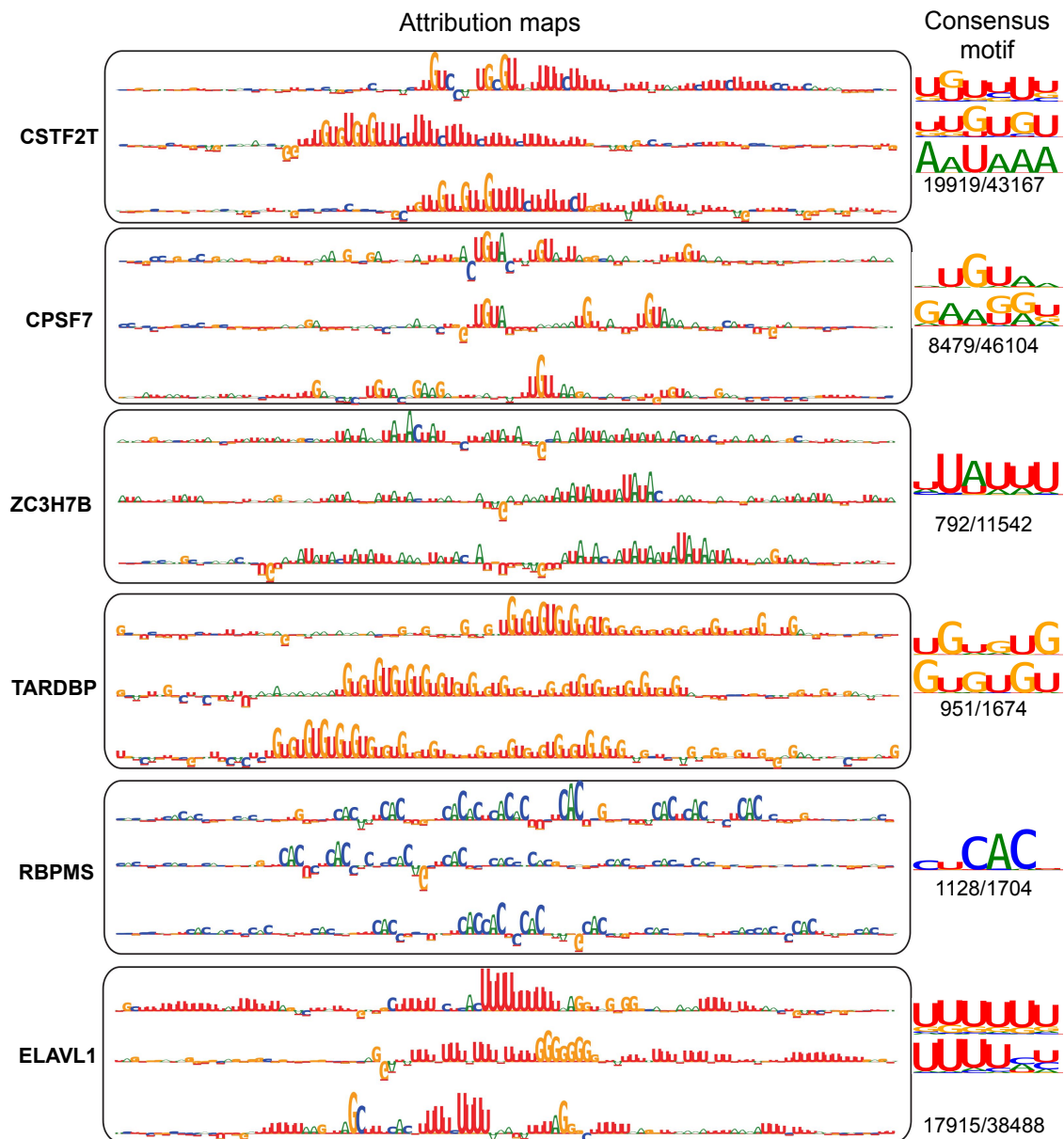
Supplemental Table S1: Classification performance of DeepRiPe: AUROC as well as AP scores for all 59 PAR-CLIP datasets.



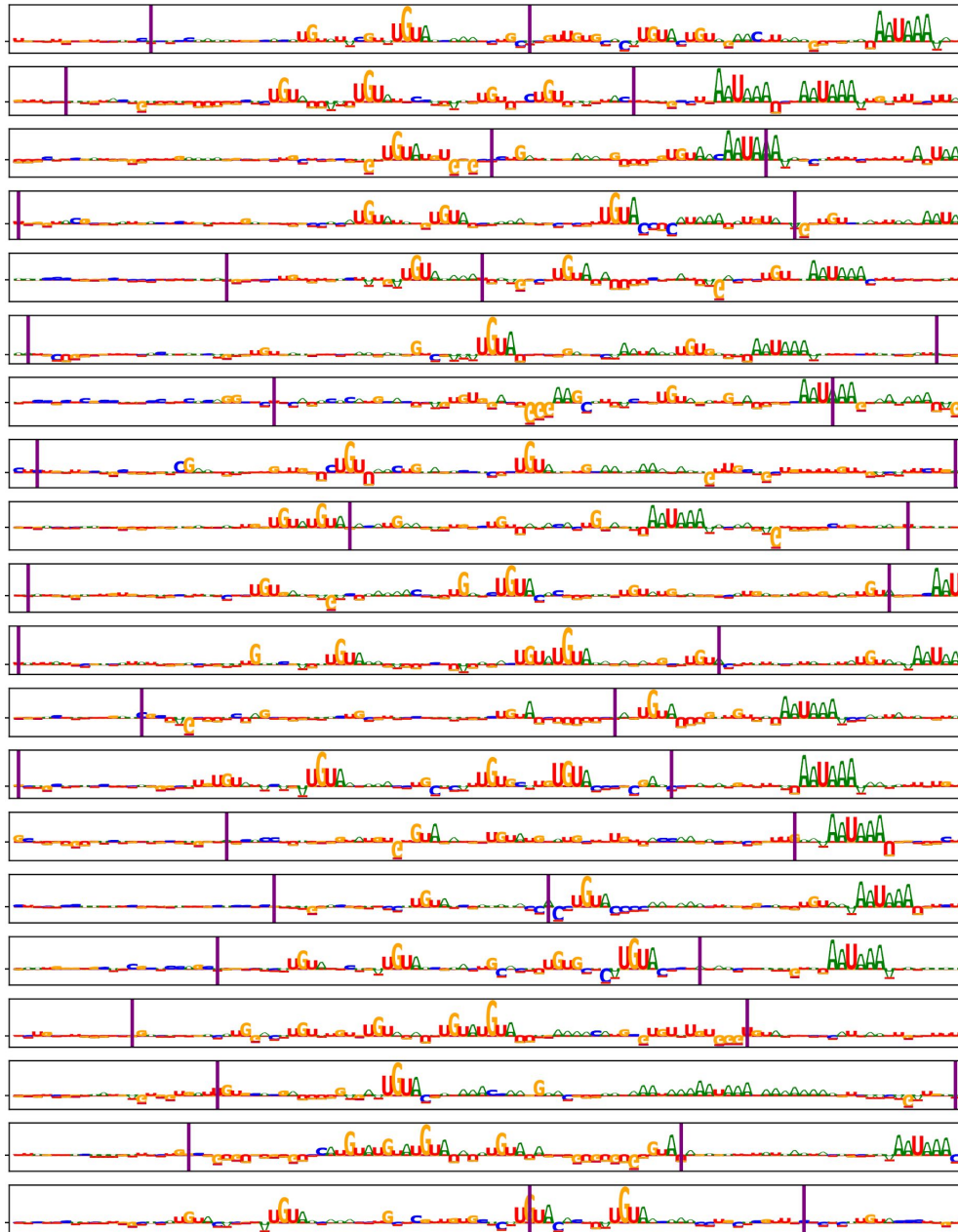
Supplemental Figure S1: Overview of datasets: A) The number of PAR-CLIP peaks for RBPs used in this study. We divided RBPs into 3 categories: RBPs with more than 10^5 peaks (high), RBPs that have between 15000 and 10^5 peaks (mid) and RBPs with less than 15000 peaks (low). B) Overlap between peaks of RBPs in terms of Jaccard index. For each pairs of RBPs, we calculate the Jaccard index = number of genome bins that both RBPs bind / number of genome bins that at least RBP binds.



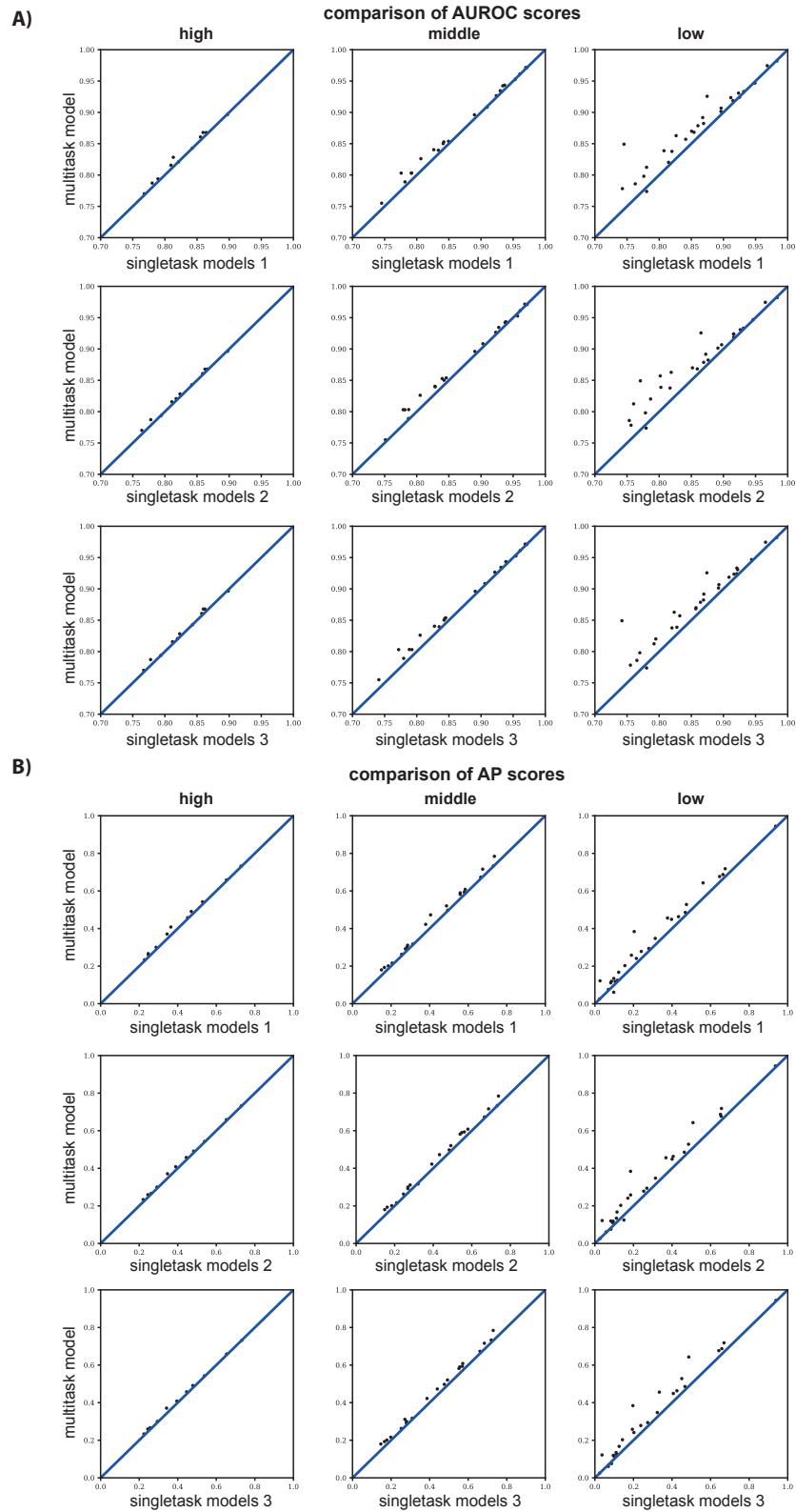
Supplemental Figure S2: Assessing the performance of the DeepRiPe when using GRU instead of CNN in the multitask module. Scatter plots comparing the AUROC (A) and AP scores (B) of DeepRiPe with CNN vs DeepRiPe with GRU model. Each data point represents an RBP and it falls above the diagonal when model with CNN outperforms the one with GRU. The results show that GRU does not help the model specially for low-model, most likely due to the lack of data for training GRU with more parameters compare to CNN.



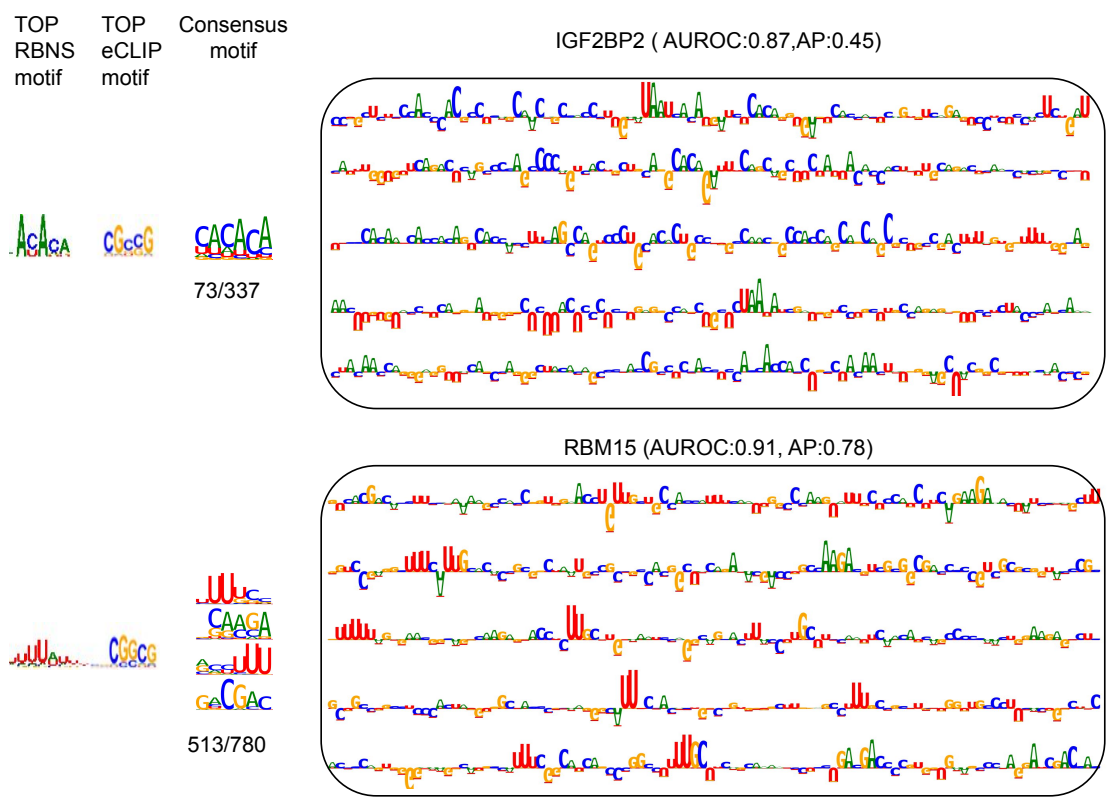
Supplemental Figure S3: Attribution maps of several RBPs. For each RBP, the sequence logos corresponding to attribution maps of three true binding sites with the highest DeepRiPe prediction scores are shown. Consensus motifs, obtained from attribution maps of all true positive binding sites of the RBP in the test set with prediction scores larger than 0.5, are shown next to attribution maps. The ratio of the number of binding sites larger than 0.5 to the total number of CLIP binding sites in the test set is listed below the consensus motif



Supplemental Figure S4: Attribution maps of CPSF6. The sequence logos corresponding to attribution maps for 20 true binding sites of CPSF6 with the highest DeepRiPe prediction scores. The lines indicate the position of actual peaks along input sequences. UGUA motif is always located inside the peak, while this is not the case for AAUAAA motif.

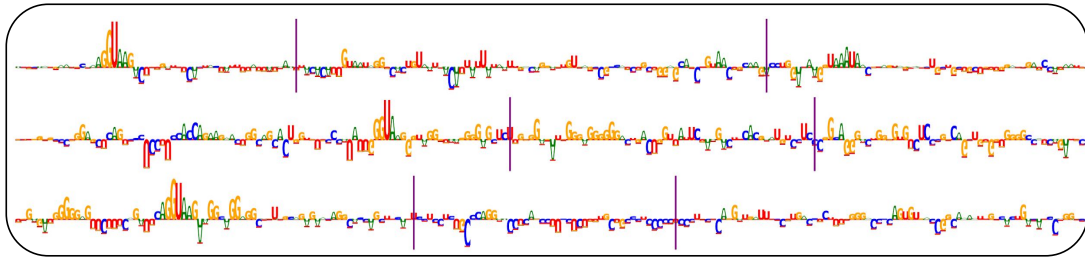


Supplemental Figure S5: Assessing the performance of multitask model vs singletask models. We subsample from negative samples of the training and validation datasets to ensure an equal number of negative samples as positive samples in these datasets (single models 3). Using all negative samples for training singletask models that have less positives samples leads to a bad performance due to imbalanced data. , A) Scatter plots comparing AUROC scores of DeepRiPe and singletask models. , B) Scatter plots comparing AP scores of DeepRiPe and singletask models.

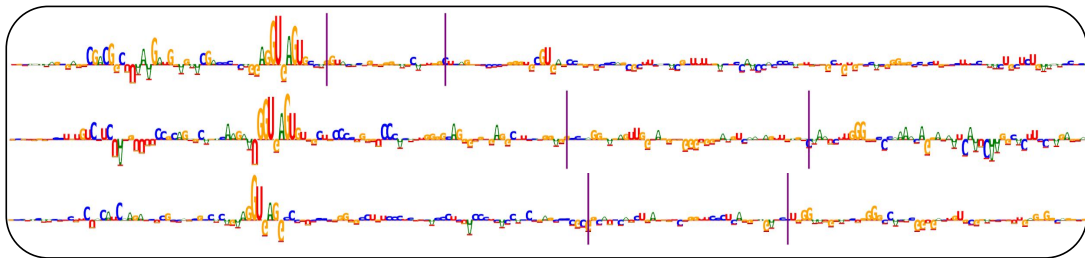


Supplemental Figure S6: Comparison of motifs obtained from in vitro (RBNS) and in vivo (eCLIP) experiments with patterns observed in attribution maps. For each RBP, the motifs obtained from RBNS, eCLIP and attribution maps along with attribution maps for top five inputs with highest prediction scores are shown. The consensus motifs obtained from attribution maps correspond to all true binding sites with prediction scores larger than 0.5. The ratio of the number of binding sites used to obtain consensus motif to the number of all true binding sites is mentioned along with corresponding consensus motif.

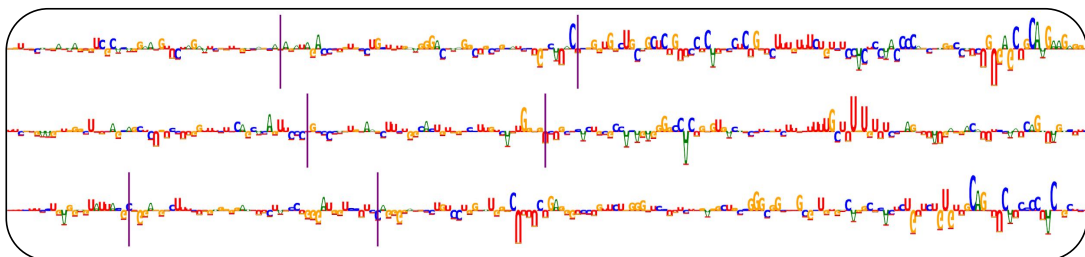
EFTUD2



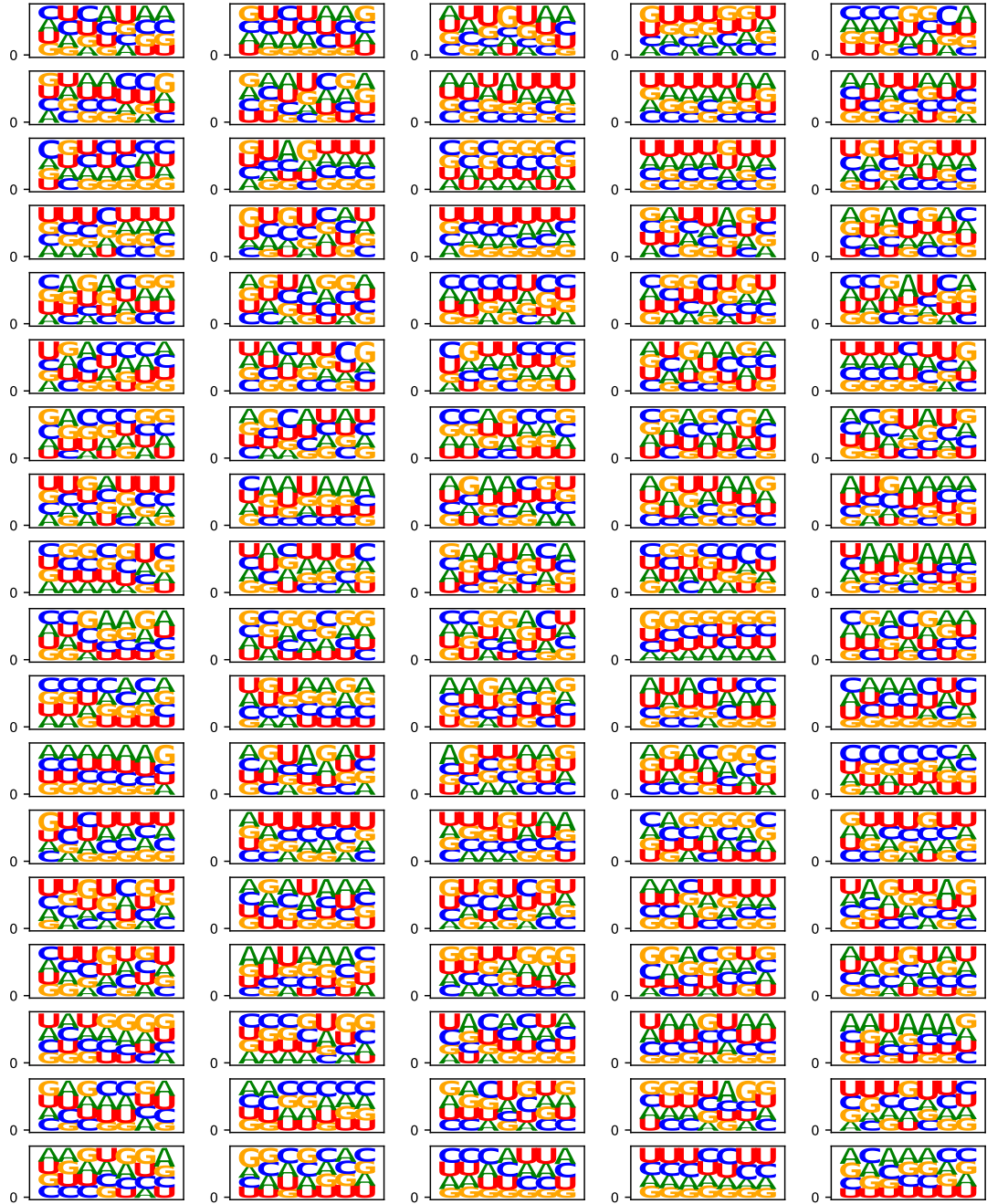
AQR



SF3B4



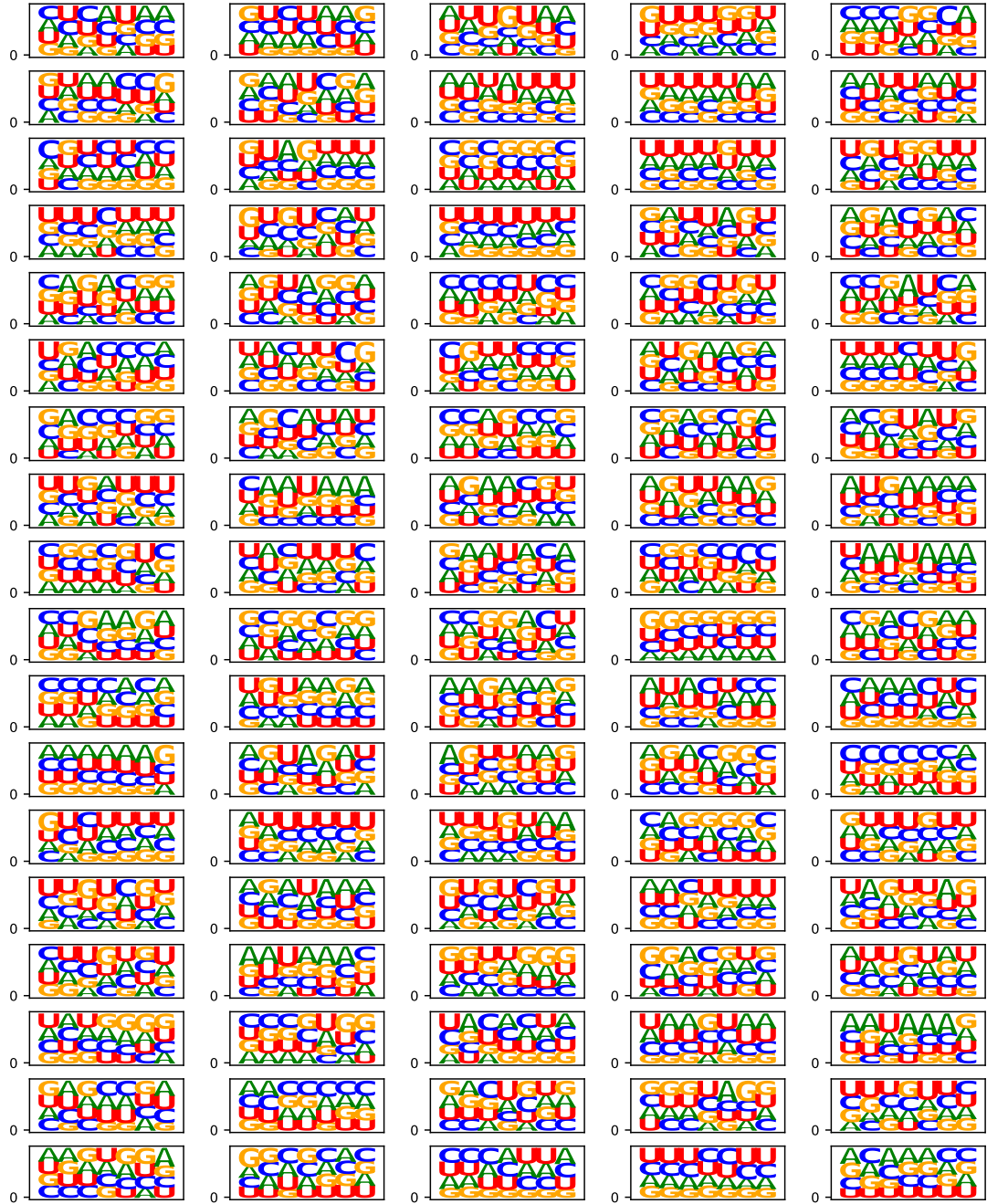
Supplemental Figure S7: Attribution maps of some splicing factors. 3' and 5' splice site motifs (CAG, GGUAAG) are observed in the attribution maps of EFTUD2, AQR and SF3B4. The lines indicate the position of actual peaks along input sequences. The observed motifs are not always located inside the peaks and they are not involved in direct interactions.



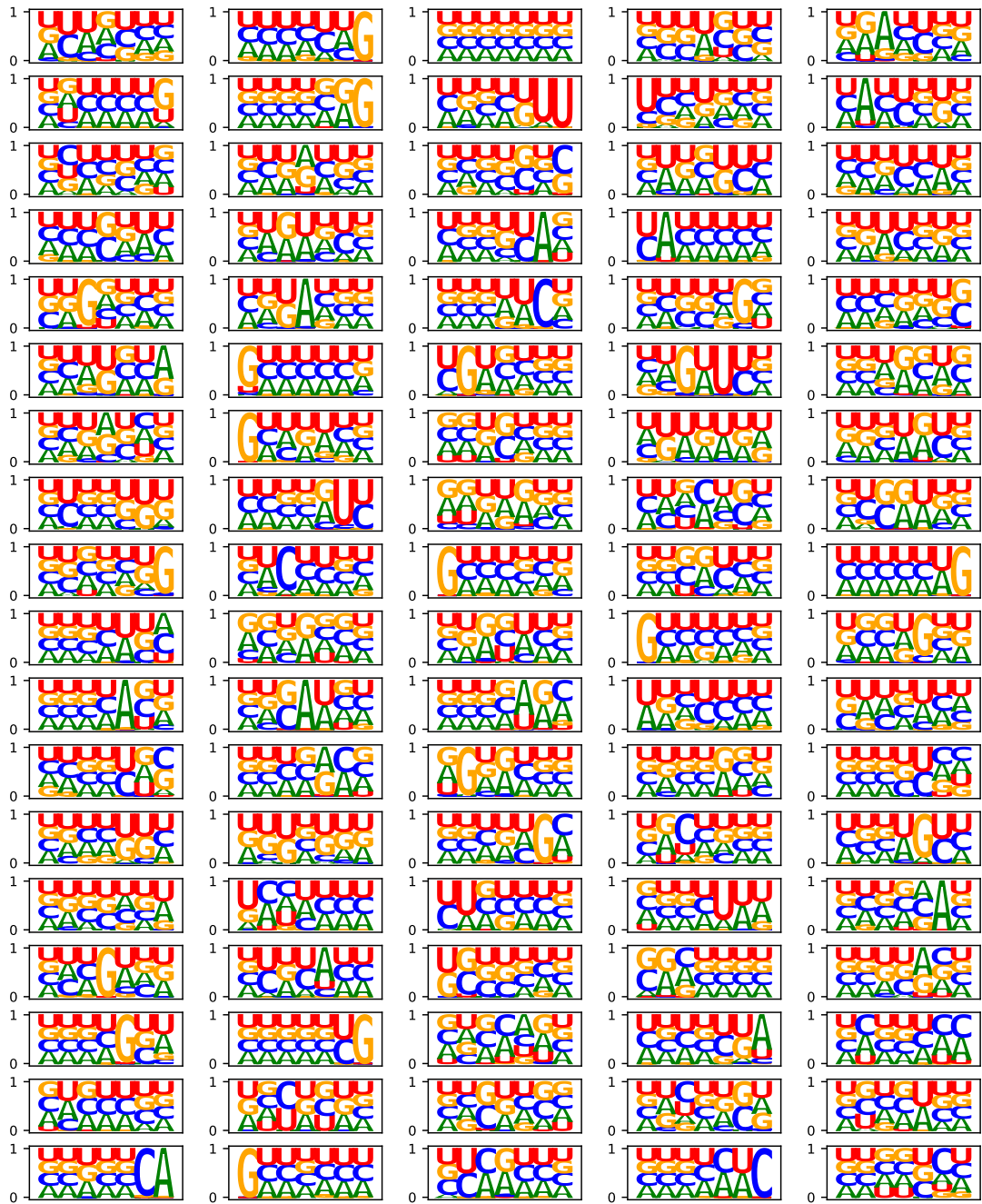
Supplemental Figure S8: Visualization of the filters' weights in the first convolutional layer of low-model in the form of PWM.



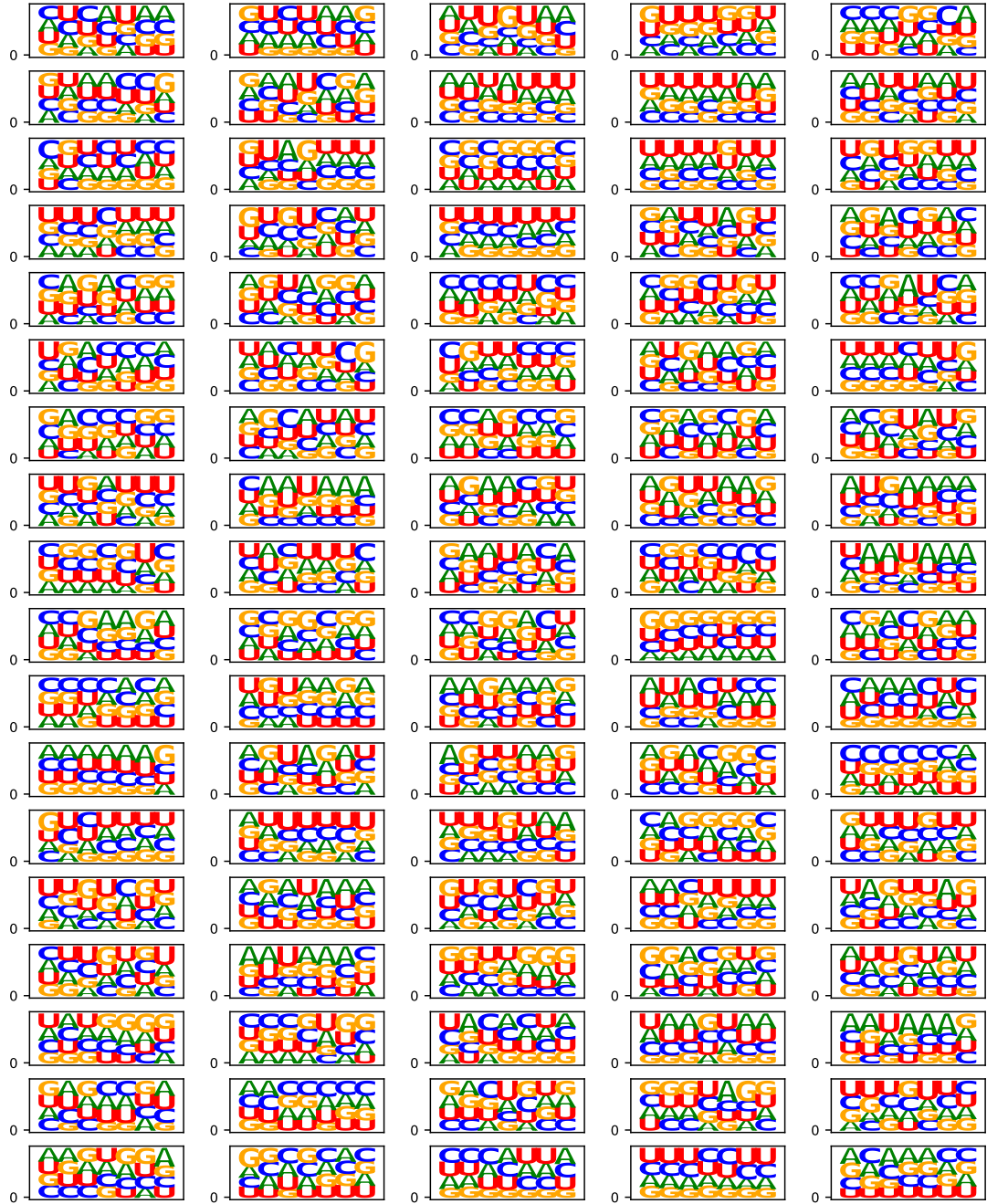
Supplemental Figure S9: Visualization of the filters in the first convolutional layer of low-model by averaging over inputs that activates the filter. For each filter, we averaged over inputs subsequences that activate the neuron corresponding to the filter.



Supplemental Figure S10: Visualization of the filters' weights in the first convolutional layer of mid-model in the form of PWM.



Supplemental Figure S11: Visualization of the filters in the first convolutional layer of mid-model by averaging over inputs that activates the filter. For each filter, we averaged over inputs subsequences that activate the neuron corresponding to the filter.



Supplemental Figure S12: Visualization of the filters' weights in the first convolutional layer of high-model in the form of PWM..



Supplemental Figure S13: Visualization of the filters in the first convolutional layer of high-model by averaging over inputs that activates the filter. For each filter, we averaged over inputs subsequences that activate the neuron corresponding to the filter.