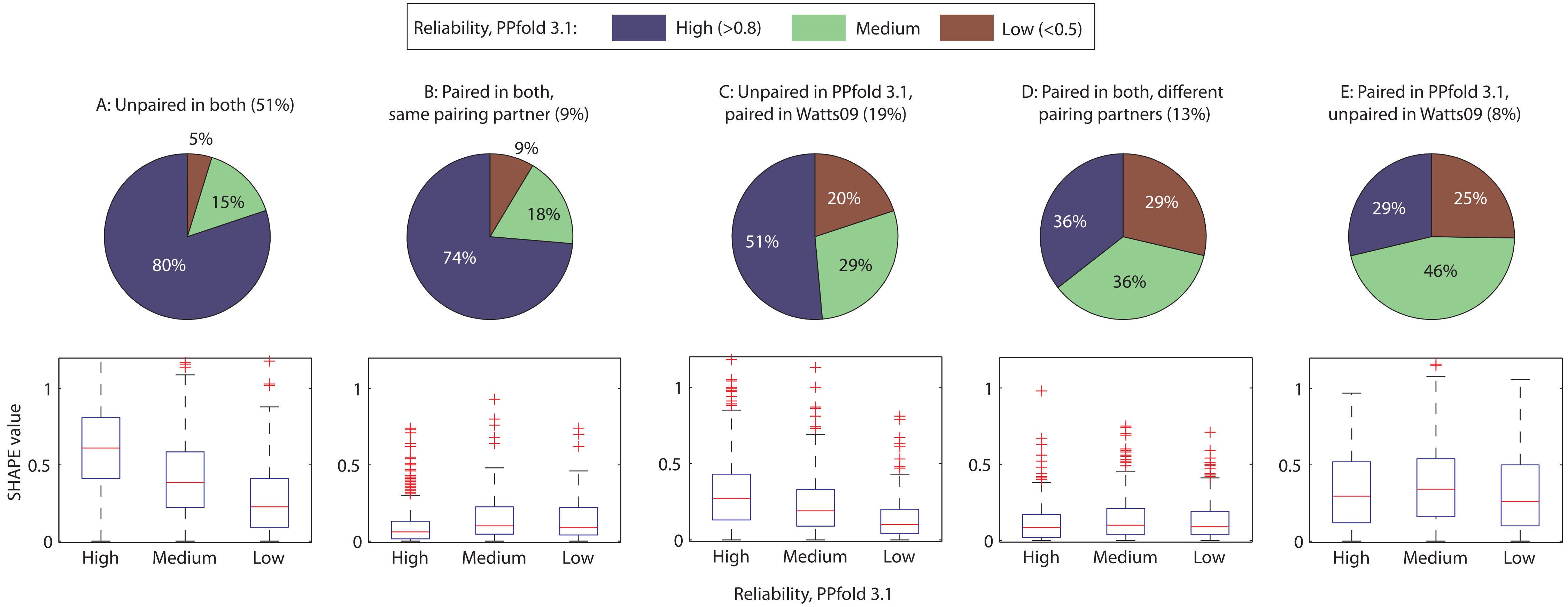
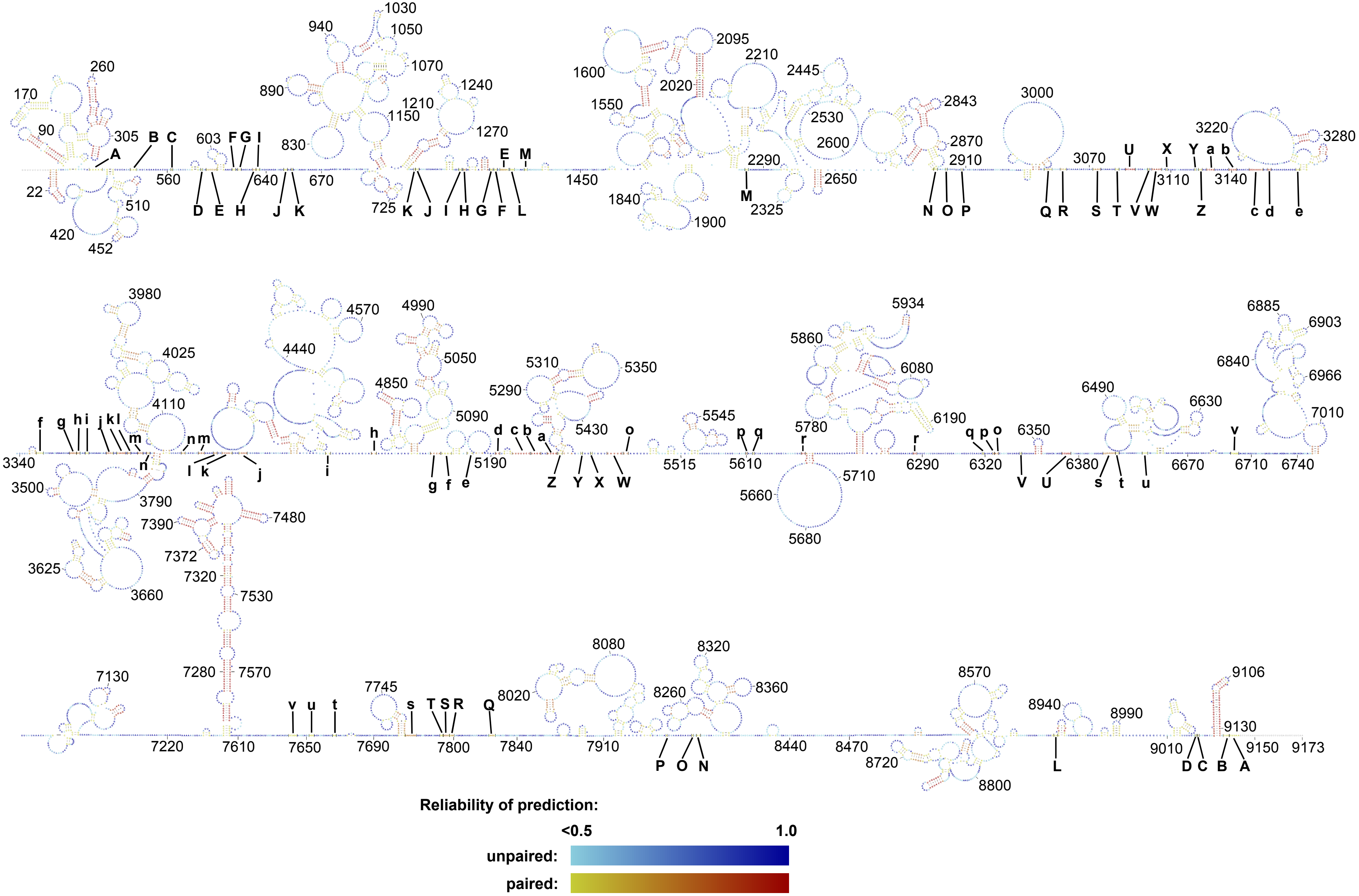
Supplementary Figures

Supplementary Figure S1: Illustration of the grouping of the nucleotides in the HIV-1 genome by structural category (top row), and boxplots of the PPfold 3.1 reliability scores and SHAPE values for each structural category (bottom row). (A) nucleotides that were unpaired in both structures (B) shared base pairs (C) nucleotides that were paired in the PPfold 3.1 structure, but unpaired in the Watts09 structure (D) nucleotides that were paired in both structures, but did not share pairing partners (E) nucleotides that were paired in the PPfold 3.1 structure, and unpaired in the Watts09 structure.


Reliability, PPfold 3.1:
High (>0.8)
Medium
Low (<0.5)
A: Unpaired in both (51%)
5%
15%
80%
B: Paired in both, same pairing partner (9%)
9%
18%
74%
C: Unpaired in PPfold 3.1, paired in Watts09 (19%)
20%
29%
51%
D: Paired in both, different pairing partners (13%)
29%
36%
36%
E: Paired in PPfold 3.1, unpaired in Watts09 (8%)
25%
29%
46%
SHAPE value
0
0.5
1
High
Medium
Low
Reliability, PPfold 3.1

Supplementary Figure S2: comparative model for the secondary structure of the HIV-1 genome, predicted with PPfold 3.1, integrating covariation information from a manually curated alignment of 38 HIV-1 genome sequences and structure probing data from the SHAPE method. Each nucleotide is coloured according to the reliability score (described in Methods). Long-distance interactions (further than 600 nucleotides apart) are indicated with letter codes.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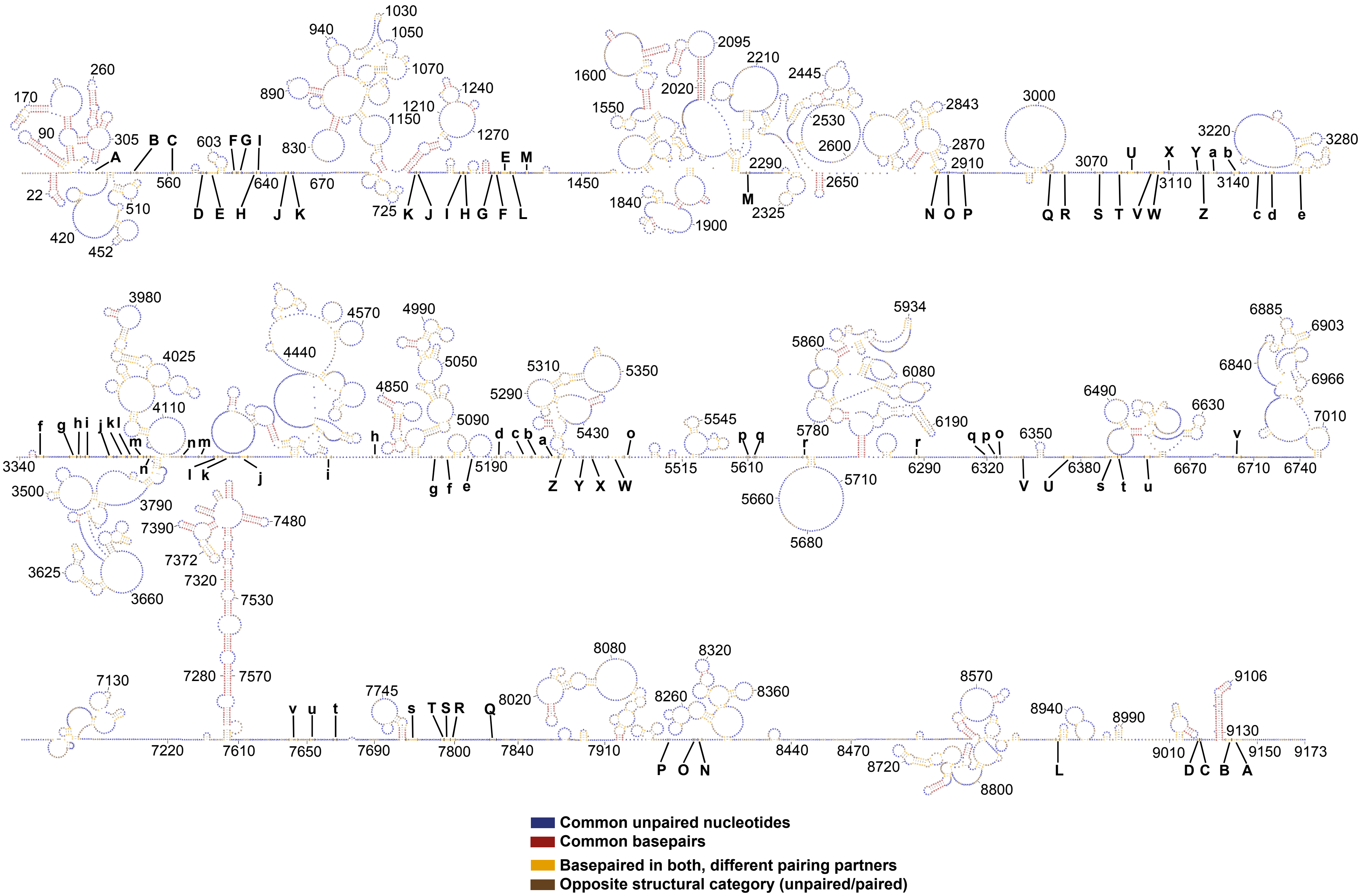
9173
Reliability of prediction:
<0.5
1.0
unpaired:
paired:

Supplementary Figure S3: The PPfold 3.1 structure colored by comparison with the Watts09 structure. The predictions were made with identical SHAPE data. Common structural components are indicated in red (base pairs) and blue (unpaired nucleotides). Different base pairing partners (but pairing in both structures) are indicated by yellow. Nucleotides paired in one but unpaired in the other are indicated in brown. 72% of all unpaired nucleotides and 31% of base paired nucleotides were found in both predictions. Over half of the genome is unpaired in both predictions (blue).



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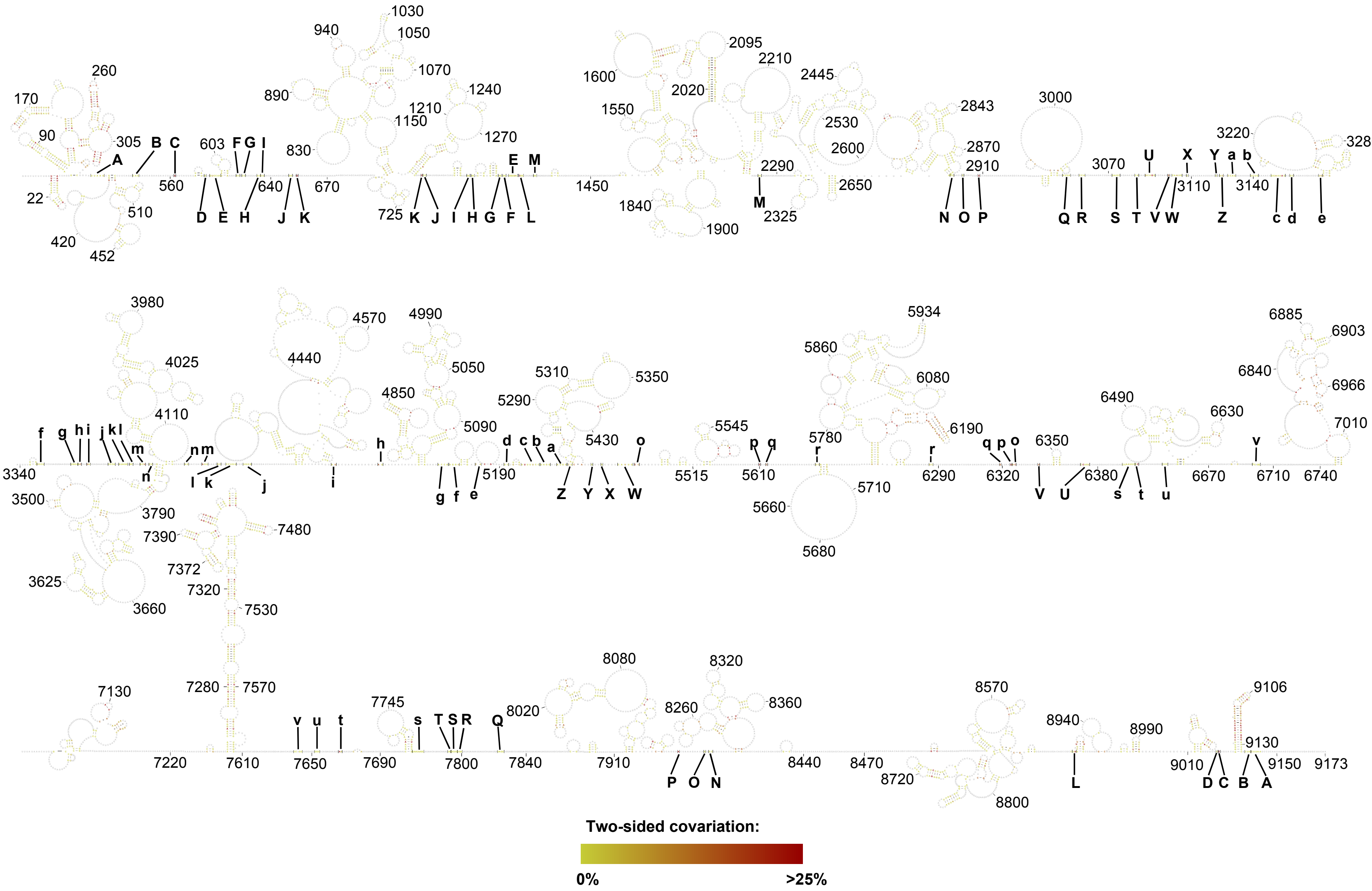
▬ Common unpaired nucleotides
▬ Common basepairs
▬ Basepaired in both, different pairing partners
▬ Opposite structural category (unpaired/paired)

Supplementary Figure S4: Phylogenetic analysis of the proposed structural model. The proportion of CBCs (two-sided covariation) is plotted. This is the proportion of base pairs consistent with the structural prediction (A-U, G-C, G-U), when removing gaps and the most frequent canonical base pair, as described in the Methods section.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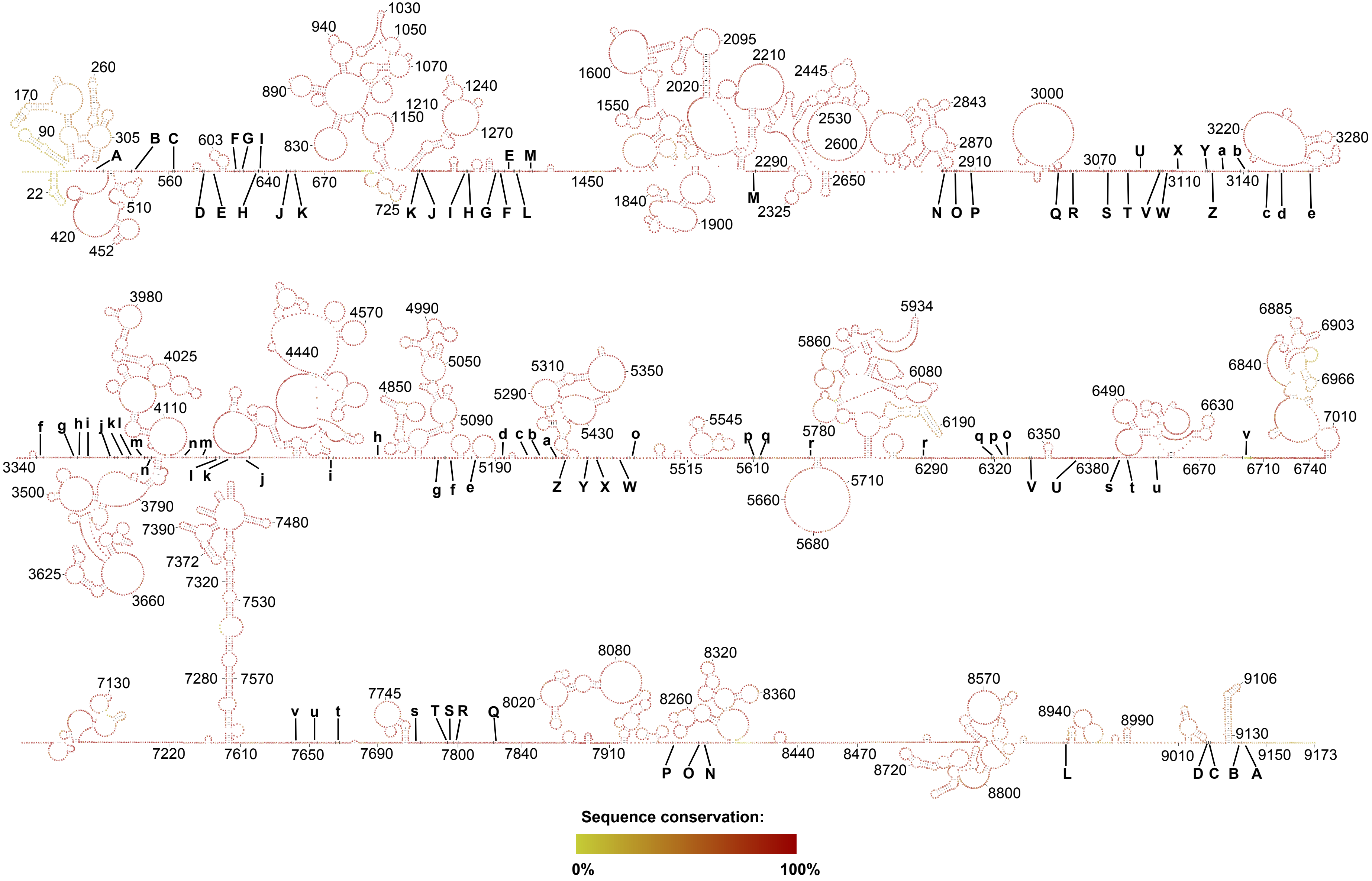
Two-sided covariation:
0%
>25%

Supplementary Figure S5: Analysis of sequence conservation along the proposed structural model.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Sequence conservation:
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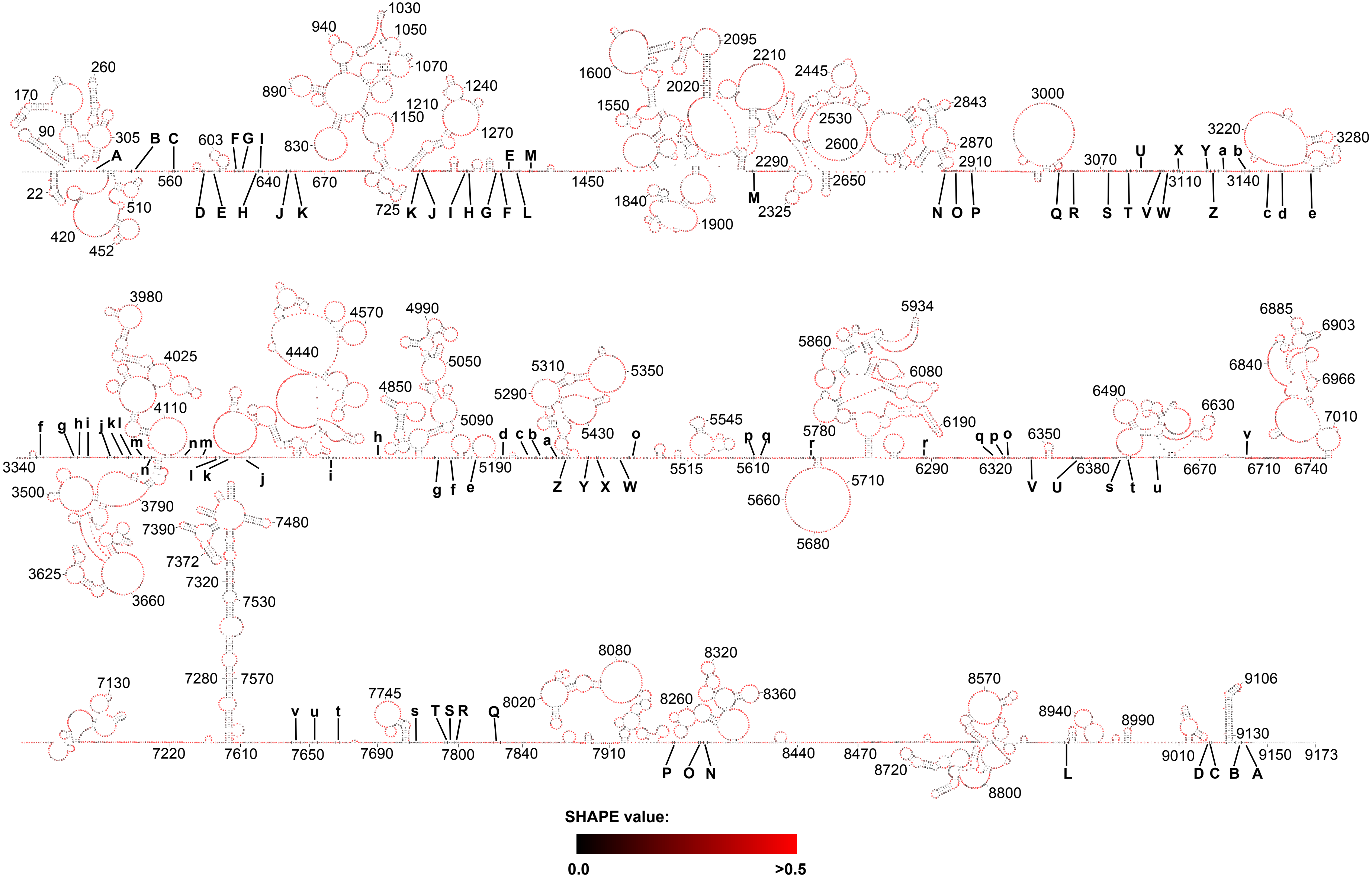
Supplementary Figure S6: The proposed structural model colored by SHAPE values.



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9010
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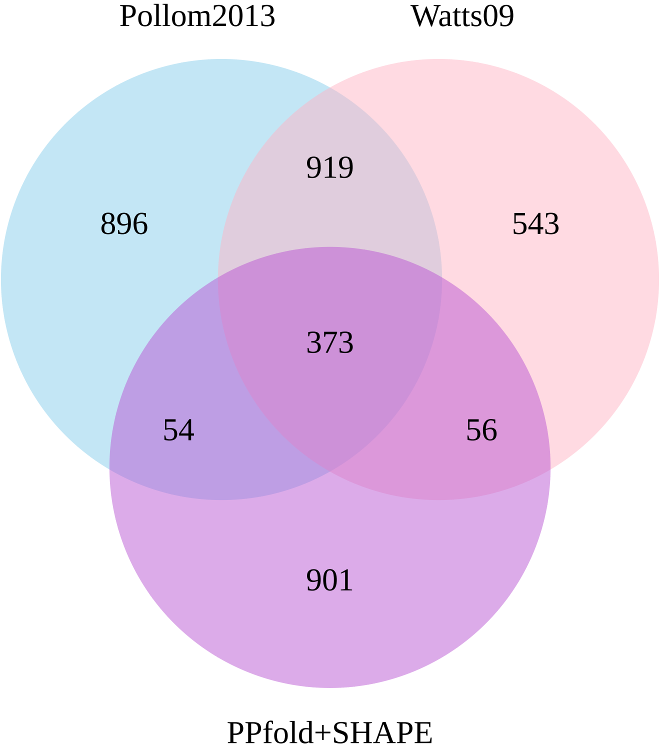
8800
SHAPE value:
0.0
>0.5

Supplementary Figure S7: The Venn diagram illustrates the number of shared base pairs between the 3 predictions: Pollom2013, Watts09 and PPfold+SHAPE. The base pair overlap of the PPfold+SHAPE prediction to the Pollom2013 dataset is highly similar to the overlap with Watts09.


Pollom2013
Watts09
896
919
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54
56
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PPfold+SHAPE