Supplementary tables and figures

**Table S1.** Version and execution details for each tool.

| Methods | Version | Execution |
|---|---|---|
| MIRANDA | MIRANDA v3.3a | MIRANDA mir_file mrna_file |
| INTARNA | INTARNA 2.3.1 using ViennaPackage 2.4.11 and boost 1.68.0 | INTARNA -q mir_file -t utr_file –out STDOUT –outMode C -n nb_predictions |
| PITA | Version 2008 64bit | PITA -utr utr_file -mir mir_file -prefix output |
| MEME | MEME suite 5.4.1 | MEME sequence_file -dna -oc script_path -nostatus -time 14400 -mod oops -nmotifs nb_motifs -minw min_size_motif -maxw max_size_motif -objfun classic -revcomp -markov_order 0 -text |
| Vienna Package | 2.4.15 | |

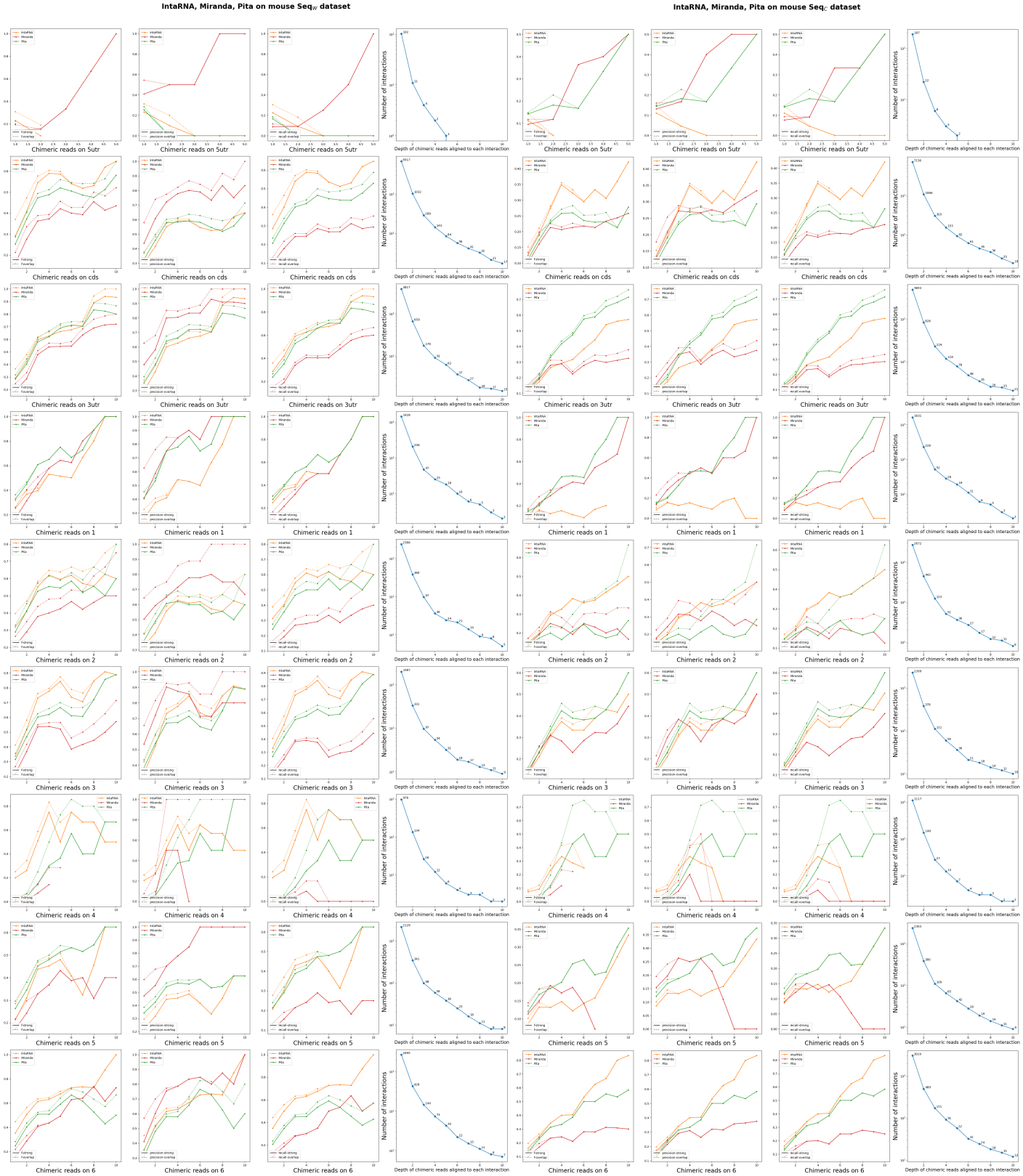



**Figure S1.** Performance of the three methods considering accessibility and seed match on the mouse Seq$_W$ and Seq$_C$ datasets.

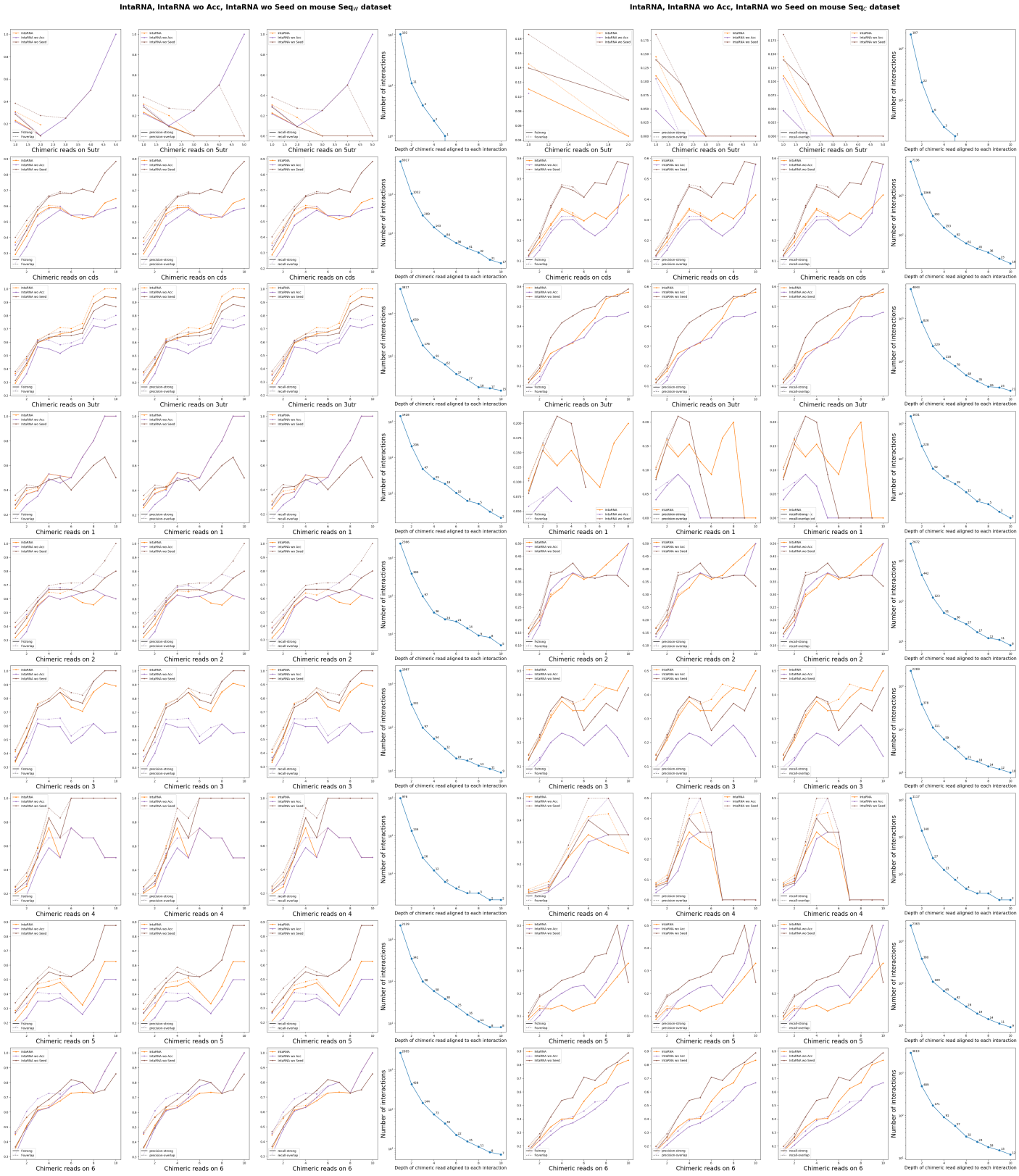



**Figure S2.** Performance of INTARNA considering or not accessibility and seed match on the mouse Seq$_W$ and Seq$_C$ datasets. The term wo in the Figure stands for WithOut.

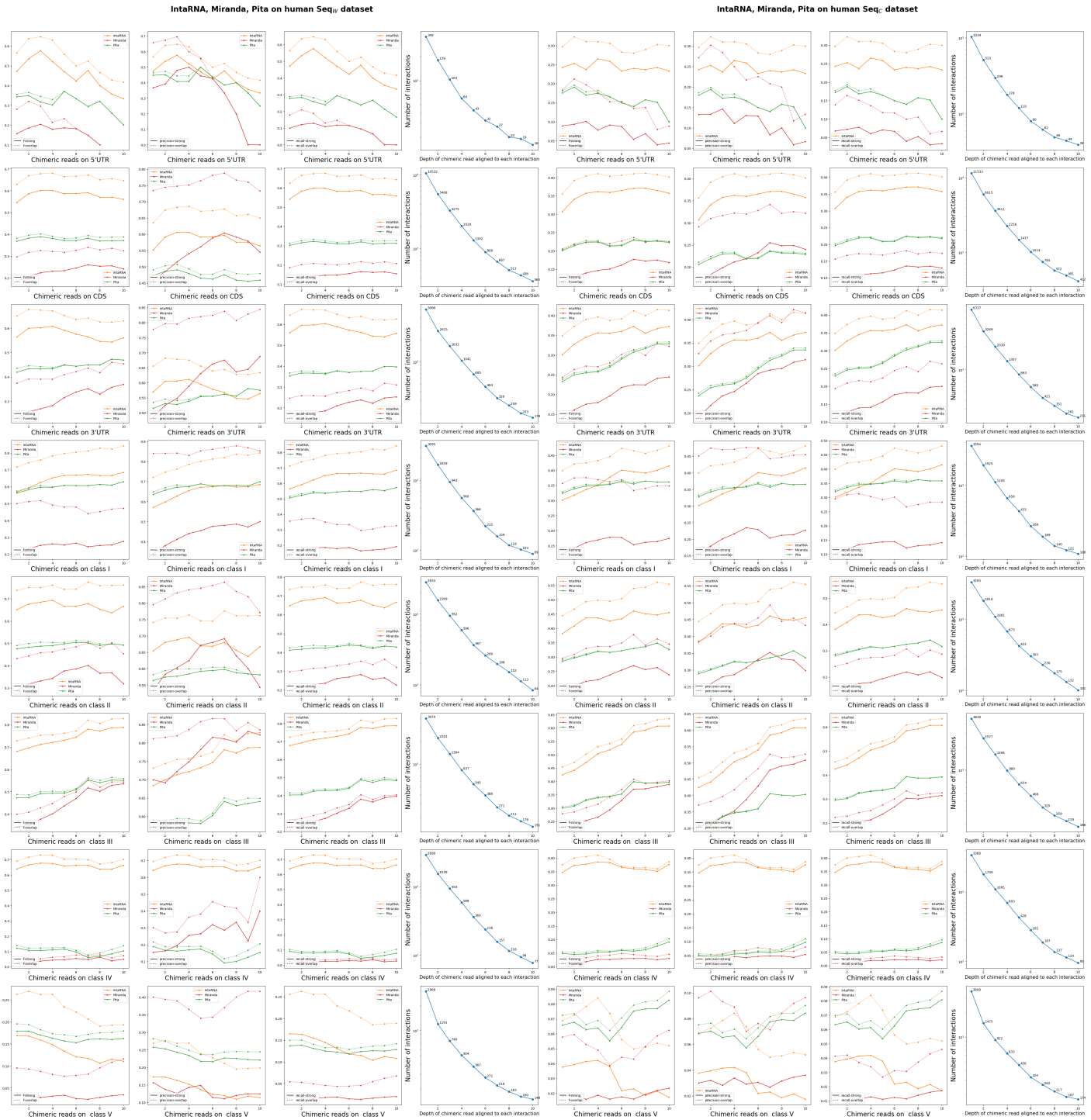



**Figure S3.** Performance of the three methods considering accessibility and seed match on the human Seq$_W$ and Seq$_C$ datasets.

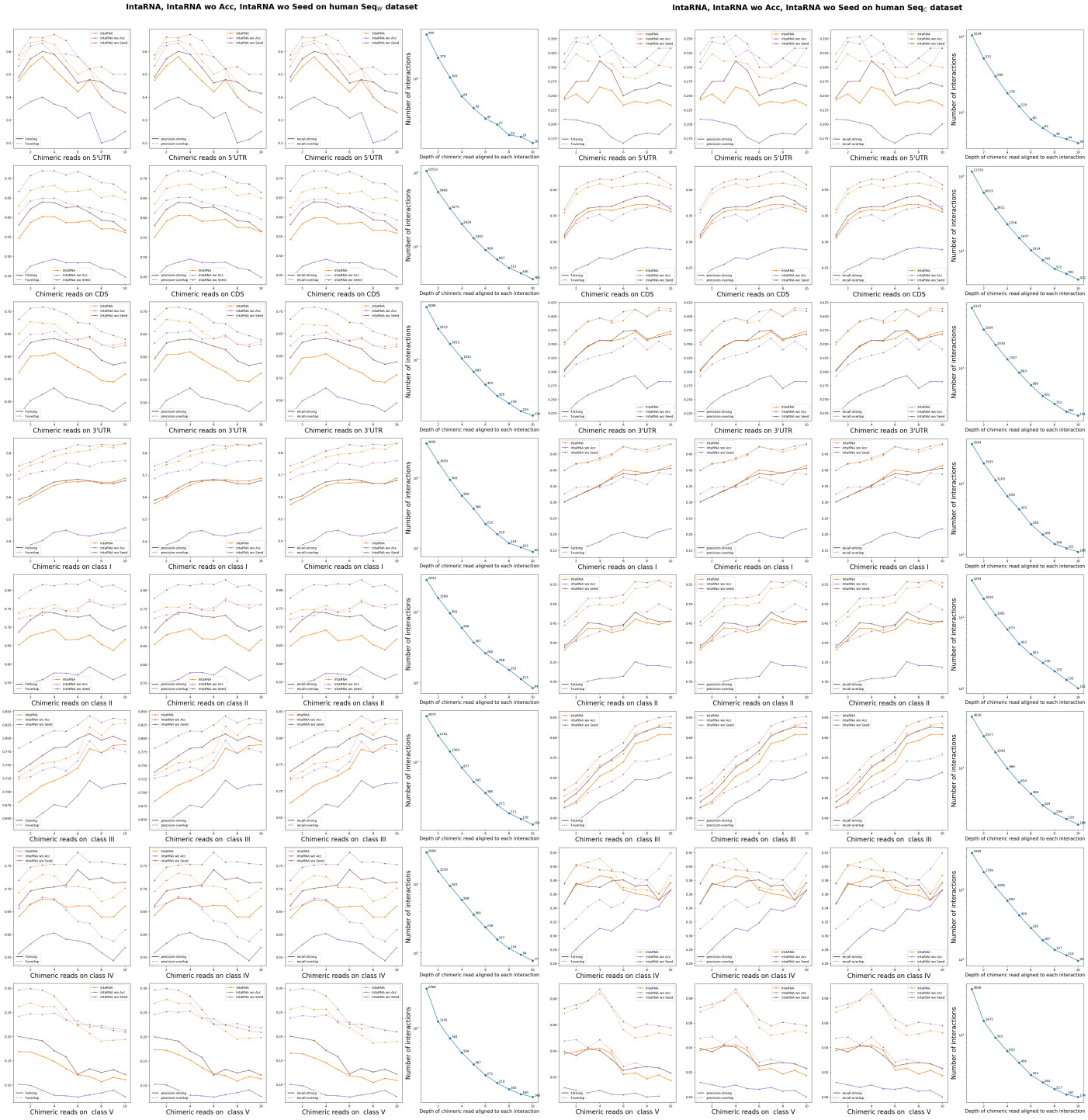



**Figure S4.** Performance of INTARNA considering or not accessibility and seed match on the human Seq$_W$ and Seq$_C$ datasets. The term wo in the Figure stands for WithOut.

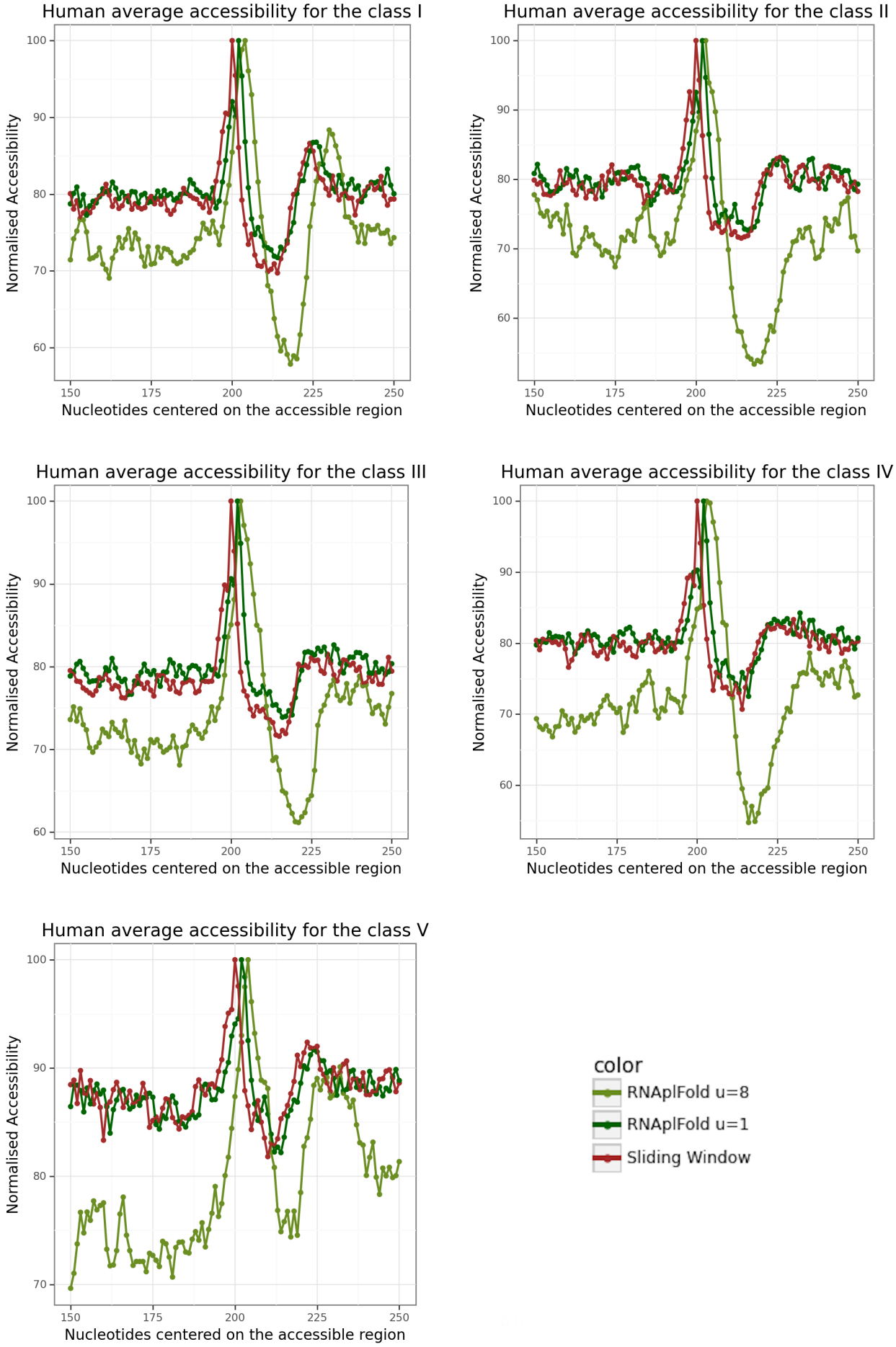



**Figure S5.** Normalised accessibility of all classes on $\text{Seq}_W$ of the human dataset. In red, the normalised accessibility when considering only the optimal structure with a sliding window. In darkgreen and in olivegreen, the normalised accessibility computed with RNAPLFOLD with an accessible window $u$ of 1 and 8.

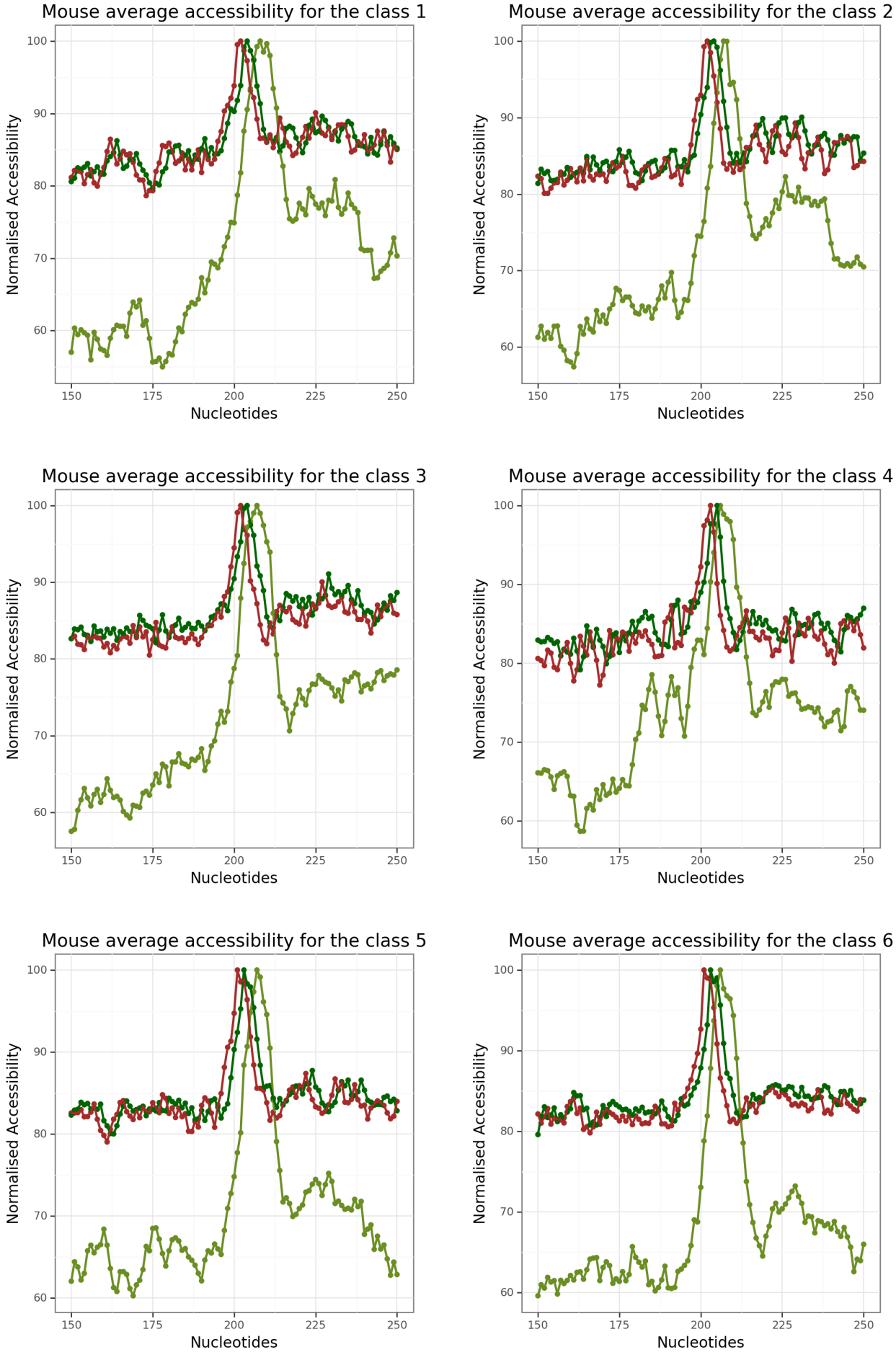



**Figure S6.** Normalised Accessibility of all classes on $\text{Seq}_W$ of the mouse dataset. In red, the normalised accessibility when considering only the optimal structure with a sliding window. In darkgreen and in olivegreen, the normalised accessibility computed with RNAPLFOLD with an accessible window $u$ of 1 and 8.

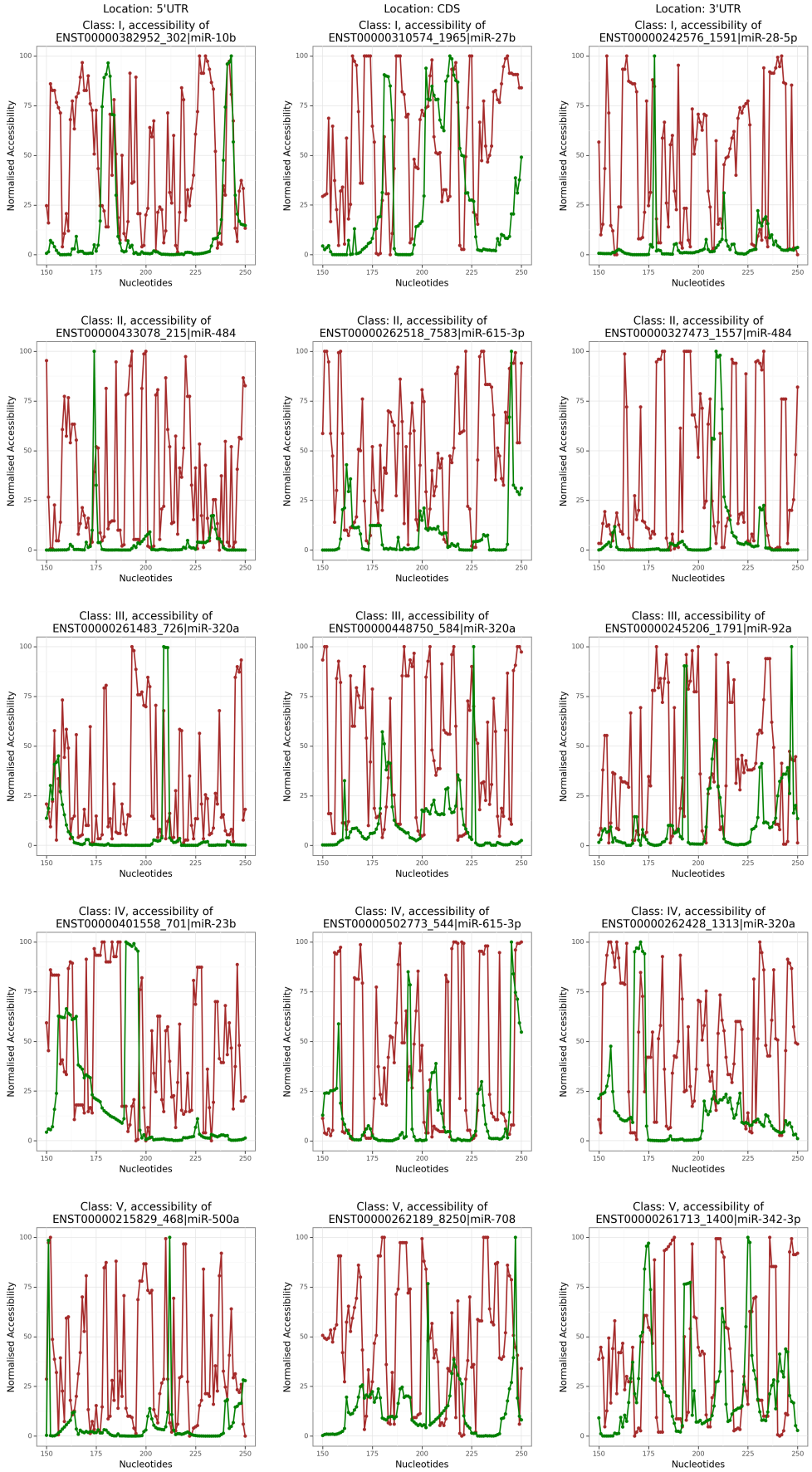



**Figure S7.** One randomly selected interaction for each class on each location on the human dataset. In red, the normalised accessibility when considering only the optimal structure with a sliding window. In green, the accessibility computed with RNAPLFOLD with an accessible window $u$ of 8.

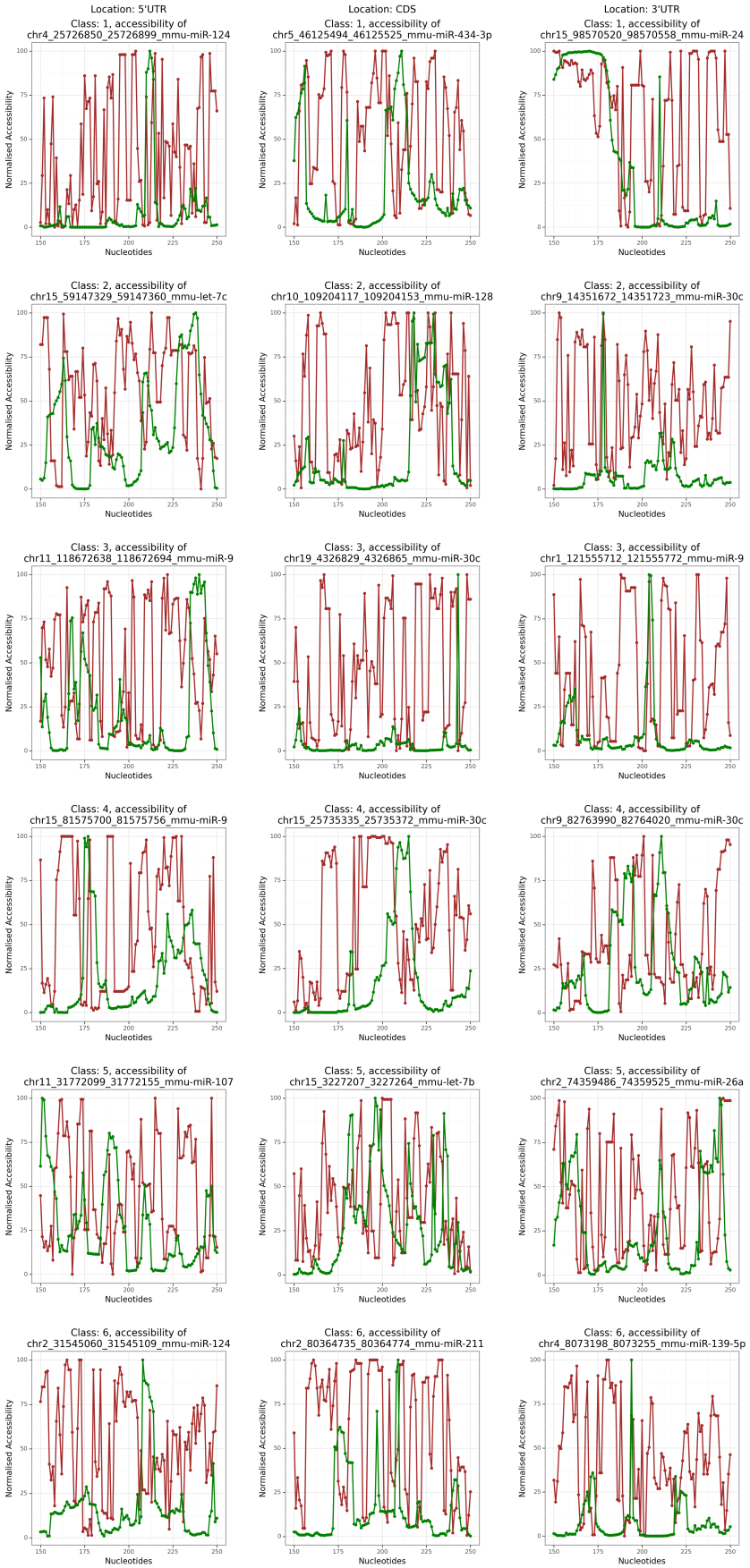
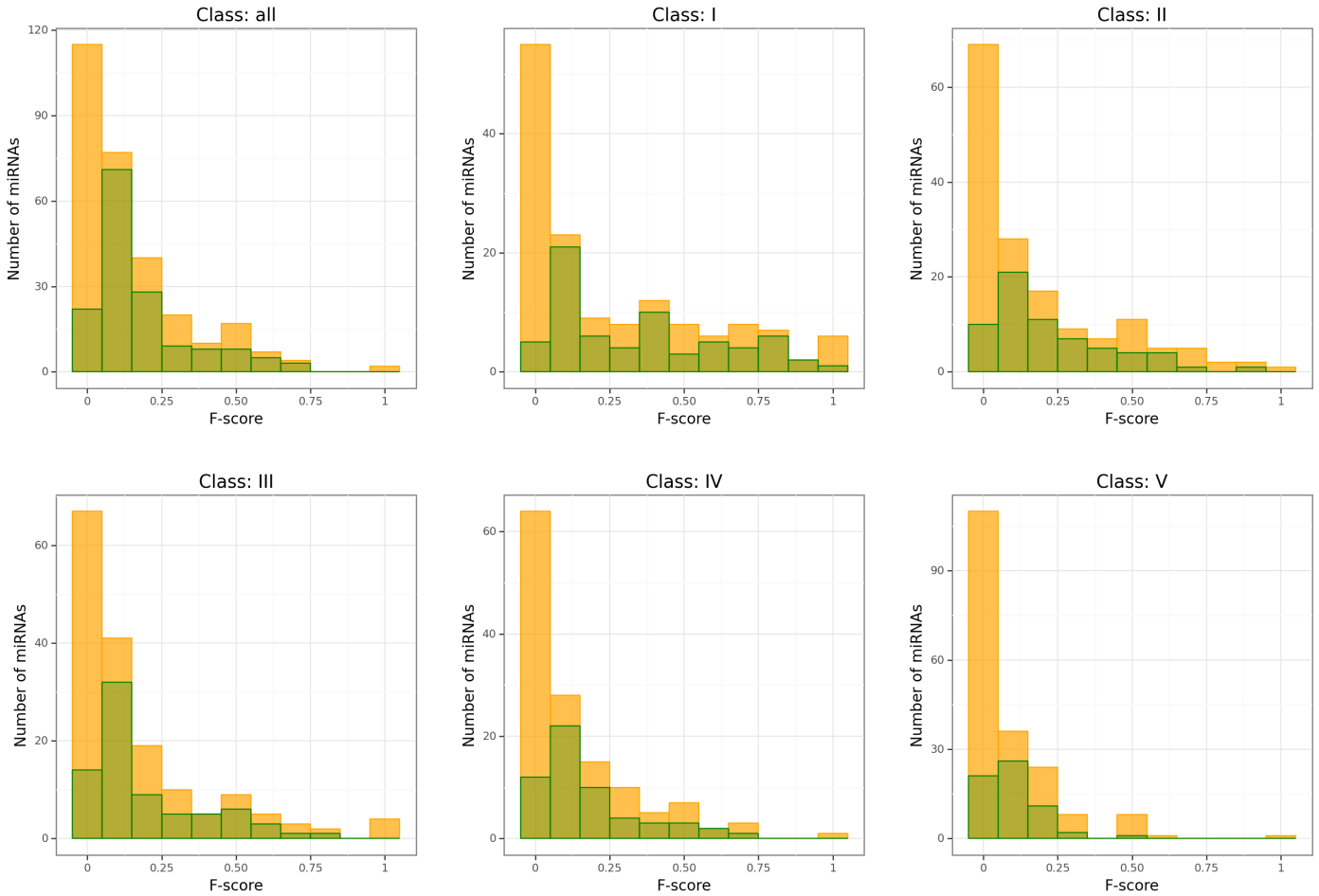
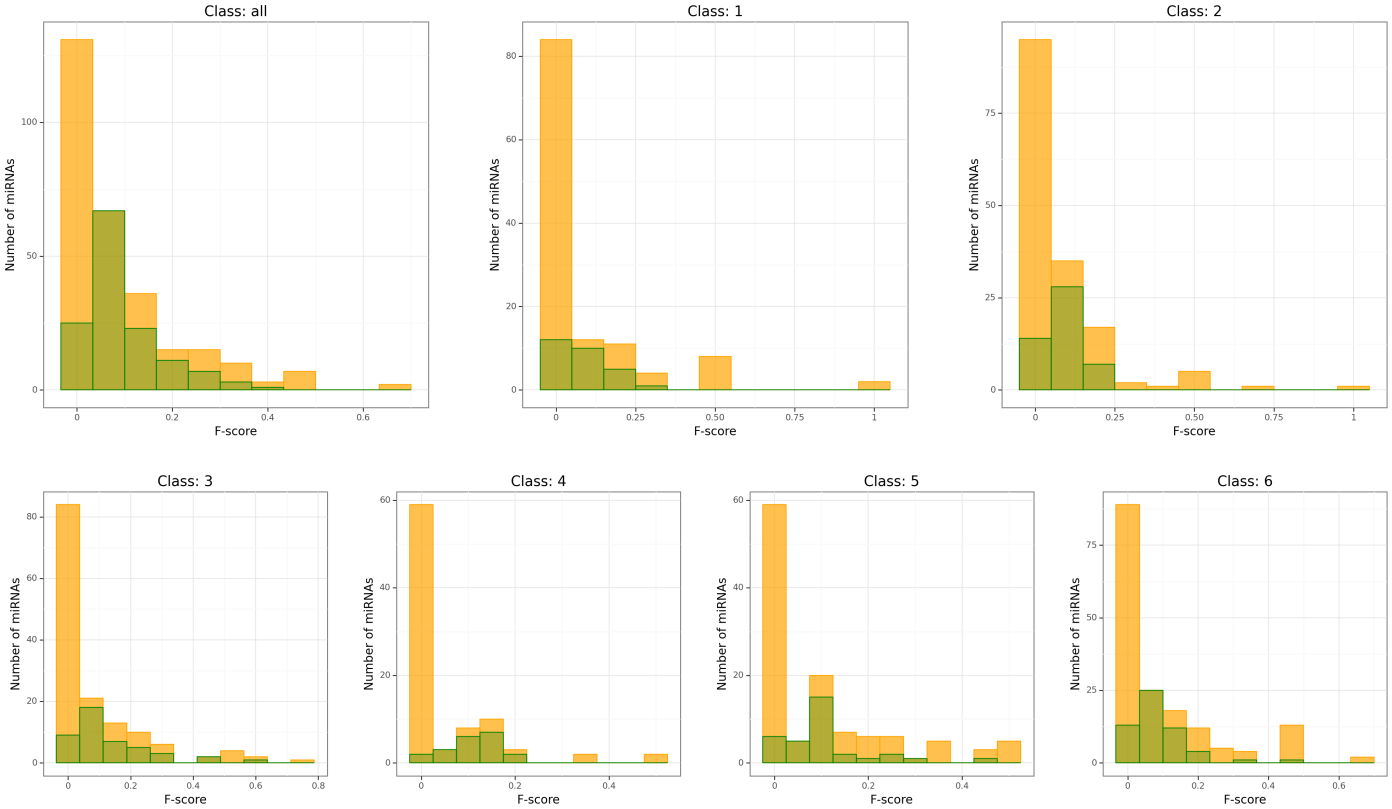



**Figure S8.** One randomly selected interaction for each class on each location on the mouse dataset. In red, the normalised accessibility when considering only the optimal structure with a sliding window. In green, the accessibility computed with RNAPLFOLD with an accessible window $u$ of 8.




**(a)** Human dataset




**(b)** Mouse dataset

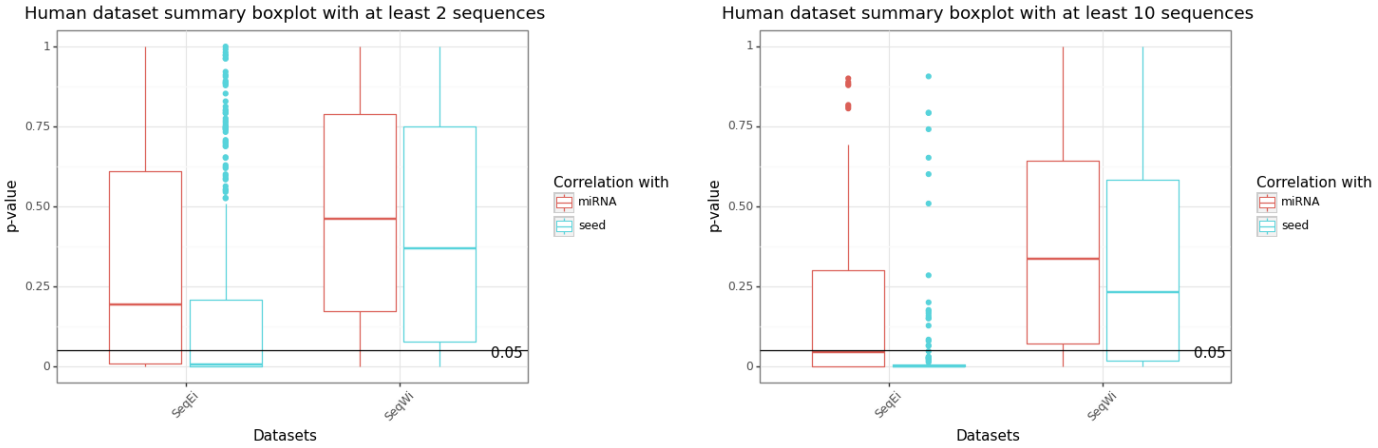
**Figure S9.** Histogram representing the number of miRNAs by f-score on $\text{Seq}_{W_i}$ for each dataset and for each class. In orange, are the datasets with at least 2 targets, and in green those with at least 10 targets. Note that the green dataset is a subset of the orange one which implies that the green number of miRNAs is equal or smaller than in the orange.

**Table S2.** Best motif of width between 6 and 23 found by MEME using the oops site distribution. The column "Av. width" corresponds to the average length of the best motif found while the column "#Seqs" corresponds to the total number of sequences for each subset (Total, and then Class I to Class V).

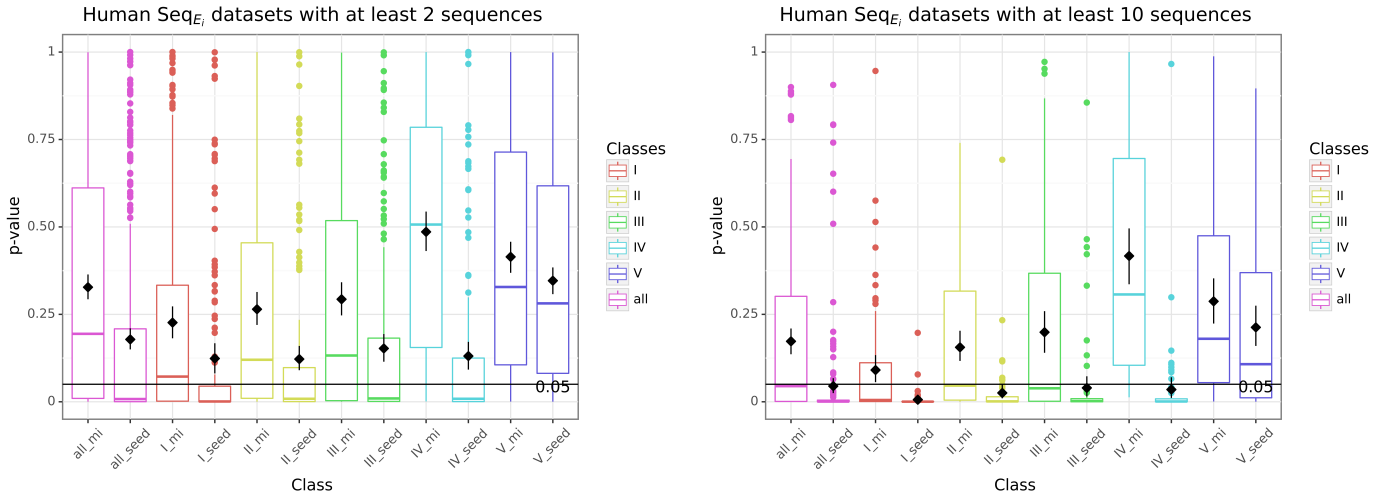
| Input: $Seq_{W_i}$ on human and associated with miRNAs targeting at least 2 mRNAs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Global numbers | | | Occurrences validation | | | | F-score | |
| **Class** | **#miRNAs** | **Av. width** | **#Seqs** | **$TP_{strong}$** | **FP** | **Over-start** | **Over-end** | **F-strong** | **F-overlap** |
| Total | 292 | 14.58 | 15670 | 2421 | 13249 | 607 | 531 | 0.15 | 0.23 |
| I | 144 | 13.77 | 3030 | 822 | 2208 | 100 | 97 | 0.27 | 0.34 |
| II | 156 | 14.84 | 2770 | 531 | 2239 | 113 | 86 | 0.19 | 0.26 |
| III | 165 | 15.12 | 3907 | 729 | 3178 | 161 | 119 | 0.19 | 0.26 |
| IV | 135 | 14.30 | 2828 | 447 | 2381 | 124 | 93 | 0.16 | 0.23 |
| V | 188 | 14.26 | 2898 | 257 | 2641 | 112 | 128 | 0.09 | 0.17 |
| Input: $Seq_{W_i}$ on human and associated with miRNAs targeting at least 10 mRNAs | | | | | | | | | |
| | Global numbers | | | Occurrences validation | | | | F-score | |
| **Class** | **#miRNAs** | **Av. width** | **#Seqs** | **$TP_{strong}$** | **FP** | **Over-start** | **Over-end** | **F-strong** | **F-overlap** |
| Total | 154 | 16.01 | 15144 | 2362 | 12782 | 595 | 517 | 0.16 | 0.23 |
| I | 67 | 14.97 | 2729 | 755 | 1974 | 91 | 85 | 0.28 | 0.34 |
| II | 64 | 16.88 | 2382 | 464 | 1918 | 101 | 72 | 0.19 | 0.27 |
| III | 76 | 16.61 | 3543 | 672 | 2871 | 145 | 112 | 0.19 | 0.26 |
| IV | 57 | 16.00 | 2520 | 412 | 2108 | 118 | 88 | 0.16 | 0.25 |
| V | 61 | 15.93 | 2372 | 205 | 2167 | 99 | 108 | 0.09 | 0.17 |

**Table S3.** Best motif of width between 6 and 23 found by MEME using the oops site distribution. The column "Av. width" corresponds to the average length of the best motif found while the column "#Seqs" corresponds to the total number of sequences for each subset (Total, and then Class 1 to Class 6).

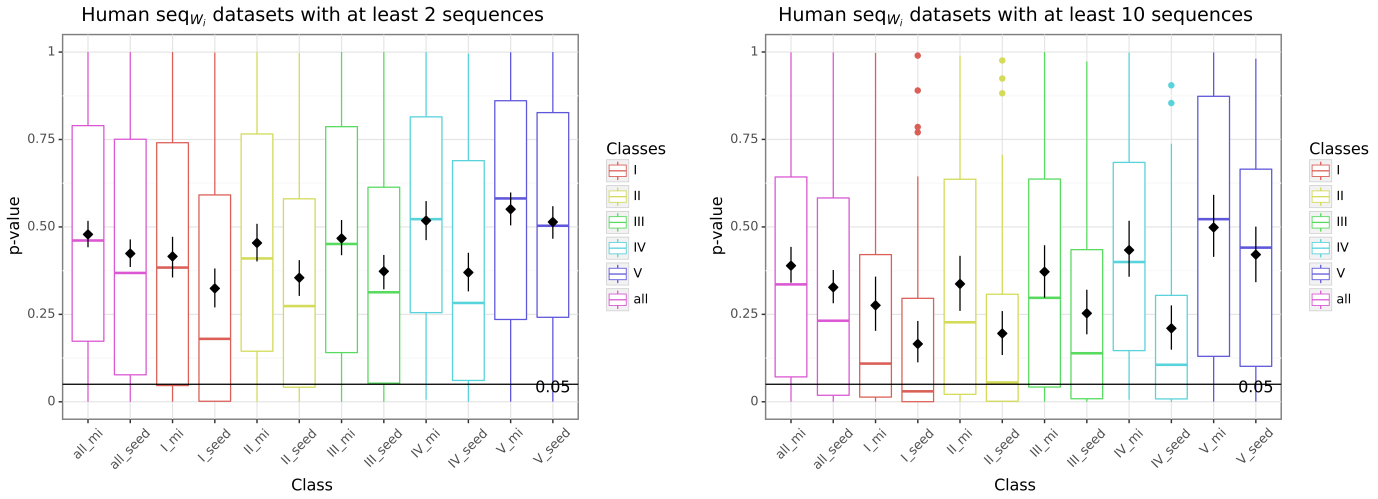
| Input: $Seq_{W_i}$ on mouse and associated with miRNAs targeting at least 2 mRNAs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Global numbers | | | Occurrences validation | | | | F-score | |
| **Class** | **#miRNAs** | **Av. width** | **#Seqs** | **$TP_{strong}$** | **FP** | **Over-start** | **Over-end** | **F-strong** | **F-overlap** |
| All | 285 | 14.72 | 9641 | 776 | 8865 | 302 | 320 | 0.08 | 0.15 |
| 1 | 121 | 13.18 | 1357 | 112 | 1245 | 34 | 32 | 0.08 | 0.13 |
| 2 | 157 | 13.40 | 2287 | 213 | 2074 | 57 | 61 | 0.09 | 0.14 |
| 3 | 143 | 14.01 | 1908 | 208 | 1700 | 55 | 55 | 0.11 | 0.17 |
| 4 | 87 | 14.36 | 922 | 81 | 841 | 30 | 33 | 0.09 | 0.16 |
| 5 | 117 | 13.62 | 2057 | 202 | 1855 | 41 | 63 | 0.10 | 0.15 |
| 6 | 168 | 14.10 | 2624 | 212 | 2412 | 88 | 101 | 0.08 | 0.15 |
| Input: $Seq_{W_i}$ on mouse and associated with miRNAs targeting at least 10 mRNAs | | | | | | | | | |
| | Global numbers | | | Occurrences validation | | | | F-score | |
| **Class** | **#miRNAs** | **Av. width** | **#Seqs** | **$TP_{strong}$** | **FP** | **Over-start** | **Over-end** | **F-strong** | **F-overlap** |
| All | 136 | 15.37 | 8982 | 719 | 8263 | 282 | 298 | 0.08 | 0.14 |
| 1 | 28 | 15.36 | 1034 | 86 | 948 | 26 | 28 | 0.08 | 0.14 |
| 2 | 49 | 14.98 | 1882 | 179 | 1703 | 49 | 55 | 0.10 | 0.15 |
| 3 | 45 | 15.36 | 1495 | 179 | 1316 | 42 | 42 | 0.12 | 0.18 |
| 4 | 20 | 15.65 | 678 | 71 | 607 | 21 | 28 | 0.10 | 0.18 |
| 5 | 33 | 15.06 | 1684 | 159 | 1525 | 33 | 57 | 0.09 | 0.15 |
| 6 | 56 | 16.55 | 2193 | 171 | 2022 | 74 | 89 | 0.08 | 0.15 |




**(a)** Correlation with the miRNA and the seed summarized.

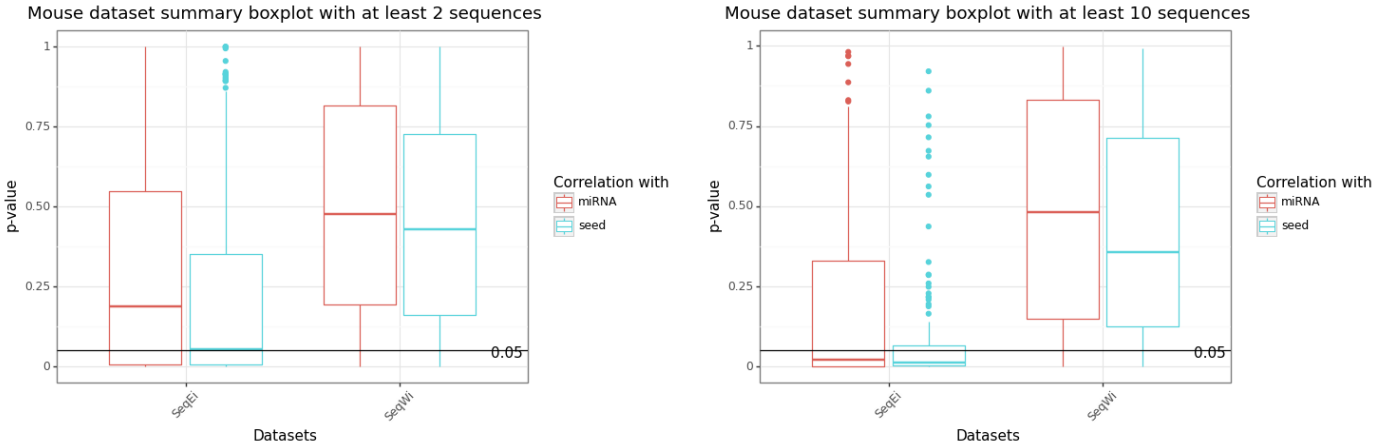



**(b)** P-value from the comparison of the motifs with the sequences given by CLASH. The boxplot indicates the distribution of the p-values for each class when comparing the best motif predicted by MEME with either the seed (seed) or the miRNA (mi) on datasets with more than 2 or 10 sequences.

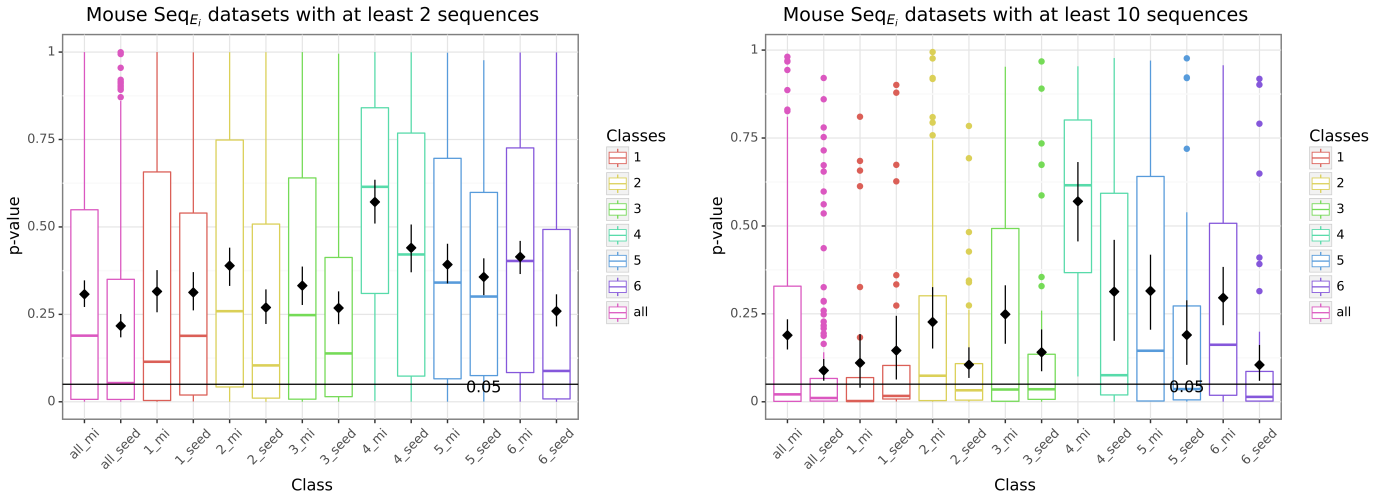



**(c)** P-value from the comparison of the motifs with Seq$_{W_i}$ datasets. The boxplot indicates the distribution of the p-values for each class when comparing the best motif predicted by MEME with either the seed (seed) or the miRNA (mi) on datasets with more than 2 or 10 sequences.

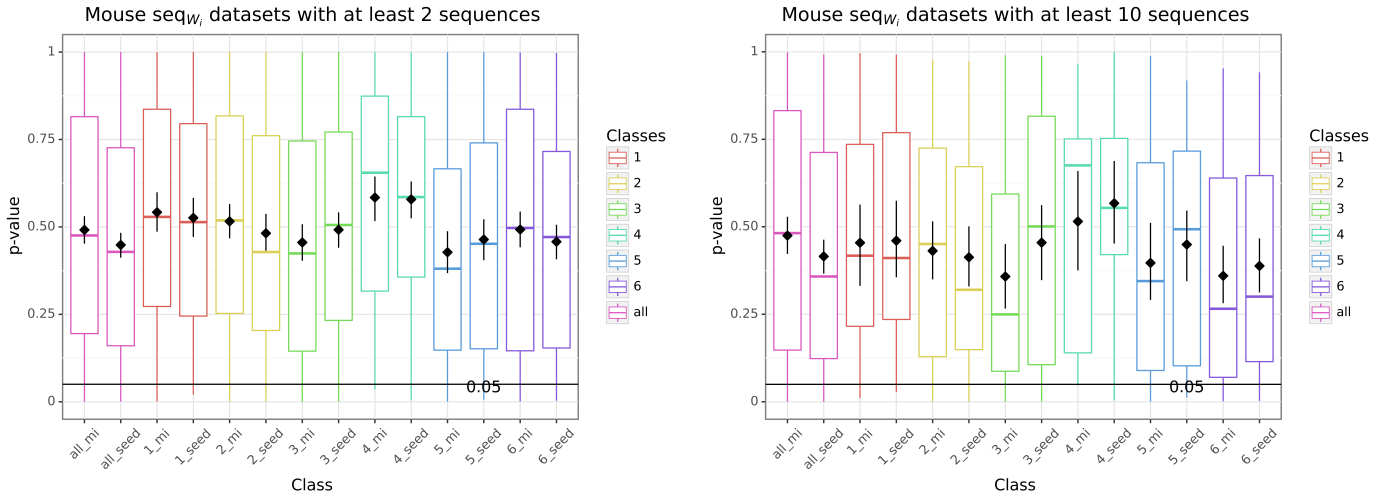
**Figure S10.** Boxplots on the human dataset.




**(a)** Correlation with the miRNA and the seed summarized.




**(b)** P-value from the comparison of the motifs with the sequences given by CLASH. The boxplot indicates the distribution of the p-values for each class when comparing the best motif predicted by MEME with either the seed (seed) or the miRNA (mi) on datasets with more than 2 or 10 sequences.




**(c)** P-value from the comparison of the motifs with Seq$_{W_i}$ datasets. The boxplot indicates the distribution of the p-values for each class when comparing the best motif predicted by MEME with either the seed (seed) or the miRNA (mi) on datasets with more than 2 or 10 sequences.

**Figure S11.** Boxplots on the mouse dataset.