CMV - Supplement and User Guide

Florian Eggenhofer[1,2], Ivo L. Hofacker[1,3], Rolf Backofen[1,6], Christian Höner zu Siederdissen[4,1,5]

[1] Bioinformatics Group, Department of Computer Science University of Freiburg, Georges-Köhler-Allee ,79110 Freiburg, Germany
[2] Institute for Theoretical Chemistry, University of Vienna, Währingerstrasse 17,A-1090 Vienna, Austria
[3] Bioinformatics and Computational Biology research group, University of Vienna, Währingerstrasse 17, A-1090 Vienna, Austria
[4] Bioinformatics Group, Department of Computer Science, University of Leipzig, D-04107 Leipzig
[5] Interdisciplinary Center for Bioinformatics, University of Leipzig, Härtelstraße 16-18, D-04107 Leipzig, Germany
[6] Centre for Biological Signalling Studies (BIOSS), University of Freiburg, 79110 Freiburg, Germany.

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A Introduction

`CMV` offers tools for the visualisation of *RNA* family models, also known as covariance models (*CM*) and Hidden Markov Models (*HMM*). Moreover, comparsions between models, the multiple sequence alignments they were constructed from and, in the case of *RNA* families, the consensus secondary structure can be visualised. The aim is to simplify model construction and evaluation by providing visualisations with different levels of detail. Minimal and simple detail representations give a overview over the size of the model by showing all nodes and in case of covariance models depict the guide tree, meaning nestedness of the secondary structure elements, of the model. Detailed views show nodes, states, emission as well as transition probabilites. Comparison results are highlighted by color labels which are consistently applied to model, alignment and secondary structure visualisation, allowing to inspect found similarities between models in their context. The tools can be applied to already existing *HMM*s (in `HMMER` [1] format) and *CM*s (in `Infernal` [2,3] format) from the `Pfam` [4,5] and `Rfam` database [6], as well as newly constructed models from `RNAlien` [7]. Comparsions between covariance models can be computed via `CMCompare` [8] and its webservice [9]. The first section describes installation and how to obtain the source code, see also the Tool subpage of the webservice. The second part of the guide explains the application of the tools for hidden markov models `HMMV` (Hidden markov model visualisation tool) and their comparisons `HMMCV` (Hidden markov model comparison visualisation tool) on the command line, as well as on the web service. The third part addresses the usage of the tools for covariance models `CMV` (Covariance model visualisation) and their comparisons `CMCV` (Covariance model comparison visualisation). For each of these for tools an example is depicted in this guide, which is also available as single click-example submission on the webservice, complete with input files. The fourth part introduces the two auxiliary tools, `CMCtoHMMC` mapping `CMCompare` output on *HMM*s and `HMMCtoCMC` mapping `HMMCompare` output on *CM*s. This document is included with the tool as manual.pdf and as a variant serves as Help section of the webservice.

B Installation

The visualisation tools are available as a commandline tool and as a webservice. For *Linux* we recommend installation via bioconda, for *macOS* usage of the docker container. The example input files used in the webservice (EGF, Piwi, Hammerhead Clan, tRNA Clan) can be retrieved here: Example input

B.1 Source availibility

The source code is open source and available via GitHub and Hackage both licenced with GPL-3.

B.2 Usage via biocontainer - *macOS*

`CMV` can be retrieved and used as docker container with all dependencies via docker. Once you have docker installed simply type:
docker run -i -t quay.io/biocontainers/cmv:1.0.7--0 /bin/bash

B.3 Installation via bioconda - *Linux*

The package can be installed via conda. Once you have conda installed simply type:
conda install -c bioconda -c conda-forge cmv

B.4 Installation via cabal-install

The package is implemented in Haskell and can be installed via the Haskell package distribution system cabal. Once you have cabal installed simply type:
cabal install CMV

B.5 Precompiled Executables

Linux x86_64: HMMV
Linux x86_64: HMMCV
Linux x86_64: CMV
Linux x86_64: CMCV

Auxiliary tools:
Linux x86_64: CMCtoHMMC
Linux x86_64: HMMCtoCMC

C HMM-Tools

Hidden Markov models are used to represent the sequence information of biopolymers. Nodes of the model represent columns of a multiple sequence alignment. The guide first describes the program flow and then the required input and parameters for the commandline and webserver instances of both tools. A visualisation for the *EGF*-protein `Pfam` [4,5] family and a comparison visualisation for the *hammerhead-RNA* `Rfam` clan [6] with corresponding command line calls are used as output examples. Detailed model view has been inspired by visualisation provided by `SAM` (drawmodel) [10].

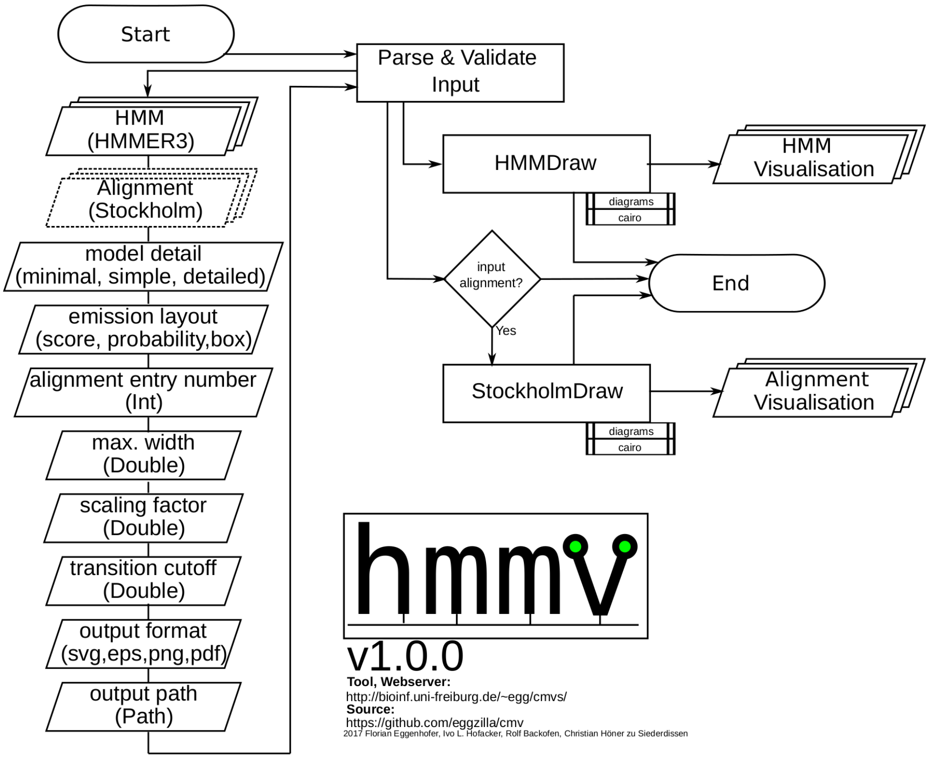

Fig. 1. Detailed flowchart representation of `HMMV`, showing options on the left, processing in the center and output on the right.

C.1 Program flowcharts

Flowchart representation of `HMMV` (see Figure 1) showing the possible options for the commandline tool and the processing of input models via HMMDraw. Optional input alignments trigger the output of alignment visualisation via StockholmDraw. Both modules are based on the diagrams library and a cairo backend. Flowchart representation of `HMMCV` (see Figure 2) showing possible options for the commandline tool and the processing of input models and input comparisons via HMMDraw. Linked nodes are highlighted in both alignment and model visualisation. Both modules are based on the diagrams library and a cairo backend.

C.2 Input

Example inputs can be found in the Help section of the webservice and on the webserver submission (HMMV, HMMCV) pages for each tool.

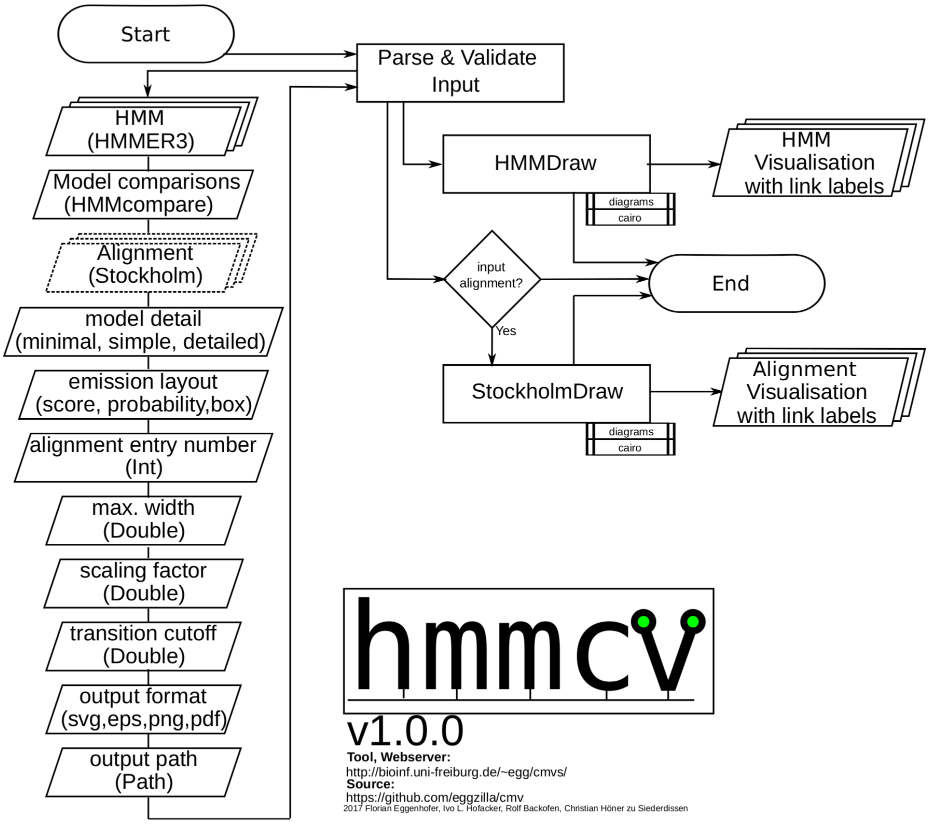

Fig. 2. Flowchart representation of `HMMCV`, showing options on the left, processing in the center and output on the right.

HMM (-m) Input models are supported in `HMMER3` [11] (see HMMER User-guide) format, as used by `Pfam` [4,5] and as part of `Rfam` [12] `Infernal` [2] models. Multiple input models can be provided by concatenating them in one file, see *hammerhead-RNA* family clan sample file. The webservice accepts a file upload, the commandline tool a absolute filepath.

Alignment (-s) Optionally the multiple sequence alignment used to construct the input model can be provided in Stockholm format, e.g. *EGF* alignment. For multiple input models the same number of alignments must be provided. The alignments must be concatenated into one file, in the same order as the models (e.g. *hammerhead-RNA*). Provide a file upload for the webservice or a absolute filepath for the commandline tool.

Comparison (-r) `HMMCV` requires a comparison file, detailing the relationship between the input models. The commandline tool requires an absolute filepath. This format is derived from the CMCompare output format and contains on each line following white space separated fields: model1Name model2Name linkscore1 linkscore2 linksequence model1matchednodes model2matchednodes
Here is a example line from a hammerhead clan comparison, the whole file can be found here: hammerheadClan-comparsion.
Hammerhead_1 Hammerhead_3 6.168 5.244 GUCCCAGUAAUAGGAC [17,18,19,20,21,22,23,23,24,25,26,27,28] [36,37,38,39,40,41,42,43,44,45,46,47,48]

Detail level (-d) Three detail level for each node are available:

- minimal - showing the node number.
- simple - showing emission probabilites
- detailed - showing emission and transition probabilities

Emission layout (-e) Controls display of emission probabilities for detail levels simple and detailed. The selected variant is shown next to the emitted symbol.

- box - fill state of a box
- score - bit score, as a floating pint number
- probability - as a floating point number

Output format (-f) Available output formats are pdf, png, svg and ps. The webservice always generates svg by default for rendering of the preview.

Max. number of alignment entries (-n) This controls how many entries are displayed for optionally uploaded alignments.

Image size scaling factor (-c) Scales the result image by set factor. Please consider that resulting .svg output can be easily rescaled.

Transition probability cutoff (-t) Minimum necessary cutoff for a transition probability to be displayed.

Output directory path (only cmdline, -o) Absolute path to output directory

Help (only cmdline, –help) Prints help with all default options and commandline parameters

C.3 Commandline usage

`HMMV` visualisation for the Piwi protein family, as used for the webservice, can be obtained with the following commandline call:

```
HMMV -d detailed -m Piwi.hmm -s /home/user/PF02171_seed.txt
```

`HMMCV` comparsion visualisation for the hammerhead-*RNA* clan can be computed like this:

```
HMMCV -d detailed -m /home/user/hammerhead.hmm -s /home/user/hammerhead.stockholm.txt
-r /home/user/hammerhead.hmmc -f pdf
```

C.4 Output

`HMMV` output For each input model a outputfile in the requested format is generated. Als filename the modelname encoded in the file is used and as file extension the request output format (.png,.svg,.ps,.pdf). If stockholm alignments have been provided, then for each model a alignment visualisation with index colums is created. The alignment file name is the model name, followed by ".aln" and then the requested file format extension. The webservice gzips all results and provides a download link. Following are minimal (see Figure 3), simple (see Figure 4) and detailed (see Figure 5 6) visualisations for the *EGF* protein `Pfam` family. The results for this and the other models can be viewed by clicking the sample button of the `HMMV` webservice. The webservice also creates a zoom- and panable preview, that can be expanded by clicking.

, showing nodes with their index and emission probabilities.

`HMMCV` output While also providing visualisation output for each model and corresponding alignment, `HMMCV` additionally annotates regions found to be linked by model comparison via color tags. Each provided model is associated with a color that is depicted in the legend table. The nodes of each model visualisation are then tagged with the color of the linked model. The coloring is also applied to the running index of the alignment visualisation. This allows to study in detail which parts of models are connected, or shared in e.g. clans and which not. The file naming scheme is similar to `HMMV`. The following example comparison was computed for the whole Hammerhead clan from `Rfam`, pairwisely comparing Hammerhead_HH9, Hammerhead_3, Hammerhead_1, Hammerhead_II and Hammerhead_HH10 with the CMCompare webserver. The comparison results from the covariance models were mapped on the prefilter *HMM*s supplied with each covariance model with the included auxiliary `CMCtoHMMC` tool. The result for the Hammerhead_HH9 *RNA* with the linked regions of the other models is shown in minimal (see Figure 8), simple (see Figures 9, 10) and detailed (see Figures 11, 12, 13) visualisations and in the alignment visualisation (see Figure 14). The results for this and the other models can be viewed by clicking the sample button of the `HMMCV` webservice.

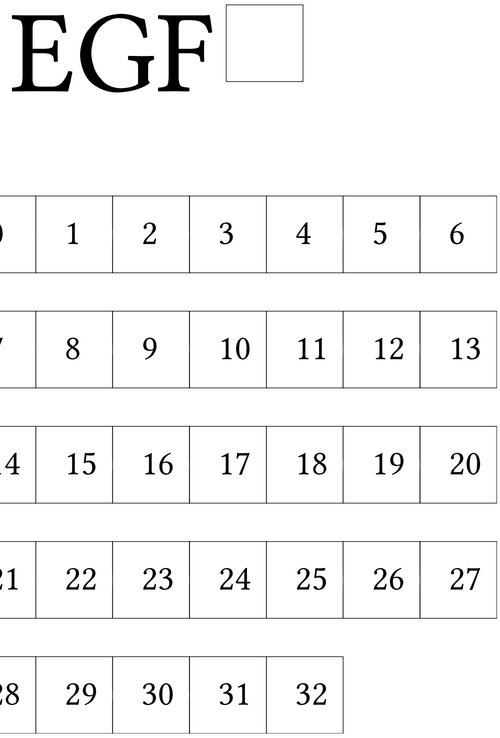

Fig. 3. Minimal detail *EGF* `Pfam` family visualisation, just showing model nodes with their index.

C.5 Examples

Additional examples for the first 1600 models from `Pfam` in 3 detail labels can be found here: Link.

D CM-Tools

Covariance, also called *RNA* family, models are used to represent the sequence and structure information of *RNA* molecules. The guide first describes the program flow and then the required input and parameters for the commandline and webserver instances of both tools. Parameters that only work for the command line tool and not on the webserver are annotated with "cmdline-only". This guide uses the *tRNA* family for a demonstration of `CMV` (Covariance model visualisation) in minimal the hammerhead-*RNA* clan for demonstration of `CMCV` (Covariance model comparison visualisation) also in three levels of detail. Layout of the detailed output has been inspired by depections used in the `Infernal` user guide and the book 'Biological sequence analysis' [13]. For both tools a webserver corresponding command line calls are use

D.1 Program flowcharts

The flowchart representation of `CMV` (see Figure 15) shows that the tool accepts multiple covariance models and optionally the corresponding Stockholm alignments as input. After parsing and validating the input, for each provided model a visualisation output is created via the CMDraw module, which is based on the diagrams library and a cairo backend. The optional input alignments are used for creating a visualisation of the input alignment via StockholmDraw module.

Flowchart representation of `CMCV` (see Figure 16) showing possible options for the commandline tool and the processing of input models and input comparisons via CMDraw. Optional input alignments trigger the output of alignment visualisation via StockholmDraw. Linked nodes are highlighted in both alignment and model visualisation. Both modules are based on the diagrams library and a cairo backend.

D.2 Input

Example inputs can be found in the Help section of the webservice and on the webserver submission (CMV, CMCV) pages for each tool.

CM (-m) Input models are supported in `Infernal` (see Infernal User-guide) format, as used by `Rfam` or constructed by `RNAlien` [7] or the *RNA* workbench [14,15]. Here is the *tRNA* family as example. Multiple input models can be provided by concatenating them in one file, see *hammerhead-RNA* family clan sample file. The webservice accepts a file upload, the commandline tool a absolute filepath.

Alignment (-s) Optionally the multiple sequence alignment used to construct the input model can be provided in Stockholm format, e.g. *tRNA* alignment. For multiple input models the same number of alignments must be provided. The alignments must be concatenated into one file, in the same order as the models (e.g. *hammerhead-RNA*). Provide a file upload for the webservice or a absolute filepath for the commandline tool.

Comparison (-r) `CMCV` requires a comparison file, detailing the relationship between the input models. The commandline tool requires an absolute filepath. The used `CMCompare` output format contains on each line following white space separated fields:
model1Name model2Name linkscore1 linkscore2 linksequence model1matchednodes model2matchednodes
Here is a example line from a hammerhead clan comparison, the whole file can be found here: hammerheadClan-comparsion.
Hammerhead_1 Hammerhead_3 6.168 5.244 GUCCCAGUAAUAGGAC ((((...,....)))) ((((........)))) [17,18,19,20,21,22,23,23,24,25,26,27,28] [36,37,38,39,40,41,42,43,44,45,46,47,48]
The `CMCompare` Webserver [9] offers cmcv.result files that can be directly used as input for (-r) Link.

Detail level (-d) Three detail level for each node are available:

- minimal - showing the node number.
- simple - showing node number and node type
- detailed - showing node number, type, emission and transition probabilities

Emission layout (-e) Controls display of emission probabilities for detail levels simple and detailed. The selected variant is shown next to the emitted symbol.

- box - fill state of a box
- score - bit score, as a floating point number
- probability - as a floating point number

Model layout (-l)

- tree - model is branched at each bifurcation according to guide tree
- flat - nodes are all arranged on a line

Secondary structure visualisation tool *(only commandline, -x)* `CMV` and `CMCV` can create input files for the secondary structure visualisation tools `forna` [16] and `R2R` [17]. This input file containes the consenus secondary structure of the input alignment. Moreover `CMCV` labels nucleotides that are annotated to be similar with compared models in the input files and in case of `R2R` color encodes them according to the color scheme used for the model comparison visualisation. In case of the webservice both visualisations are triggered on providing a input alignment.

- `forna` - for each model a input structure file and a color scheme is generated for upload to forna
- `R2R` - for each model a input file for `R2R` is generated

Output format (-f) Available output formats are pdf, png, svg and ps. The webservice always generates svg by default for rendering of the preview.

Max. number of alignment entries (-n) This controls how many entries are displayed for optionally uploaded alignments.

Image size scaling factor (-c) Scales the result image by set factor. Please consider that resulting .svg output can be easily rescaled.

Transition probability cutoff (-t) Minimum necessary cutoff for a transition probability to be displayed.

Output directory path (only cmdline, -o) Absolute path to output directory

Help (only cmdline, –help) Prints help with all default options and commandline parameters

D.3 Commandline usage

`CMV` visualisation for the tRNA family, as used as sample for the webservice, can be obtained with the following commandline call:
CMV -m tRNA.cm -s RF00005.stockholm.txt -f pdf

`CMCV` comparsion visualisation for the hammerheadRNA clan can be computed like this:
CMCV -d simple -m /home/user/hammerheadClan.cm -s /home/user/hammerheadClan.sto -r /home/user/hammerheadClan.cmcompare -f pdf -l tree

D.4 Output

`CMV` output For each input model a outputfile in the requested format is generated. Also filename the modelname encoded in the file is used and as file extension the request output format (.png,.svg,.ps,.pdf). If stockholm alignments have been provided, then for each model a alignment visualisation with index colums is created. The alignment file name is the model name, followed by ".aln" and then the requested file format extension. The webservice compresses all results and provides a download link. Extensive information about the node types (with abbreviations MATP, MATL, MATR, BIF, ROOT, BEGL, BEGR, END) and state types (with abbreviations P, L, T, B, D, S, E) used by covariance models can be found in the `Infernal` user guide, specifically pages 52 and 53. The webservice also creates a zoom- and panable preview, that can be expanded by clicking. Following is the minimal (see Figure 17), simple (see Figure 18) and detailed (see Figures 19, 20, 21, 22, 23, 24, 28) *tRNA* `Rfam` family model visualisation. For the corresponding alignment visualisation see Figure 26.

Secondary structure visualisation Table provides the consensus secondary structure visualisation of the structural alignment for each model by `R2R` as well as `forna`.

`CMCV` output `CMCV` also provides visualisation output for each model and corresponding alignment. The naming scheme is similar to `CMV`. However it annotates regions found to be linked by model comparison via color tags. Each provided model is associated with a color that is depicted in the legend table. The nodes of each model visualisation are then tagged with the color of the linked model. The coloring is also applied to the running index of the alignment visualisation. This allows to study in detail which parts of models are connected, or shared in e.g. clans and which not. Extensive information about the node types (with abbreviations MATP, MATL, MATR, BIF, ROOT, BEGL, BEGR, END) and state types (with abbreviations P, L, T, B, D, S, E) used by covariance models can be found in the `Infernal` user guide, specifically pages 52 and 53. The following example shows the result for the *Hammerhead_HH9 RNA* `CMCV` output as minimal (see Figure 29), simple (see Figures 30, 31) and detailed (see Figures 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42) visualisation. The alignment is shown in Figure 43.

The webservice also creates a zoom- and panable preview, that can be expanded by clicking.

Secondary structure visualisation Moreover linked nodes are also annotated in the consensus secondary structure of the provided models, if a stockholm alignment with consensus structure has been provided. This allows to identify specific secondary structure elements that are linked between families. This is done for pairs of models with `R2R` as well as `forna`.

D.5 Examples

Additional examples for all models from `Rfam` in three detail labels can be found here: Link. Examples for comparisons of Rfam clans can be found here: Link.

D.6 Benchmark

Runtime and memory consumption for the first 100 Rfam families are shown in Table 1 and were computed on a *Intel(R) Xeon(R) CPU E5-2630 v4 @ 2.20GHz* cpu with a single thread.

Rfam family name	Elapsed real time [seconds]	Maximum resident set size [kbytes]
5S_rRNA	12.79	715140
5_8S_rRNA	13.36	784956
U1	16.41	867316
U2	17.77	1071648
tRNA	06.61	444100
Vault	08.85	550828

U12	15.04	850800
Hammerhead_3	06.40	389308
RNaseP_nuc	24.38	1391292
RNaseP_bact_a	39.83	1953500
RNaseP_bact_b	34.91	1963264
U3	23.86	1220600
6S	19.19	1063516
DsrA	09.75	558360
U4	12.97	765668
SNORD14	09.33	565648
Metazoa_SRP	31.33	1810600
CsrB	29.43	1770356
Y_RNA	10.02	555420
U5	12.99	698060
Spot_42	10.88	729424
GcvB	18.18	1115148
tmRNA	34.49	1799168
Telomerase-vert	42.88	2172452
Telomerase-cil	16.64	895780
U6	06.99	527964
let-7	08.84	555552
Intron_gpI	24.16	1257588
Intron_gpII	08.05	539248
RNase_MRP	23.07	1353624
SECIS_1	05.71	409756
Histone3	03.95	302612
MicF	08.60	543284
RprA	10.39	574844
OxyS	12.28	683444
RRE	35.82	1939584
IRE_I	03.95	302136
PrfA	12.39	702136
DicF	05.22	363060
rne5	30.26	1812964
Entero_OriR	09.44	717796
CopA	08.12	561304
Plasmid_R1162	06.33	513064
Phage_pRNA	20.36	1241372
SNORA73	19.07	1180256
snoR30	07.31	513408
mir-2	06.97	443128
Entero_CRE	06.05	385656
SNORD36	06.58	399556
FMN	10.97	744152
mir-17	08.44	536708
lin-4	06.78	443840
mir-7	08.95	557020

SNORD25	06.24	423344
SNORD96	05.78	416272
SNORA71	12.44	777396
RyhB	05.67	405092
HgcF	17.56	880720
TPP	09.58	593776
HgcE	12.84	714416
IRES_HCV	24.23	1378276
HgcC	11.61	738716
SscA	08.23	545260
HgcG	25.36	1362644
snoR9	12.48	706812
U7	06.34	386840
SNORD15	10.51	607972
SNORD21	06.94	452528
SNORD24	06.20	397048
SNORD29	05.18	366832
SNORD73	05.72	389652
SNORA75	11.00	747536
mir-156	08.46	541540
mir-29	06.40	440452
mir-166	11.40	690084
mir-181	07.29	520416
SraB	14.83	880924
MicA	06.16	434544
OmrA-B	08.18	538008
yybP-ykoY	13.90	816788
ArcZ	10.06	566836
SraG	16.49	872468
GlmZ_SraJ	19.11	1173580
CsrC	22.38	1325628
SNORD28	05.76	397704
SNORD27	05.78	384396
SNORD26	06.35	397440
SNORD30	05.43	395044
SNORD31	05.16	374096
SNORA74	20.63	1195224
SNORA62	12.20	798120
SNORA63	10.27	723496
SNORD18	05.42	390436
HDV_ribozyme	07.85	551132
snoPyro_CD	04.42	315896
U8	10.19	728664
snoR71	09.31	539732
SNORD22	09.48	570696
7SK	30.55	1778300
SraC_RyeA	12.30	768748

Table 1: Benchmark table showing the runtimes and memory consumption for computing a detailed covariance model visualisation with *CMV* on a *Intel(R) Xeon(R) CPU E5-2630 v4 @ 2.20GHz* cpu with a single thread.

E Auxiliary tools

We created two auxiliary tools to simplify the handling of comparison results.

E.1 CMCtoHMMC

`CMCompare` results contain the node intervals of linked models. Since both the `Infernal` covariance models and the `HMMER` hidden markov models have the alignment columns the were derived from annotated, it is possible to map these intervals from a *CM* to a *HMM* of the same family. This tool was used to create the `HMMCompare` files used for the `HMMCV`. Here is a example call:
CMCtoHMMC -c /home/user/models.cm -h /home/user/models.hmm -r /home/user/model.cmcwsresult

E.2 HMMCtoCMC

`HMMCompare` results contain the node intervals of linked models. Since both the `Infernal` covariance models and the `HMMER` hidden markov models have the alignment columns the were derived from annotated, it is possible to map these intervals from a *HMM* to a *CM* of the same family. Here is a example call:
HMMCtoCMC -c /home/user/models.cm -h /home/user/models.hmm -r /home/user/model.cmcwsresult

References

1. Robert D Finn, Jody Clements, and Sean R Eddy. Hmmer web server: interactive sequence similarity searching. *Nucleic acids research*, page gkr367, 2011.
2. Eric P Nawrocki and Sean R Eddy. Infernal 1.1: 100-fold faster RNA homology searches. *Bioinformatics*, 29(22):2933–2935, 2013.
3. Eric P. Nawrocki, Sarah W. Burge, Alex Bateman, Jennifer Daub, Ruth Y. Eberhardt, Sean R. Eddy, Evan W. Floden, Paul P. Gardner, Thomas A. Jones, John Tate, and Robert D. Finn. Rfam 12.0: updates to the rna families database. *Nucleic Acids Research*, 43(D1):D130–D137, 2015.
4. Robert D Finn, Jaina Mistry, Benjamin Schuster-Böckler, Sam Griffiths-Jones, Volker Hollich, Timo Lassmann, Simon Moxon, Mhairi Marshall, Ajay Khanna, Richard Durbin, et al. Pfam: clans, web tools and services. *Nucleic acids research*, 34(suppl 1):D247–D251, 2006.
5. Robert D. Finn, Penelope Coggill, Ruth Y. Eberhardt, Sean R. Eddy, Jaina Mistry, Alex L. Mitchell, Simon C. Potter, Marco Punta, Matloob Qureshi, Amaia Sangrador-Vegas, Gustavo A. Salazar, John Tate, and Alex Bateman. The pfam protein families database: towards a more sustainable future. *Nucleic Acids Research*, 44(D1):D279–D285, 2016.
6. Paul P Gardner, Jennifer Daub, John Tate, Benjamin L Moore, Isabelle H Osuch, Sam Griffiths-Jones, Robert D Finn, Eric P Nawrocki, Diana L Kolbe, Sean R Eddy, et al. Rfam: Wikipedia, clans and the decimal release. *Nucleic acids research*, 39(suppl 1):D141–D145, 2011.
7. Florian Eggenhofer, Ivo L Hofacker, and Christian Höner zu Siederdissen. RNAlien - unsupervised RNA family model construction. *Nucleic Acids Research*, 44(17):8433, 2016.
8. Christian Höner zu Siederdissen and Ivo L Hofacker. Discriminatory power of RNA family models. *Bioinformatics*, 26(18):i453–i459, 2010.
9. Florian Eggenhofer, Ivo L. Hofacker, and Christian Höner zu Siederdissen. CMCompare webserver: comparing RNA families via covariance models. *Nucleic Acids Research*, 41(W1):W499, 2013.
10. Richard Hughey and Anders Krogh. Sam: Sequence alignment and modeling software system. Technical report, Santa Cruz, CA, USA, 1995.
11. Sean R Eddy. Accelerated profile HMM searches. *PLoS Comput Biol*, 7(10):e1002195, 2011.
12. Sarah W Burge, Jennifer Daub, Ruth Eberhardt, John Tate, Lars Barquist, Eric P Nawrocki, Sean R Eddy, Paul P Gardner, and Alex Bateman. Rfam 11.0: 10 years of RNA families. *Nucleic acids research*, page gks1005, 2012.
13. Richard Durbin, Sean R Eddy, Anders Krogh, and Graeme Mitchison. *Biological sequence analysis: probabilistic models of proteins and nucleic acids.* Cambridge university press, 1998.
14. Björn A. Grüning, Jörg Fallmann, Dilmurat Yusuf, Sebastian Will, Anika Erxleben, Florian Eggenhofer, Torsten Houwaart, Bèrènice Batut, Pavankumar Videm, Andrea Bagnacani, Markus Wolfien, Steffen C. Lott, Youri Hoogstrate, Wolfgang R. Hess, Olaf Wolkenhauer, Steve Hoffmann, Altuna Akalin, Uwe Ohler, Peter F. Stadler, and Rolf Backofen. The RNA workbench: best practices for RNA and high-throughput sequencing bioinformatics in galaxy. *Nucleic Acids Research*, 45(W1):W560–W566, 2017.
15. Rolf Backofen, Jan Engelhardt, Anika Erxleben, Jörg Fallmann, Björn Grüning, Uwe Ohler, Nikolaus Rajewsky, and Peter F Stadler. RNA-bioinformatics: Tools,

services and databases for the analysis of RNA-based regulation. *Journal of Biotechnology*, 2017.

16. Peter Kerpedjiev, Stefan Hammer, and Ivo L Hofacker. Forna (force-directed RNA): simple and effective online RNA secondary structure diagrams. *Bioinformatics*, page btv372, 2015.
17. Zasha Weinberg and Ronald R. Breaker. R2R - software to speed the depiction of aesthetic consensus RNA secondary structures. *BMC Bioinformatics*, 12(1):3, 2011.

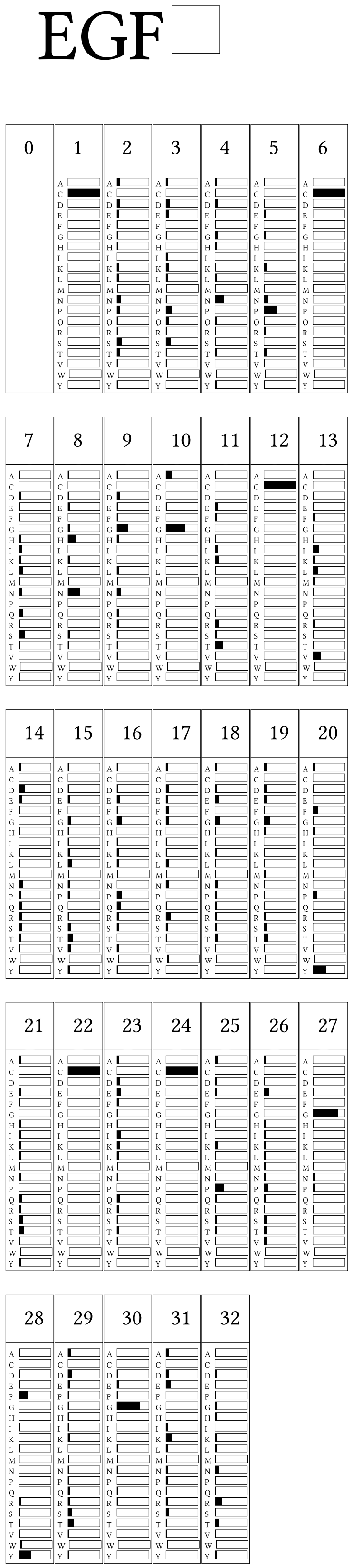

Fig. 4. Simple detail *EGF* `Pfam` family visualisation, showing nodes with their index and emission probabilities.

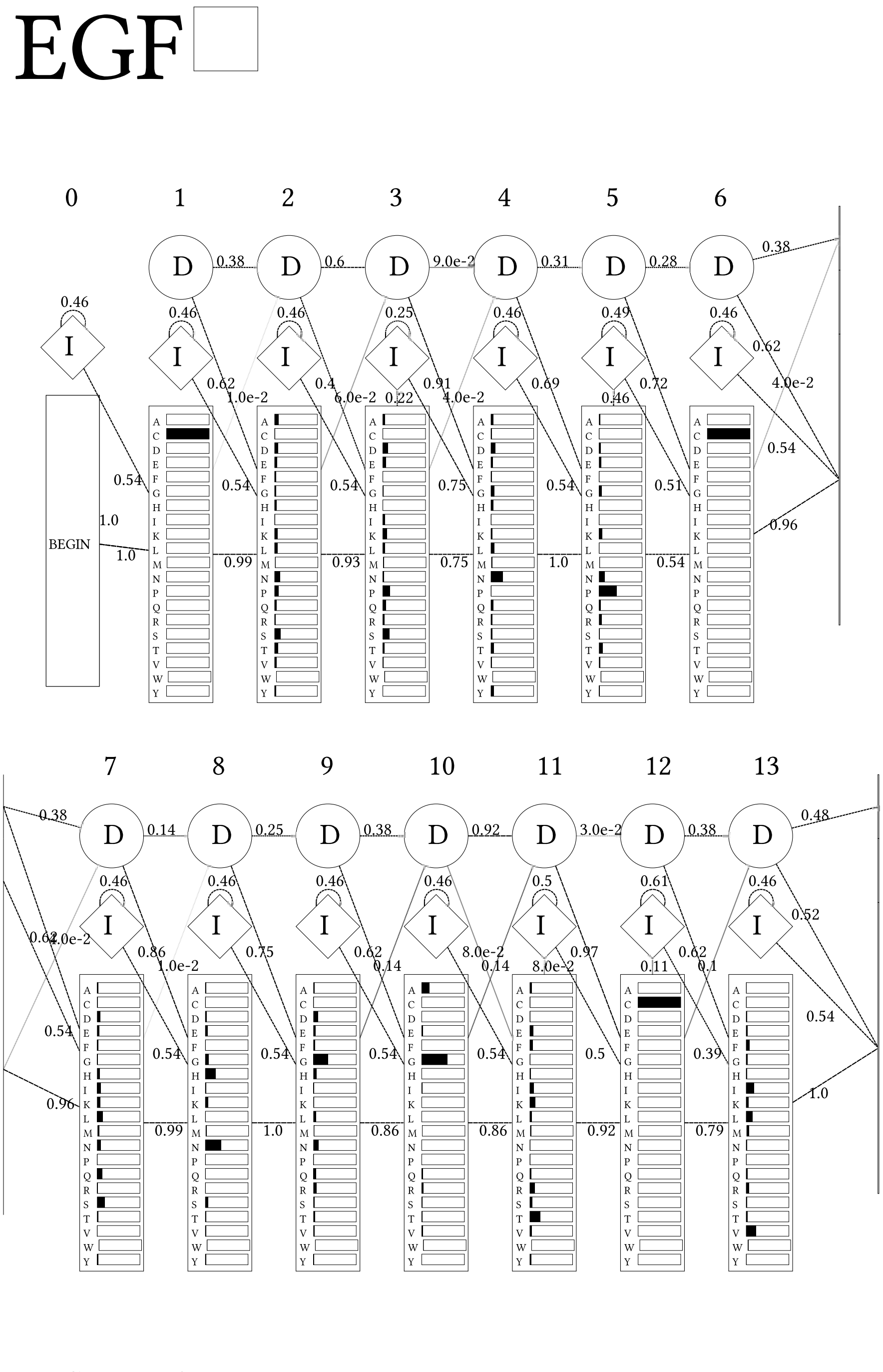

Fig. 5. Detailed *EGF* `Pfam` family visualisation, showing nodes with insertion, deletion and match states and emission and transition probabilities. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability - Part 1

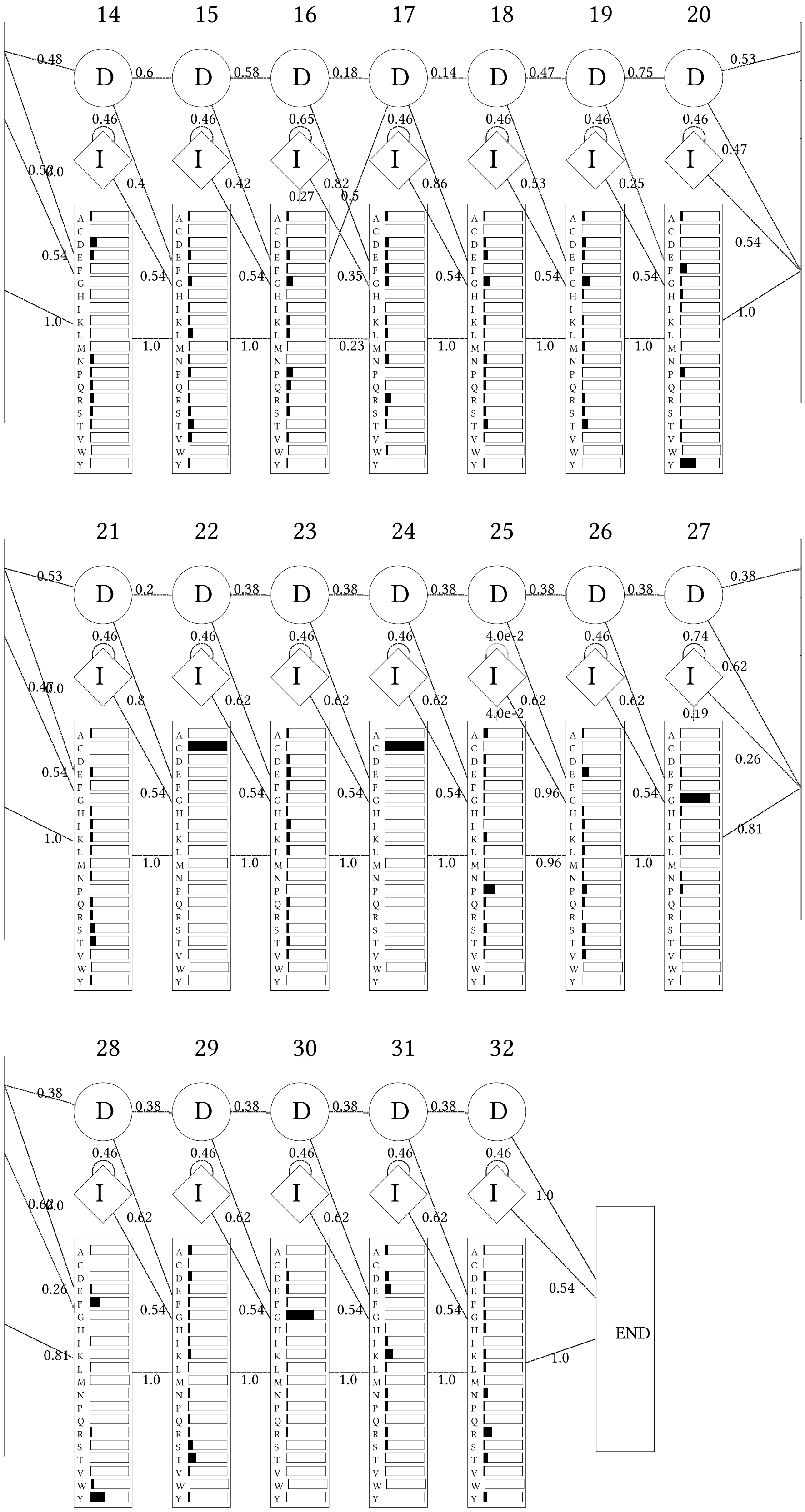

Fig. 6. Detailed *EGF* `Pfam` family visualisation, showing nodes with insertion, deletion and match states and emission and transition probabilities. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability - Part 2

```
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                            12345678901234567890123456789012345678901234567890
BM86_RHIMP/209-245          CKTKEAGFVCKHG....C...RSTG.....KAYECTCP.SGSTVAEDGIT
AGRIN_CHICK/1351-1381       CDS..HP..CLHGGT..C...EDDG.....REFTCRCP.AG....KGGAV
A4V346_DROME/260-287        CVL..EPN.CIHGT...C...........NKPWTCICN.EG....WGGLY
PROS_BOVIN/121-153          CNP..LP..CNEDGFMTC...KDGQ.....ATFTCICK.SG....WQGEK
CRB_DROME/1209-1239         CKP..NP..CHSNGE..C...TDLW.....HTFACHCP.RP....FFGHT
CRB_DROME/1483-1513         CRK..NP..CLHNAE..C...RNTW.....NDYTCKCP.NG....YKGKN
SLIT_DROME/1052-1084        CSPEFNP..CANGAK..C...MDHF.....THYSCDCQ.AG....FHGTN
O01768_CAEEL/4584-4614      CDD.....YCTNNSK..C..TITNG.....THFECDCK.PG....FKGLR
CRB_DROME/982-1017          CDQ..NP..CLNGGA..C...LPYLINEVTHLYNCTCE.NG....FQGDK
MFGM_MOUSE/68-106           CSP..NP..CYNDAK..CLVTLDTQRGDIFTEYICQCP.VG....YSGIH
M9NE67_DROME/871-903        CAS..NR..CKNEAK..C...TPSS...NFLDFSCTCK.LG....YTGRY
NOTC1_XENLA/62-97           CTIK.NQ..CMNFGT..C....EPVLQGNAIDFICHCP.VG....FTDKV
URT2_DESRO/87-119           CSE..LR..CFNGGT..C...WQAA...SFSDFVCQCP.KG....YTGKQ
M9NE67_DROME/100-134        CNS..MR..CQNGGT..CQVTFRNG....RPGISCKCP.LG....FDESL
CRB_DROME/547-577           CNA..TNGKCLNGGT..C..........SMNGTHCYCA.VG....YSGDR
NOTC1_XENLA/260-290         CPS..NN..CRNGGT..C...VDGV.....NTYNCQCP.PD....WTGQY
CRB_DROME/390-421           CAS..QP..CQNNGS..C...IDRI.....NGFSCDCSGTG....YTGAF
PROC_BOVIN/98-127           CD...LP..CCGRGK..C...IDGL.....GGFRCDCA.EG....WEGRF
LYAM1_HUMAN/160-190         C....QPWSCSGHGE..C...VEII.....NNYTCNCD.VG....YYGPQ
NOTC1_XENLA/1270-1302       CLS..NP..CDSRGTQNC...IQLV.....NDYRCECR.QG....FTGRR
NOTC1_XENLA/22-55           CTQ..TAEMCLNGGR..C...EMTP....GGTGVCLCG.NL....YFGER
O01768_CAEEL/4544-4577      CQK..QPNWCHNGGR..C...LDTP....GYPGKCKCL.PR....FAGPR
CRB_DROME/308-339           CAK..NP..CENGGS..C...LENS....RGDYQCFCD.PN....HSGQH
CRB_DROME/1993-2025         CNM..EGDYCGGLGR..C...FNKP.....GSFQCICQ.KP....YCGAY
LTBP1_HUMAN/877-908         CTV..NPDIC.GAGH..C...INLP.....VRYTCICY.EG....YRFSE
LTBP1_HUMAN/1625-1655       CGIL.NG..CE.NGR..C...VRVQ.....EGYTCDCF.DG....YHLDT
M9NE67_DROME/413-445        CTS..NP..CHADAI..C...DTSP...INGSYACSCA.TG....YKGVD
CRB_DROME/269-299           CLN..DP..CMGHGT..C...SSSP.....EGYECRCT.AR....YSGKN
FBP2_STRPU/111-147          CLS..DTSNCDGHGI..C....QLSTFGRNERYICFCA.LG....FRNNN
CRB_DROME/1760-1790         CFQ..SD..CKNDGF..C...QSPS.....DEYACTCQ.PG....FEGDD
TRBM_BOVIN/143-172          CFD..NN..CEYQ....C...QPVG....RSEHKCICA.EG....FAPVP
SLIT_DROME/935-966          CFE..QP..CQNQAQ..C...VALP....QREYQCLCQ.PG....YHGKH
CRB_DROME/2032-2066         CNA..TD.LCSNGGR..C...VESC..GAKPDYYCECP.EG....FAGKN
TSP1_HUMAN/650-686          CTD..GTHDCNKNAK..C....NYLGHYSDPMYRCECK.PG....YAGNG
NID1_HUMAN/672-705          CYI..GTHGCDTNAA..C...RPGP....RTQFTCECS.IG....FRGDG
NID1_HUMAN/390-422          CAN..NRHQCSVHAE..C...RDYA.....TGFCCSCV.AG....YTGNG
EGF_HUMAN/835-865           CAP..VG..CSMYAR..C...ISEG.....EDATCQCL.KG....FAGDG
O01768_CAEEL/4621-4650      CSE......CSNEAK..C...IKKP....SGTVICQCP.QG....LGGEY
AGRIN_CHICK/1607-1638       CDP..TP..CHISAT..C...LVLP....EGGAMCACP.MG....REGEF
EGF_HUMAN/318-353           CKL..RKGNCSSTV...C...GQDL.....QSHLCMCA.EGYALSRDRKY
EGF_HUMAN/401-435           CPR..NVSECSHD....C...VLTS.....EGPLCFCP.EGSVLERDGKT
LRP5_MOUSE/298-334          CEE..DNGGCSHL....C...LLSP...REPFYSCACP.TGVQLQDNGKT
LRP5_MOUSE/1216-1247        CAR..DNGGCSHI....C...IAKG....DGTPRCSCP.VH....LVLLQ
LRP5_MOUSE/604-638          CAD..GNGGCSHL....C...FFTP.....RATKCGCP.IGLELLSDMKT
A0A024R7D5_HUMAN/318-351    CLD..NNGGCSHV....C...NDLK.....IGYECLCP.DGFQL.VAQRR
O01768_CAEEL/3122-3155      CPK..AN..CSHF....C...IDRR....DVGHQCFCA.PGYILSENQKD
FBP2_STRPU/256-288          CSQ..GTNDCNENGE..C...VEED.....GKYWCECG.EG....YEENE
FBP2_STRPU/52-89            CES..DTNKCNNHGT..C...IEGR....WGTYYCKCE.MPFRVGIPDSS
LTBP1_RAT/1462-1496         CQ...DPNSCIDGQ...C...VNTE.....GSYNCFCT.HPMVLDASEKR
CRB_DROME/1916-1946         CEI..TP..CDNGGL..C...LTTG.....AVPMCKCS.LG....YTGRL
SS_cons                     GCST.TTTSSTTT-E..E...EEET...TTTEEEEEECTTT....EESTT
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Fig. 7. EGF Pfam family alignment visualisation, the number of alignment entries can be set via option. The displayed column indices allow association with the corresponding nodes in the model.

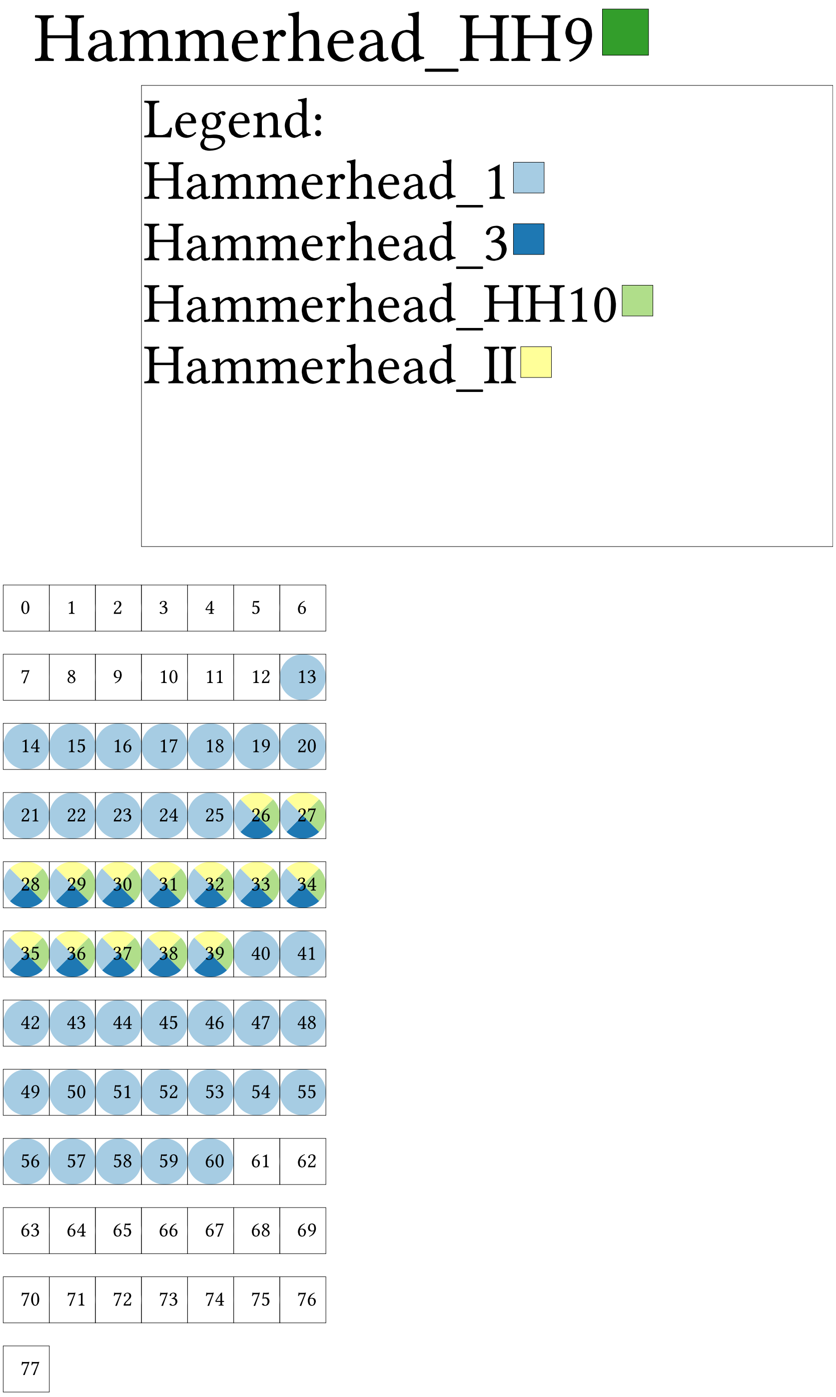


Fig. 8. Minimal detail `HMMCV` visualisation of *Hammerhead_HH9* with linked nodes highlighted by color. Families corresponding to the color can be looked up in the legend.

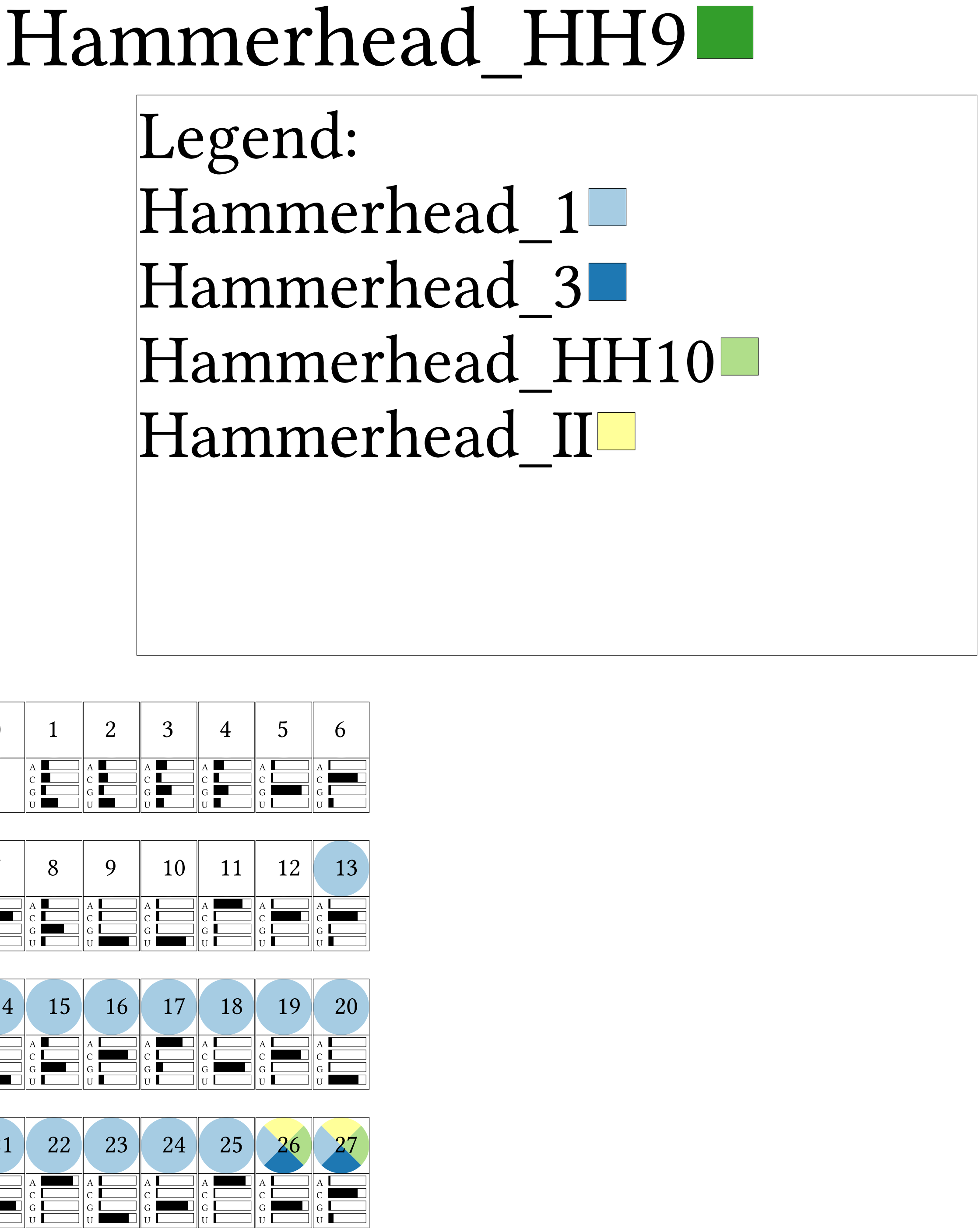


Fig. 9. Simple detail `HMMCV` visualisation of *Hammerhead_HH9* family, showing nodes with their index and emission probabilities. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part 1.

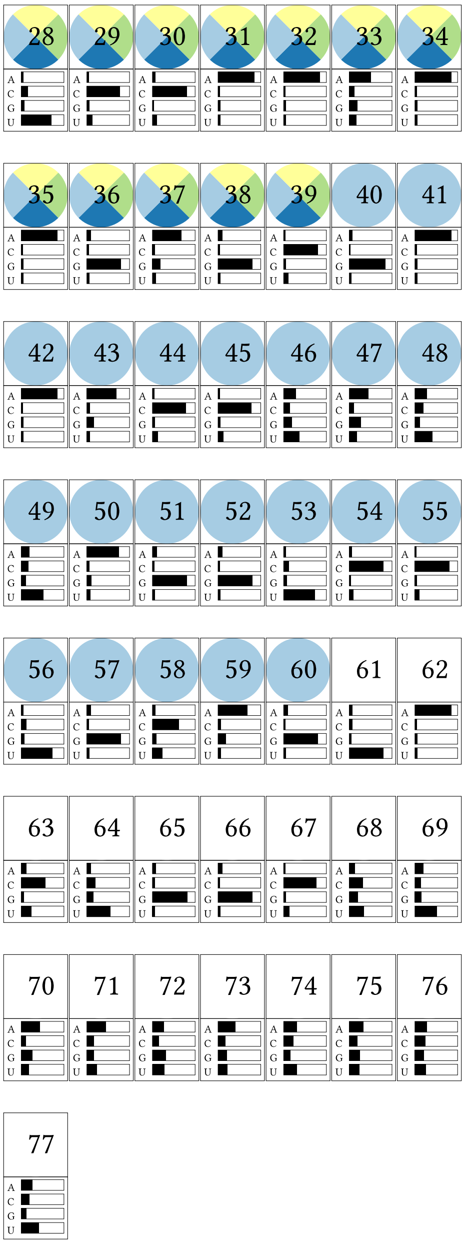


Fig. 10. Simple detail `HMMCV` visualisation of *Hammerhead_HH9* family, showing nodes with their index and emission probabilities. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part 2.

Hammerhead_HH9 🟩

Legend:

Hammerhead_1 🟦

Hammerhead_3 🟦

Hammerhead_HH10 🟩

Hammerhead_II 🟨

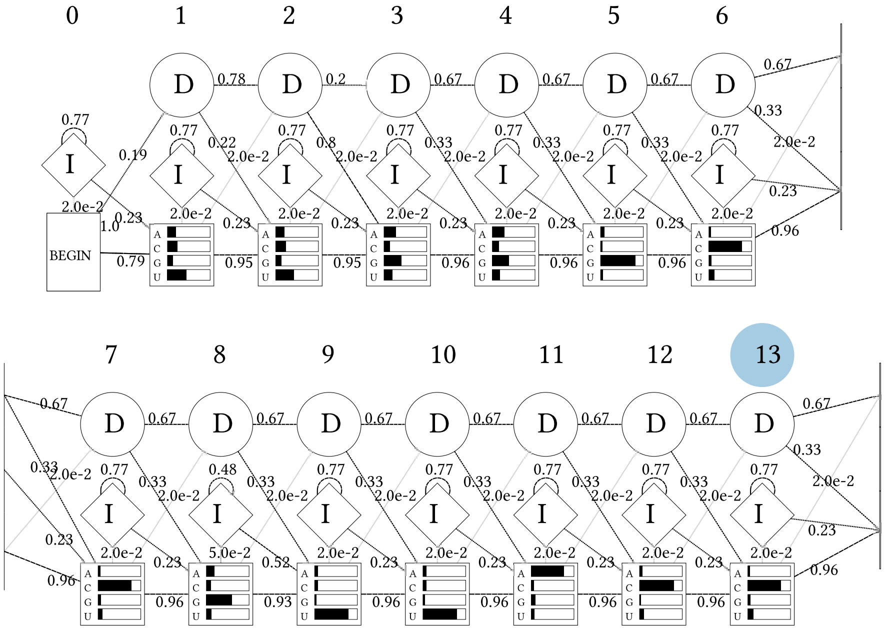


Fig. 11. Detailed `HMMCV` visualisation of *Hammerhead_HH9* family visualisation, showing nodes with insertion, deletion and match states and emission and transition probabilities. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part1.

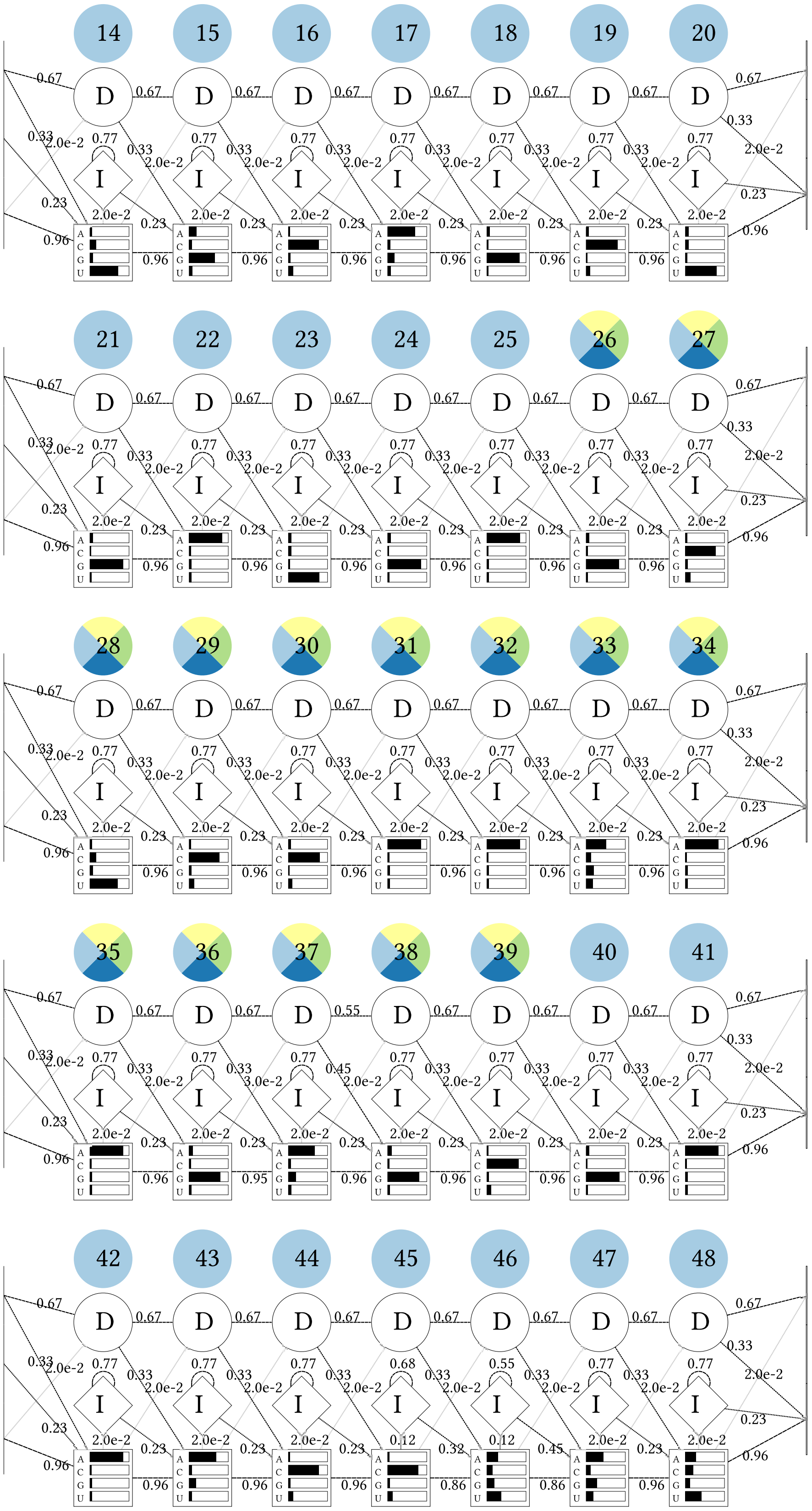


Fig. 12. Detailed `HMMCV` visualisation of *Hammerhead_HH9* family visualisation, showing nodes with insertion, deletion and match states and emission and transition probabilities. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part2.

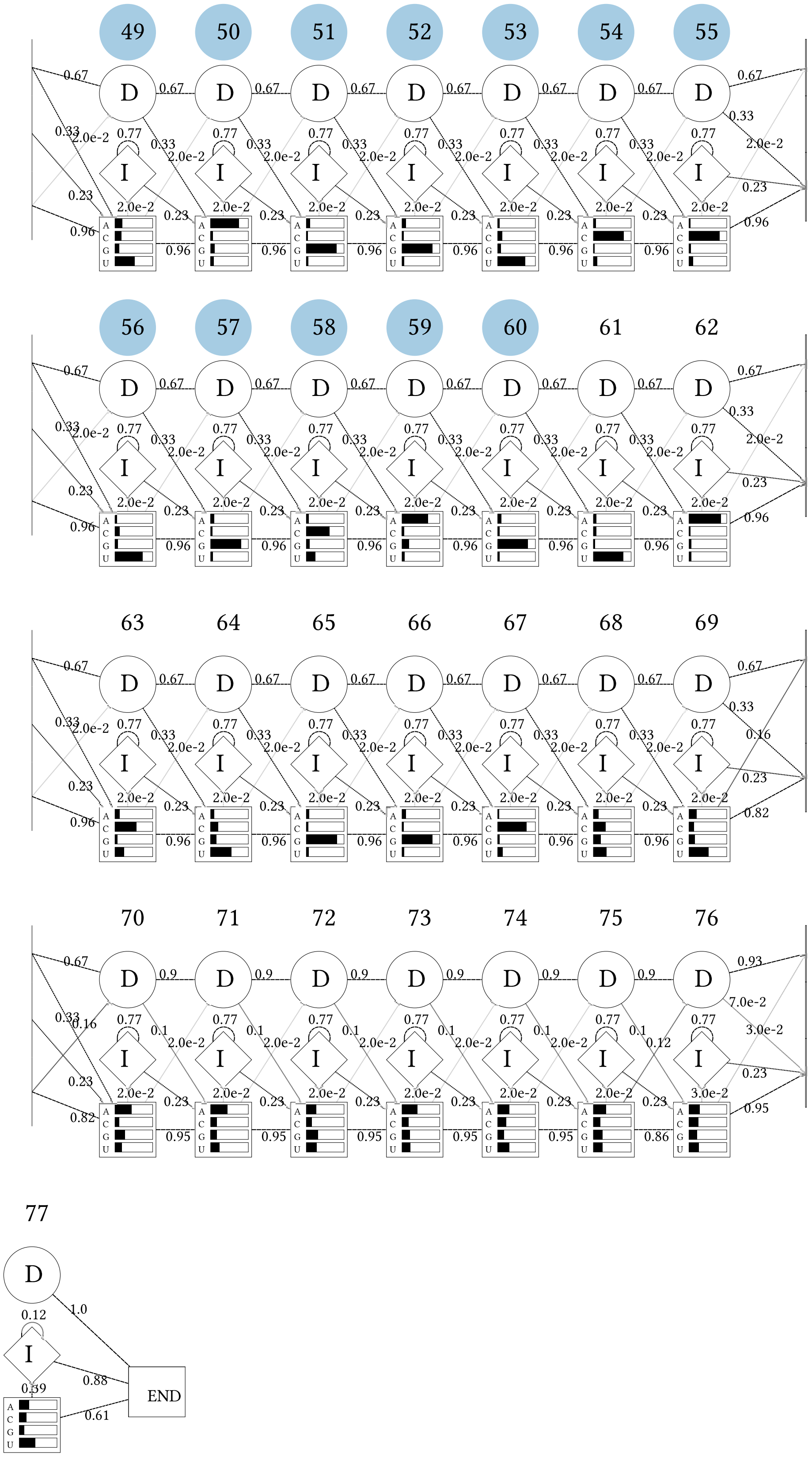
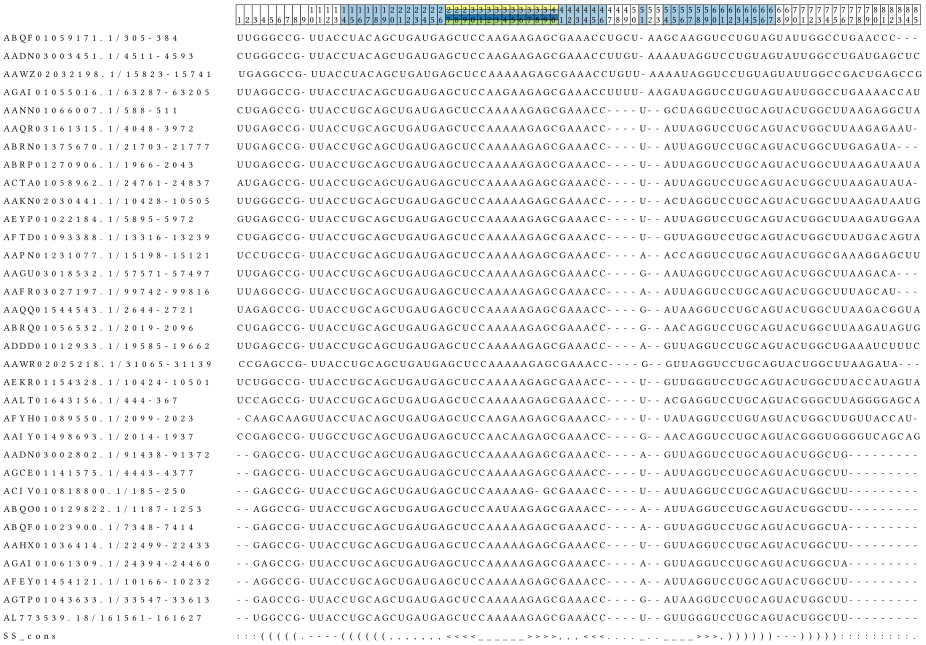


Fig. 13. Detailed `HMMCV` visualisation of *Hammerhead_HH9* family visualisation, showing nodes with insertion, deletion and match states and emission and transition probabilities. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part3.



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AL773539.18/161561-161627      --UGGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----U--GUUGGGUCCUGCAGUACUGGCUU---------
SS_cons                        :::(((((.----((((((,,,,,,,<<<<______>>>>,,,<<<...._.____>>>,))))))---))))):::::::::.
```

Fig. 14. *Hammerhead_HH9* `Rfam` family alignment visualisation, the number of alignment entries can be set via option. The displayed column indices allow association with the corresponding nodes in the model. The consensus secondary structure is shown in the last line.

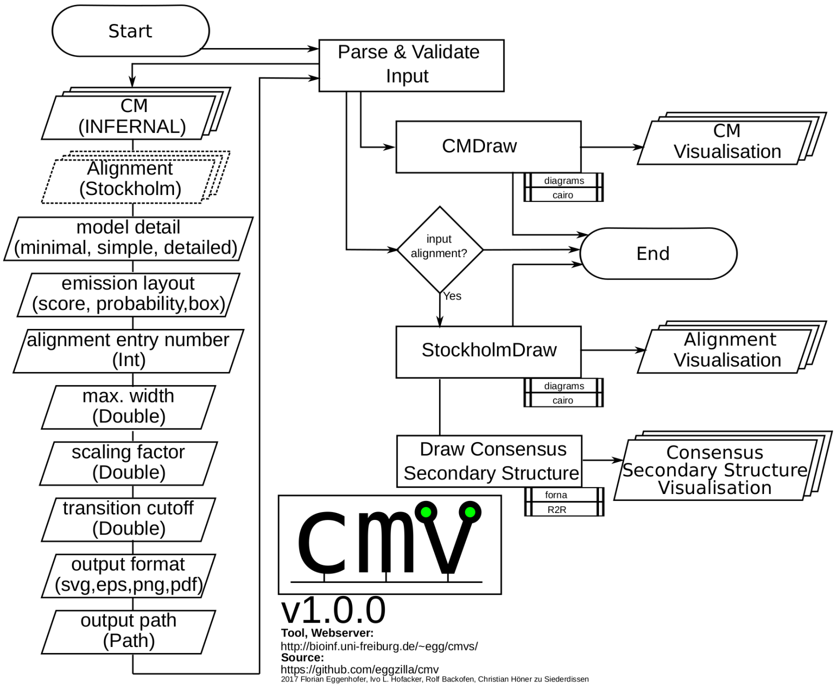


Fig. 15. Detailed flowchart representation of `CMV`, showing options on the left, processing in the center and output on the right.

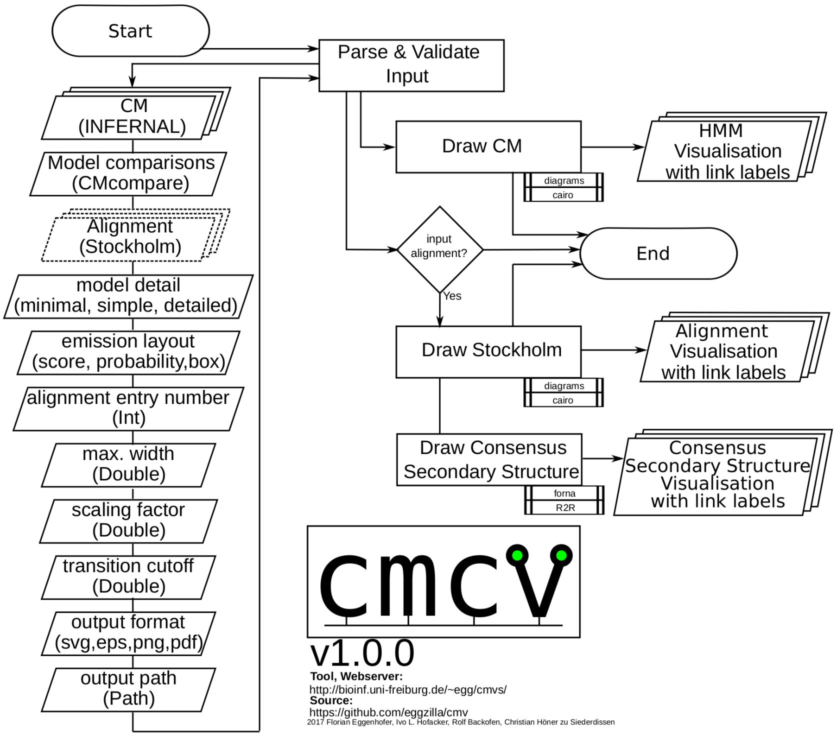


Fig. 16. Detailed flowchart representation of `CMCV`, showing options on the left, processing in the center and output on the right.

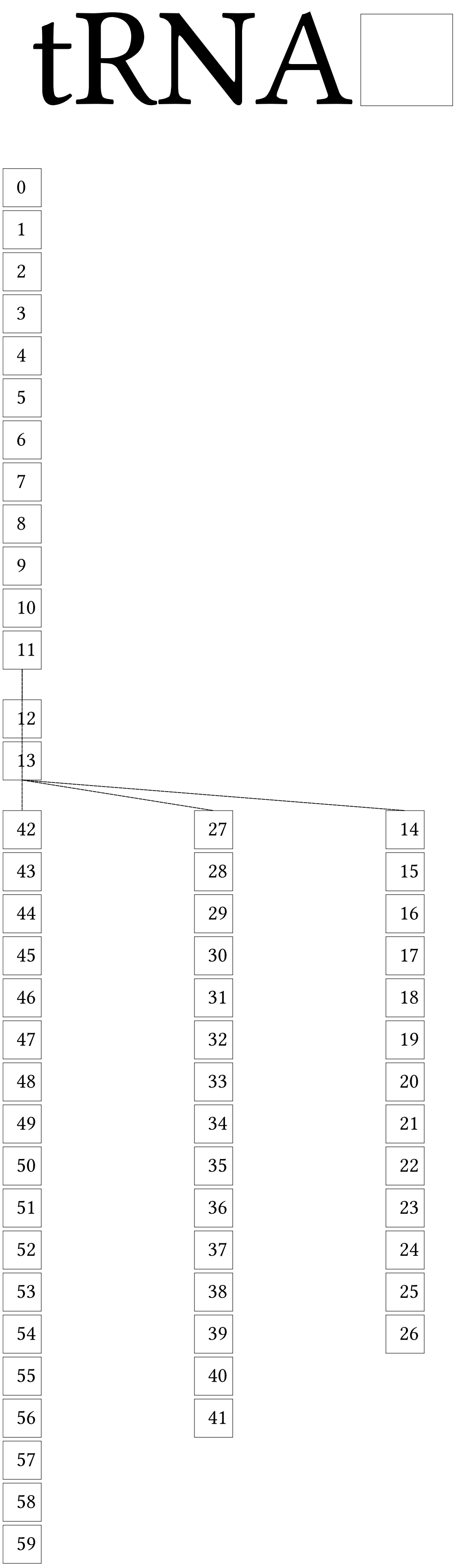


Fig. 17. Minimal tRNA `Rfam` family visualisation, showing model nodes with their index arranged according to guide tree.

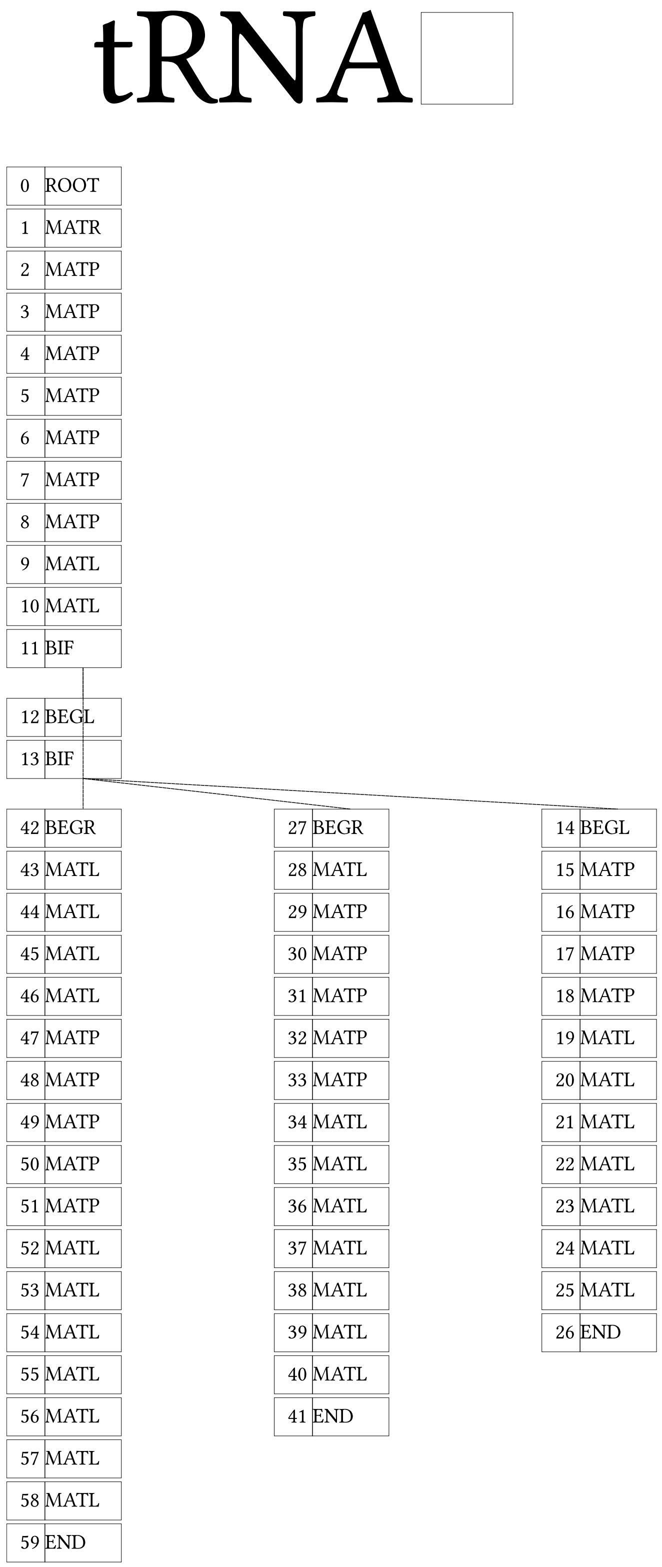


Fig. 18. Simple tRNA `Rfam` family visualisation, showing model nodes, labeled with node type and index, arranged according to guide tree.

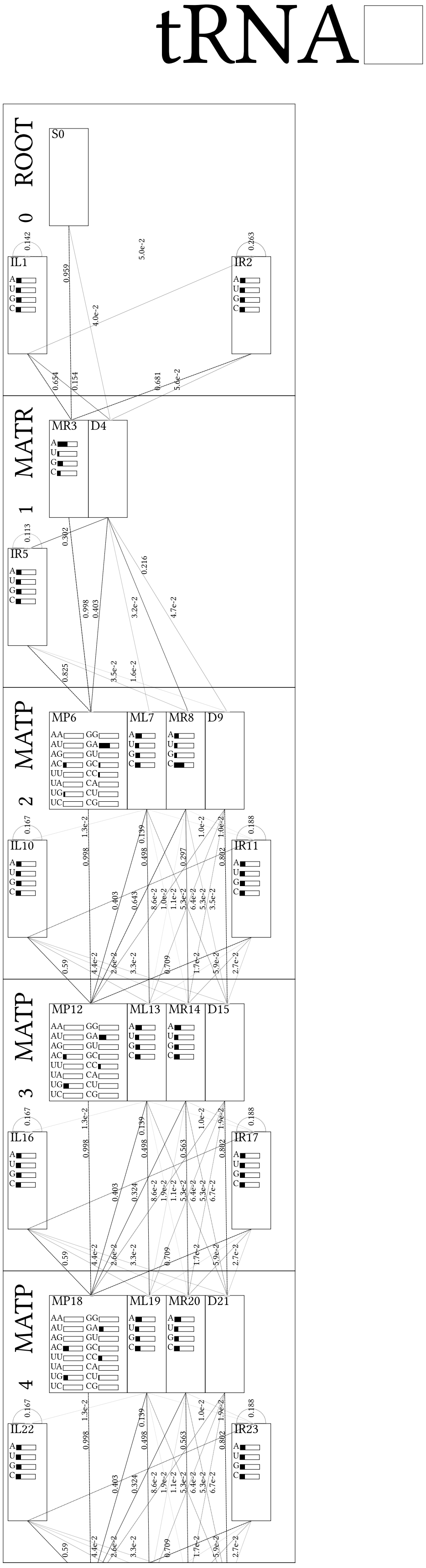


Fig. 19. Detailed tRNA `Rfam` family visualisation, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability - Part 1

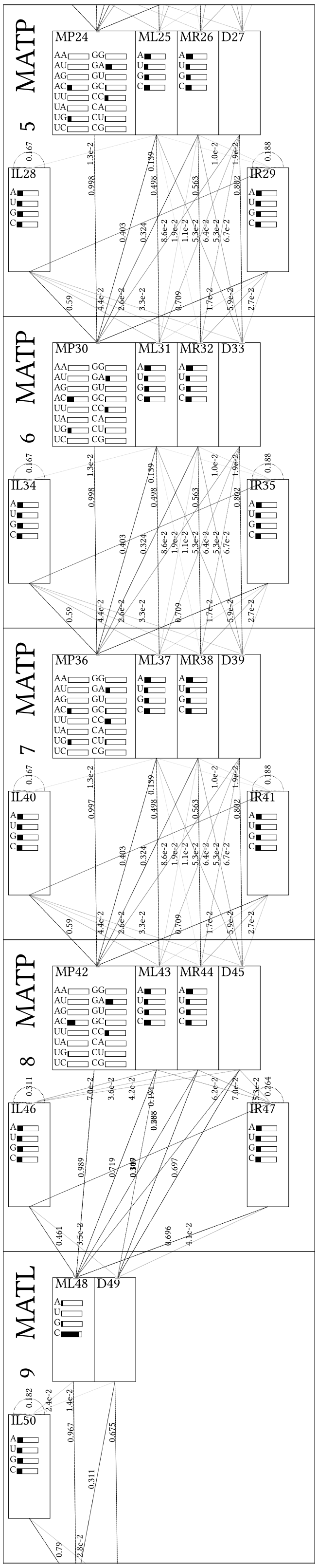


Fig. 20. Detailed tRNA `Rfam` family visualisation, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability - Part 2

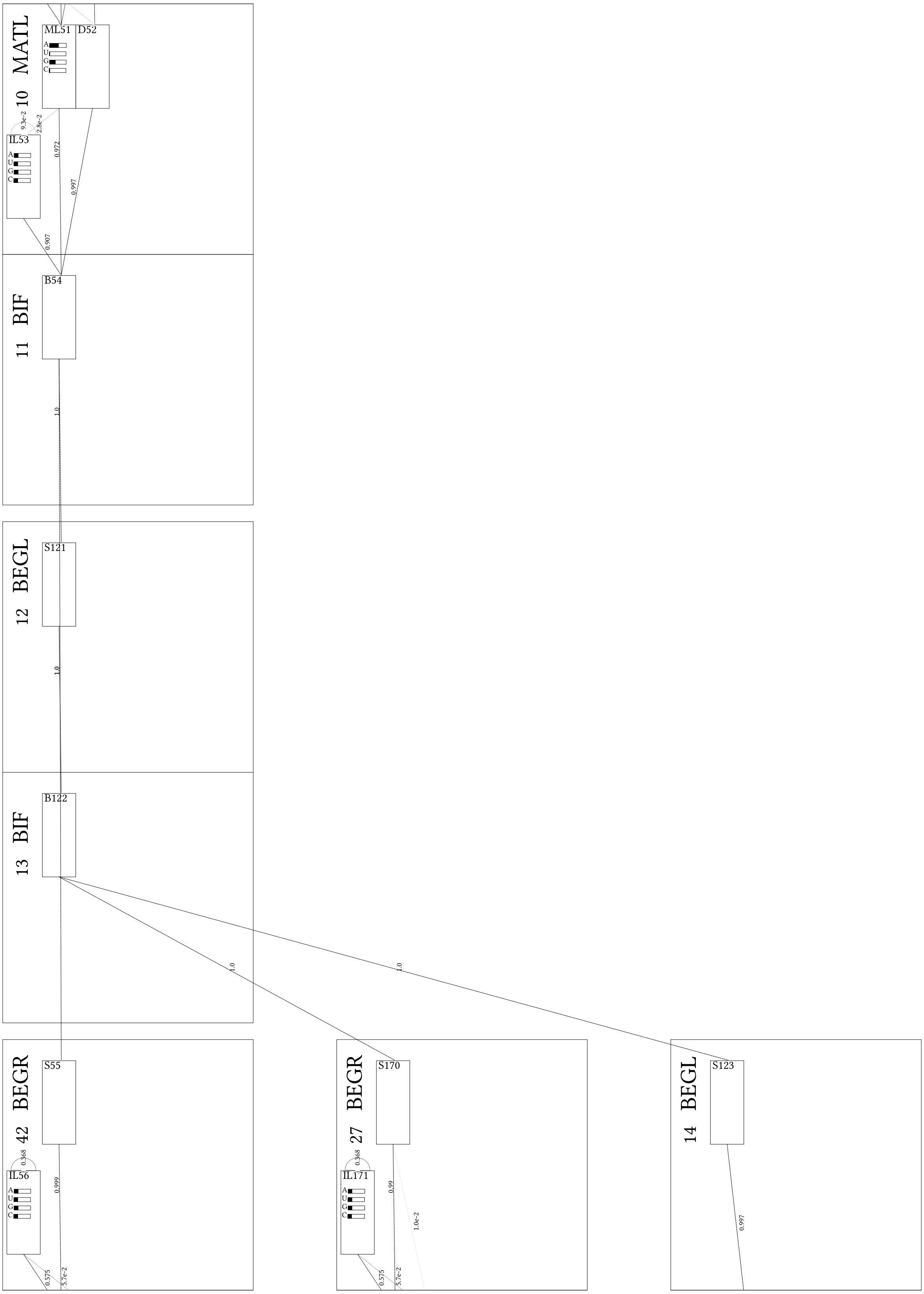


Fig. 21. Detailed tRNA `Rfam` family visualisation, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability - Part 3

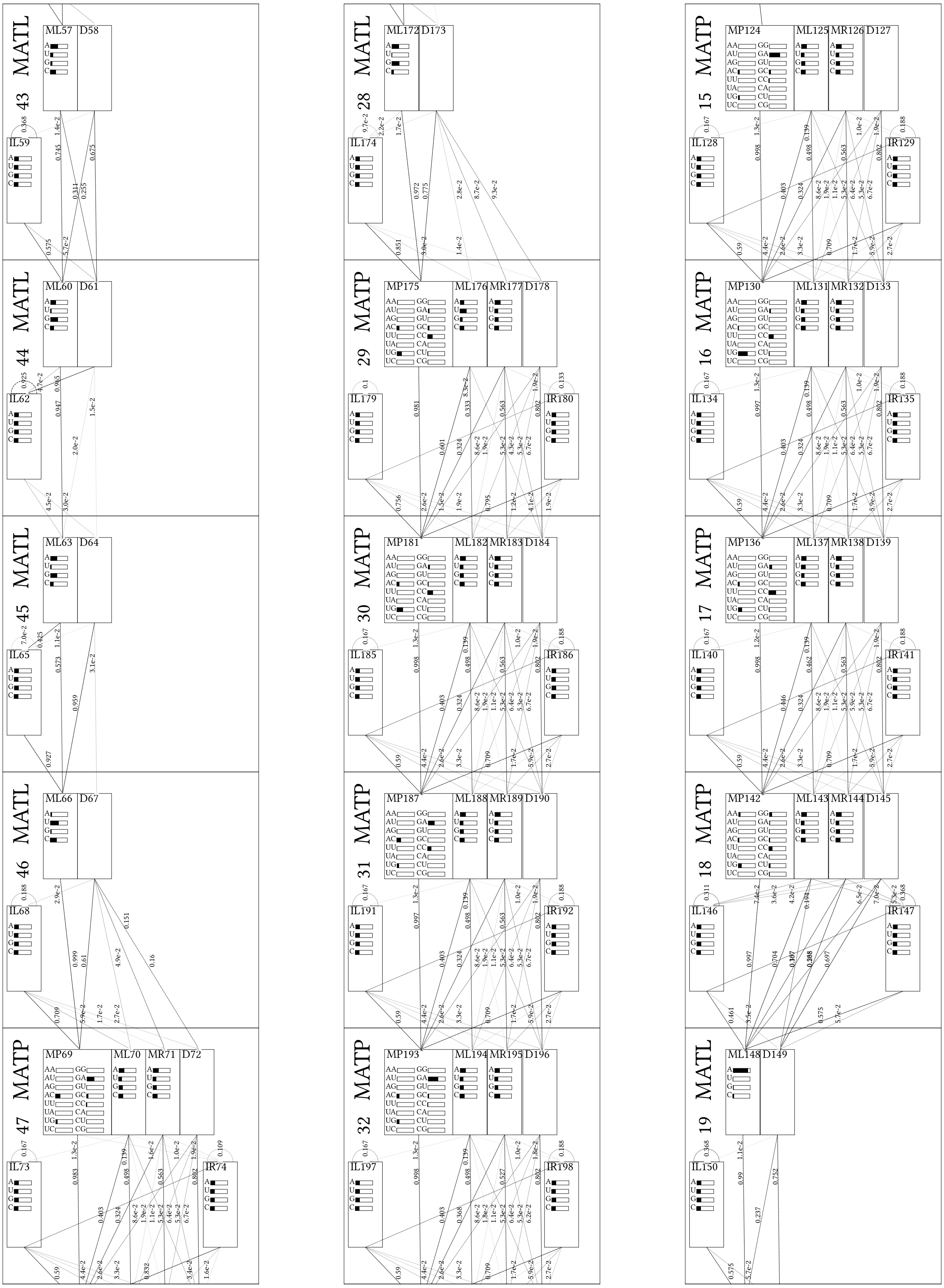


Fig. 22. Detailed tRNA `Rfam` family visualisation, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability - Part 4

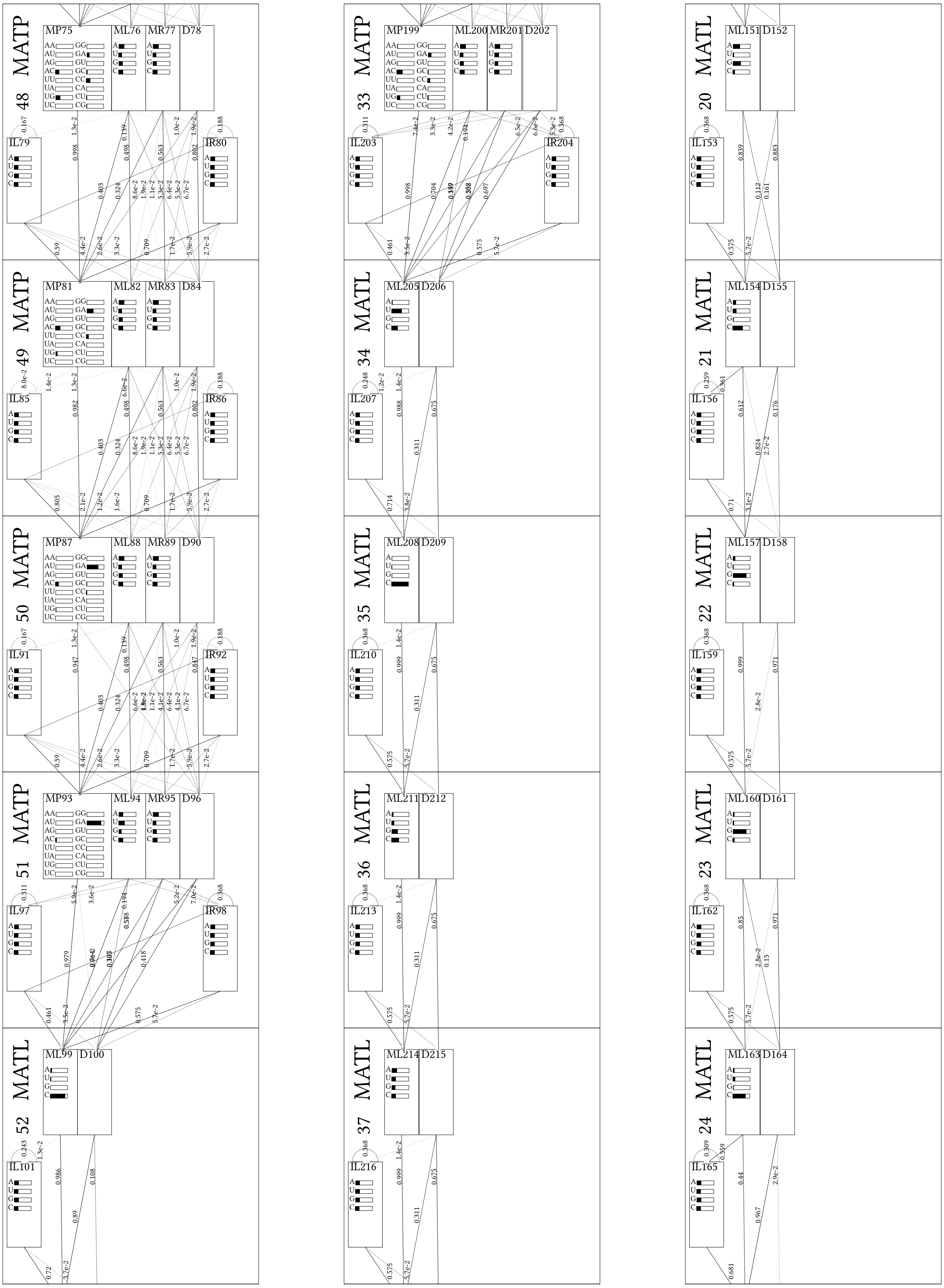


Fig. 23. Detailed tRNA `Rfam` family visualisation, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability - Part 5

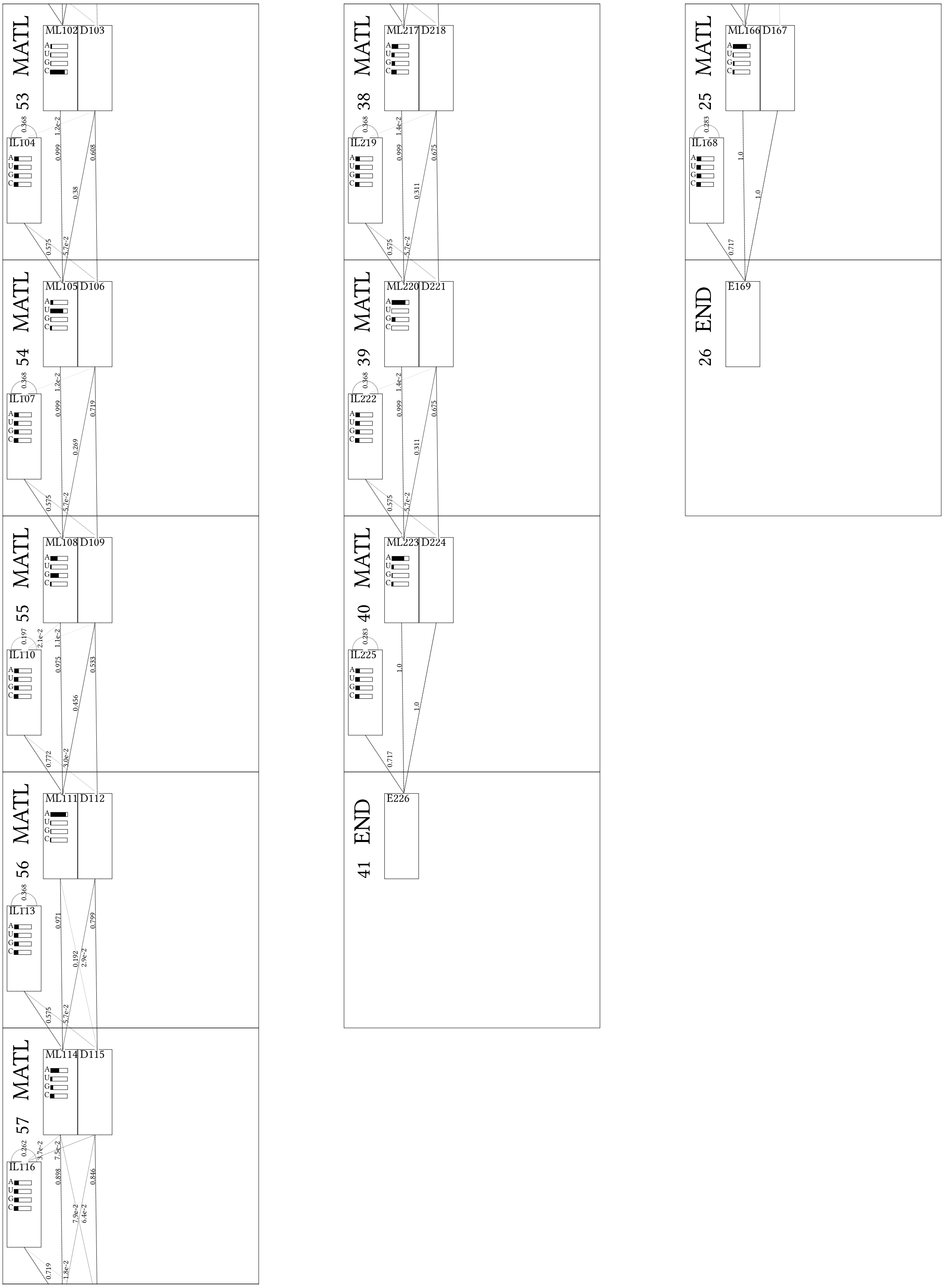


Fig. 24. Detailed tRNA `Rfam` family visualisation, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability - Part 6

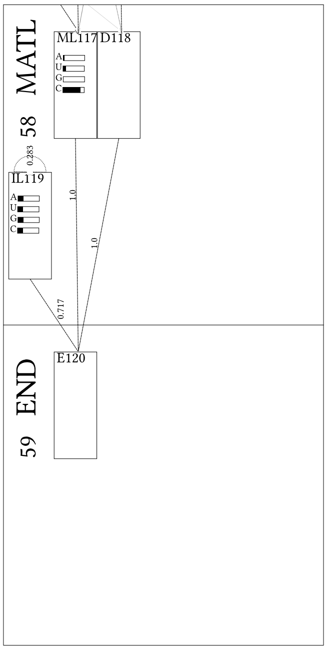
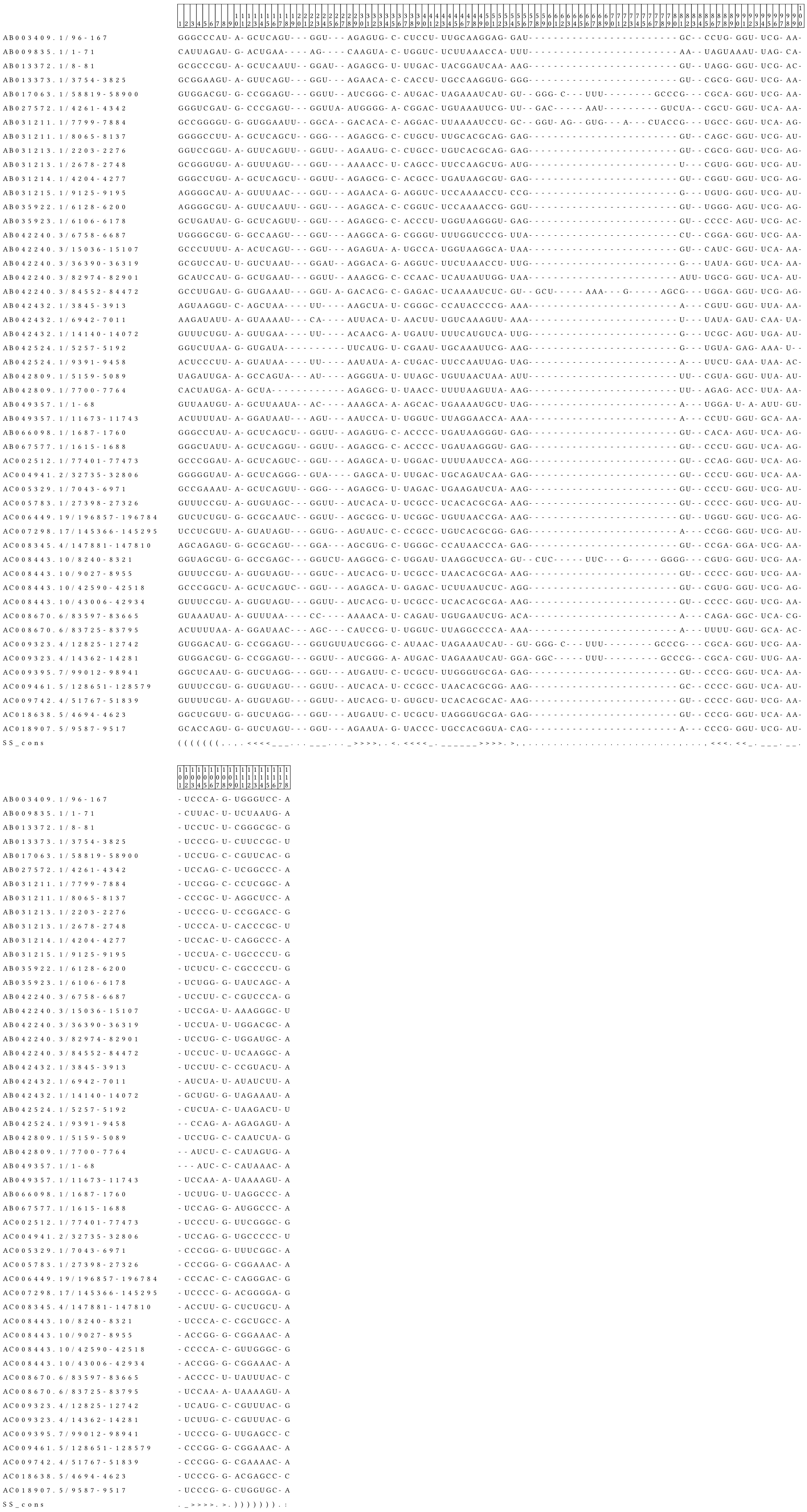


Fig. 25. Detailed tRNA `Rfam` family visualisation, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability - Part 7



```
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AB031213.1/2203-2276       GGUCCGGU-A-GUUCAGUU--GGUU--AGAAUG-C-CUGCC-UGUCACGCAG-GAG------------------------GU--CGCG-GGU-UCG-AG-
AB031213.1/2678-2748       GCGGGUGU-A-GUUUAGU---GGU---AAAACC-U-CAGCC-UUCCAAGCUG-AUG------------------------U---CGUG-GGU-UCG-AU-
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AB035923.1/6106-6178       GCUGAUAU-G-GCUCAGUU--GGU---AGAGCG-C-ACCCU-UGGUAAGGGU-GAG------------------------GU--CCCC-AGU-UCG-AC-
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AC009742.4/51767-51839     GUUUUCGU-A-GUGUAGU---GGUU--AUCACG-U-GUGCU-UCACACGCAC-AAG------------------------GU--CCCC-GGU-UCG-AA-
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AB042432.1/14140-14072     -GCUGU-G-UAGAAAU-A
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AB067577.1/1615-1688       -UCCAG-G-AUGGCCC-A
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AC018638.5/4694-4623       -UCCCG-G-ACGAGCC-C
AC018907.5/9587-9517       -UCCCG-G-CUGGUGC-A
SS_cons                    ._>>>>.>.))))))).:
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Fig. 26. tRNA Rfam family alignment visualisation, the number of alignment entries can be set via option. The displayed column indices allow association with the corresponding nodes in the model. The consensus secondary structure is shown in the last line.

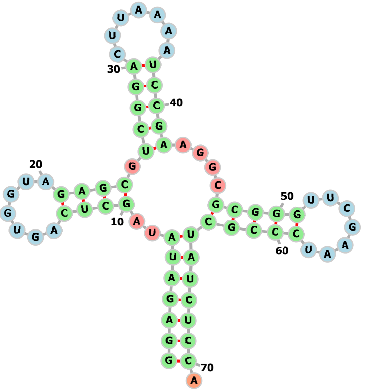


Fig. 27. Consensus secondary structure visualisation for tRNA with `forna`

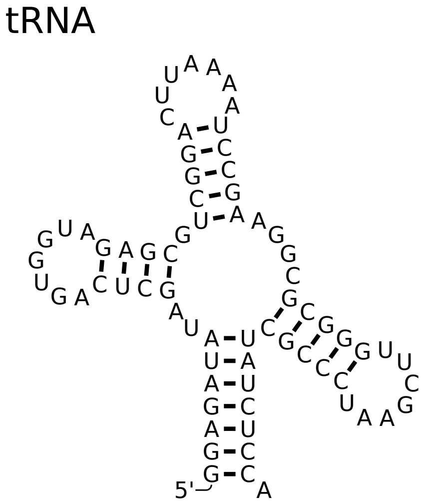


Fig. 28. Consensus secondary structure visualisation for tRNA with `R2R`

Fig. 29. Minimal detail `CMCV` visualisation of *Hammerhead_HH9*, showing model nodes with their index arranged according to guide tree.

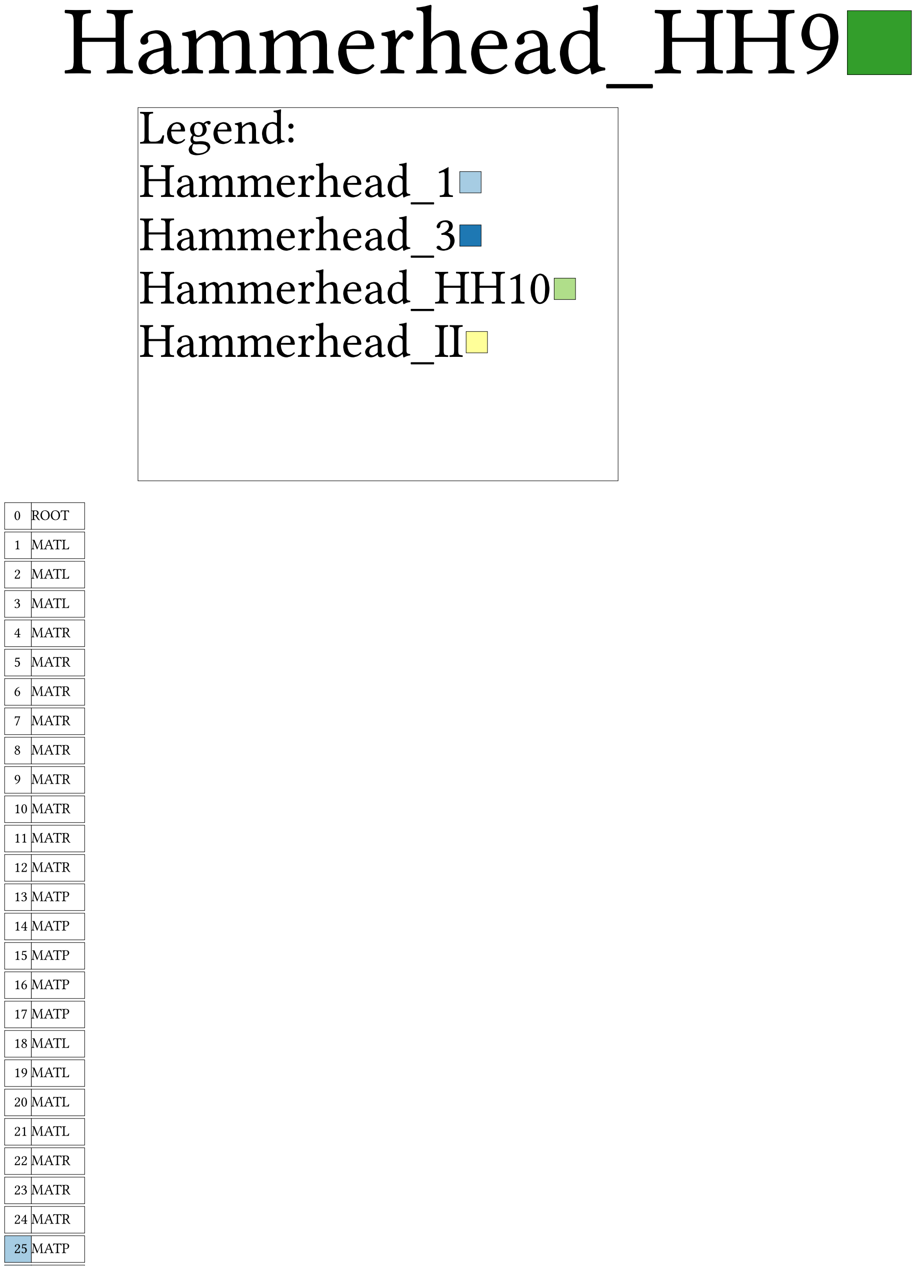


Fig. 30. Simple detail `CMCV` visualisation of *Hammerhead_HH9*, showing model nodes, labeled with node type and index, arranged according to guide tree - Part 1

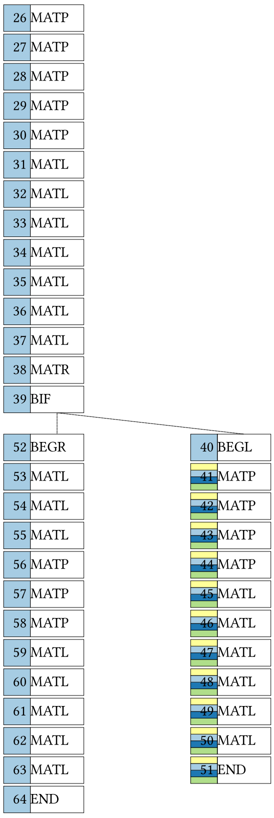


Fig. 31. Simple detail `CMCV` visualisation of *Hammerhead_HH9*, showing model nodes, labeled with node type and index, arranged according to guide tree - Part 2

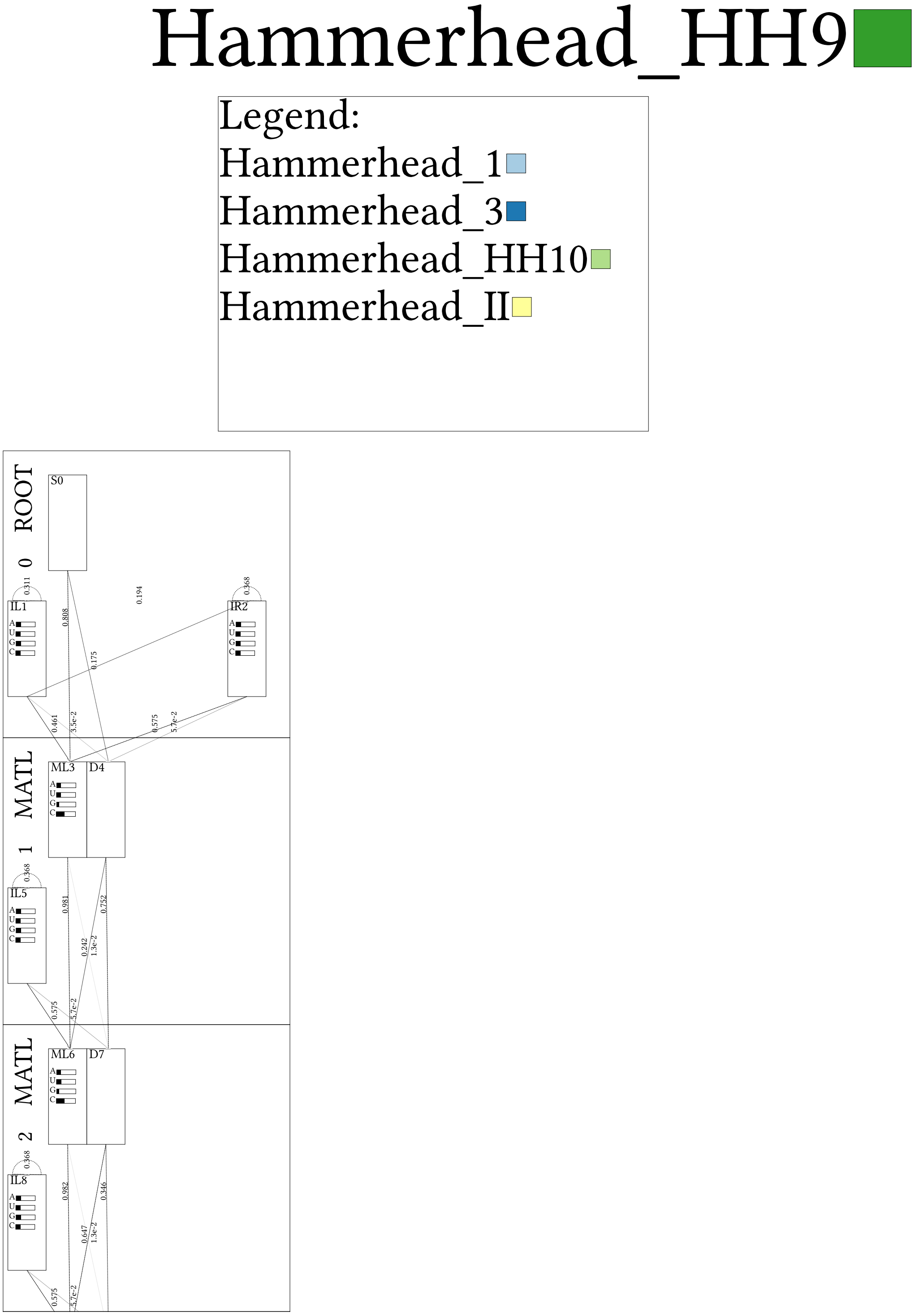


Fig. 32. Detailed `CMCV` visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part1.

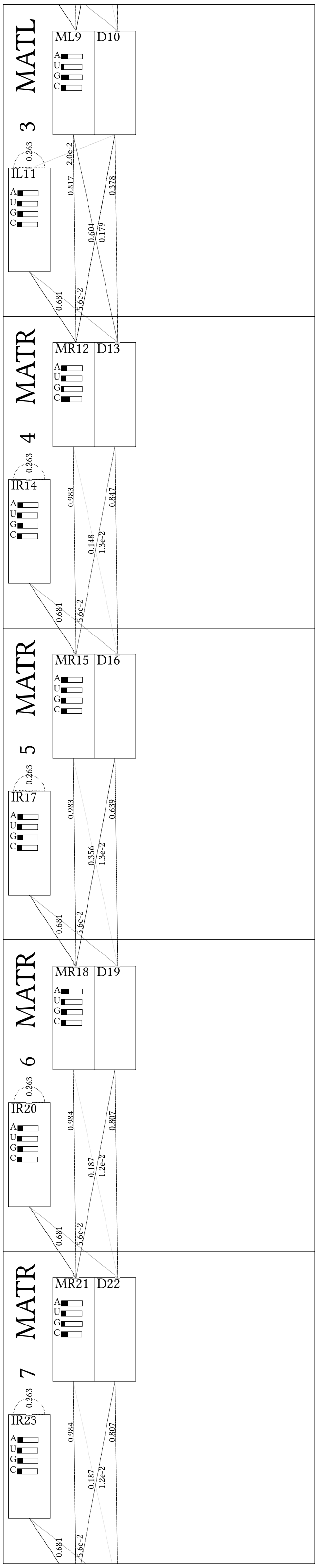


Fig. 33. Detailed `CMCV` visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part2.

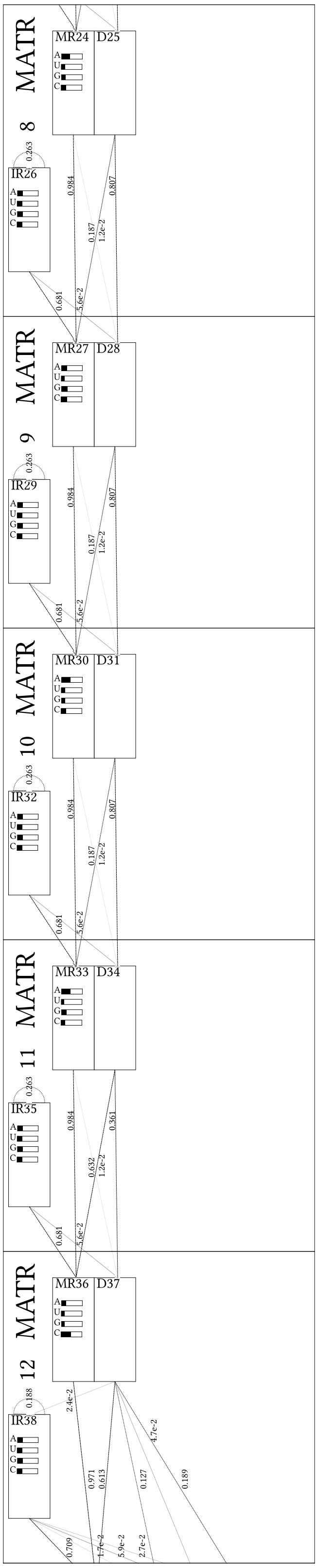


Fig. 34. Detailed CMCV visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part3.

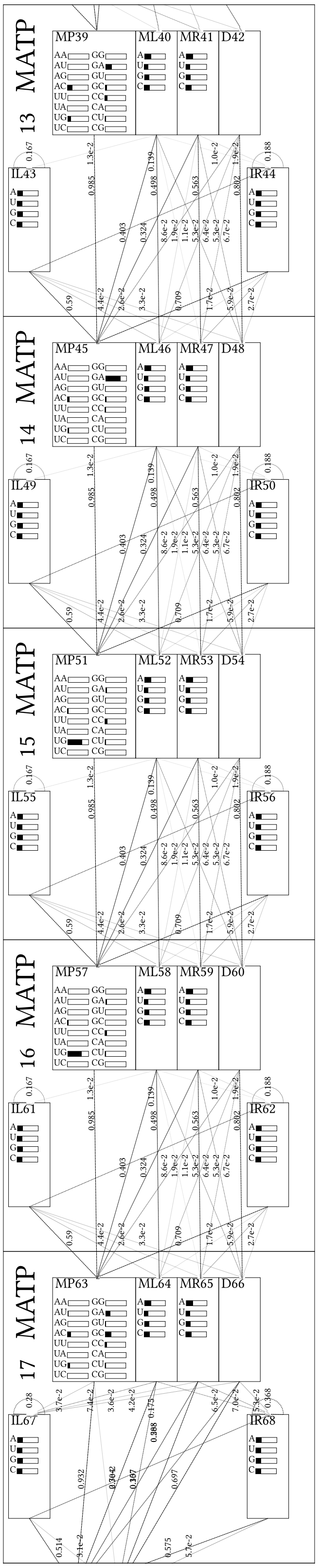


Fig. 35. Detailed `CMCV` visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part4.

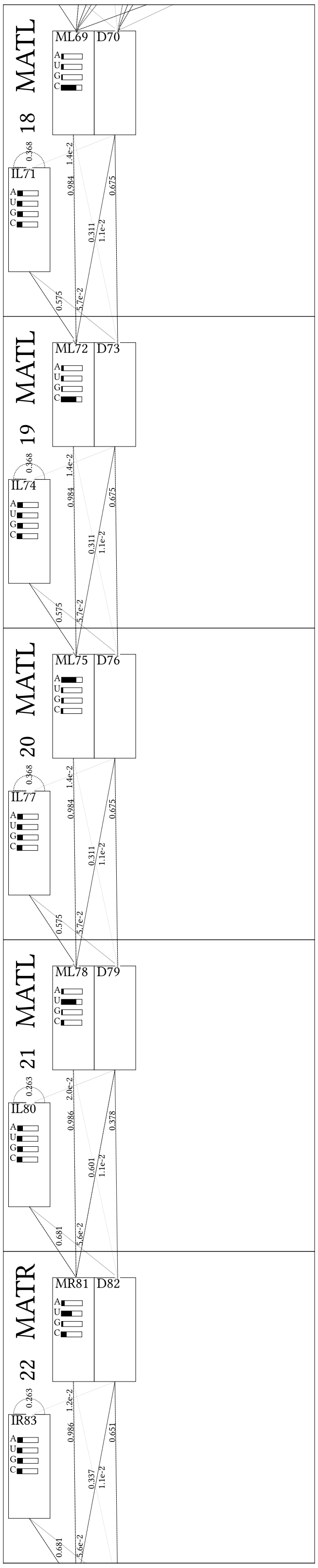


Fig. 36. Detailed CMCV visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part5.

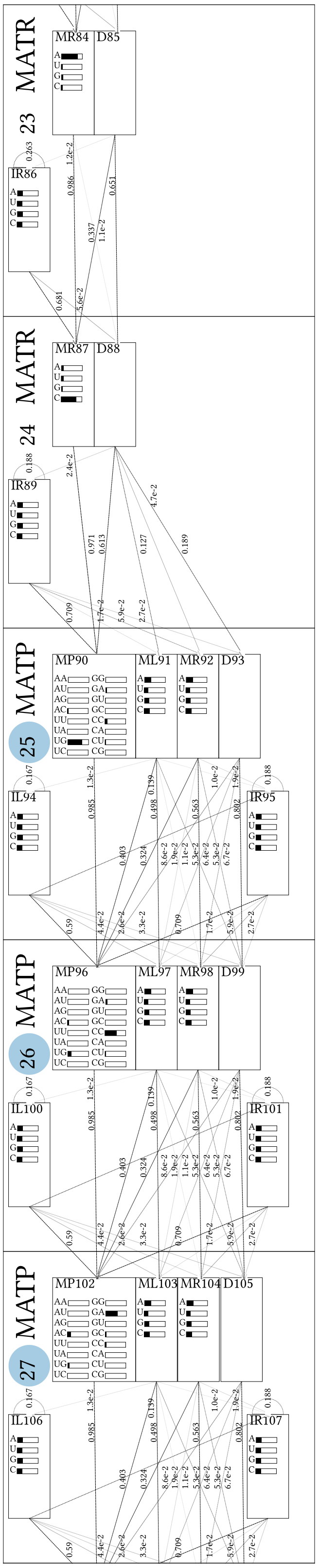


Fig. 37. Detailed `CMCV` visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part6.

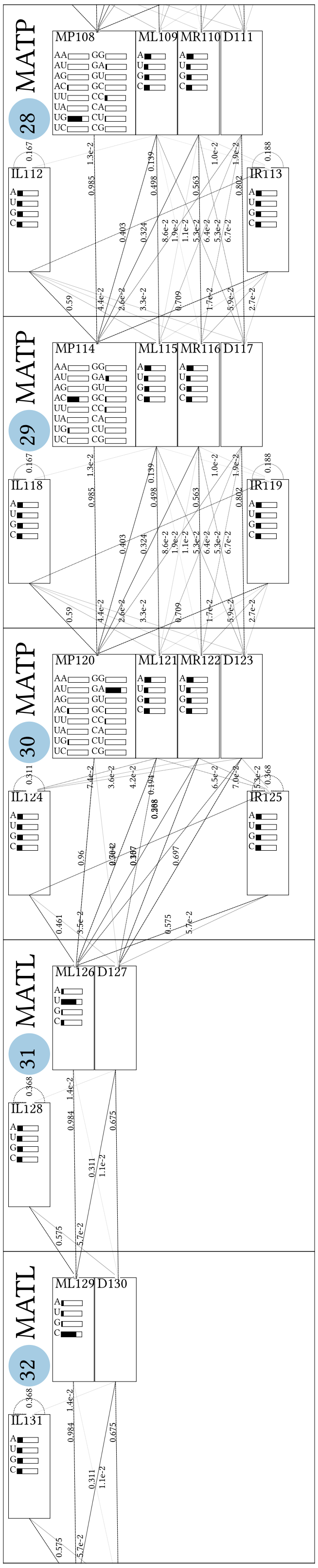


Fig. 38. Detailed CMCV visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part7.

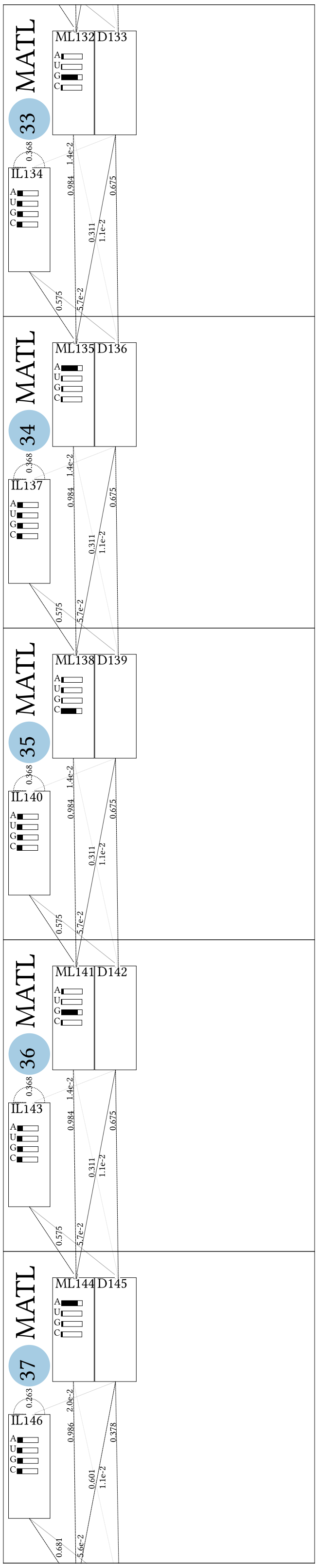


Fig. 39. Detailed `CMCV` visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part8.

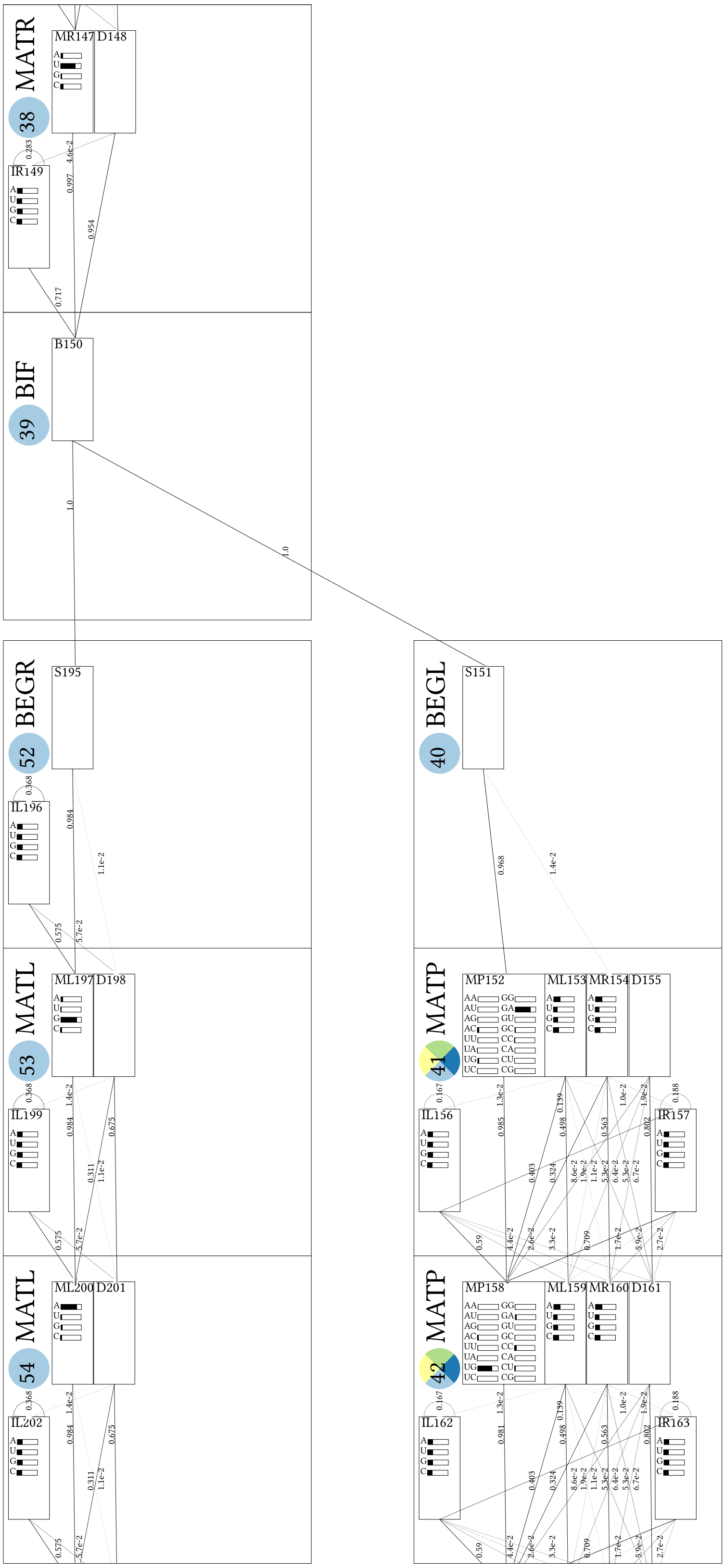


Fig. 40. Detailed `CMCV` visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part9.

Fig. 41. Detailed `CMCV` visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part10.

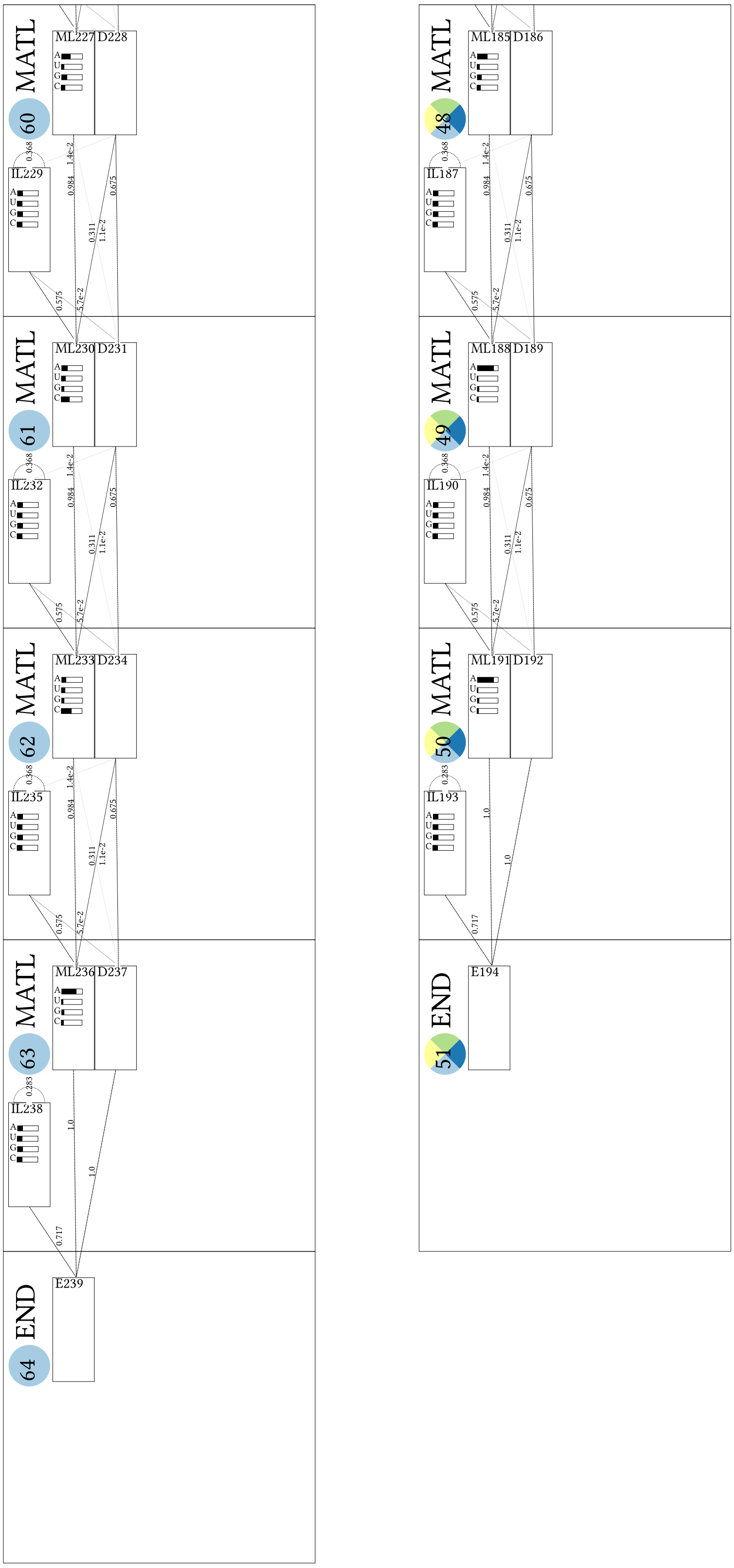
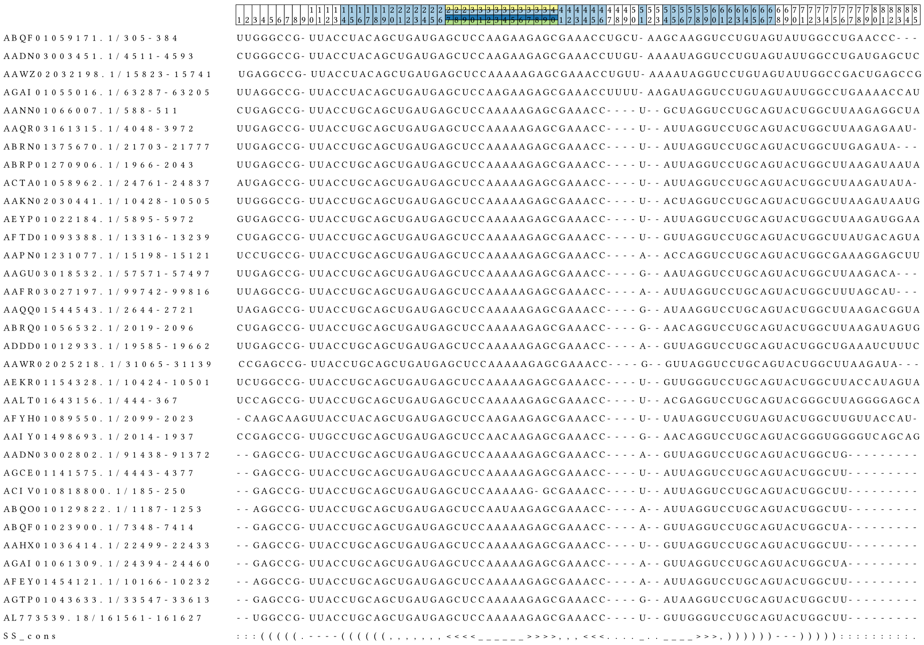


Fig. 42. Detailed `CMCV` visualisation of *Hammerhead_HH9*, showing nodes with states, emission and transition probabilities, arranged according to guide tree. Transitions below threshold that can be set via option are not shown and line strength corresponds to probability. Linked are nodes highlighted by color which correspond to the clan families in the automatically created legend - Part11.



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AAFR03027197.1/99742-99816  UUAGGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----A--AUUAGGUCCUGCAGUACUGGCUUUAGCAU---
AAQQ01544543.1/2644-2721    UAGAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----G--AUAAGGUCCUGCAGUACUGGCUUAAGACGGUA
ABRQ01056532.1/2019-2096    CUGAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----G--AACAGGUCCUGCAGUACUGGCUUAAGAUAGUG
ADDD01012933.1/19585-19662  UUGAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----A--GUUAGGUCCUGCAGUACUGGCUGAAAUCUUUC
AAWR02025218.1/31065-31139  CCGAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----G--GUUAGGUCCUGCAGUACUGGCUUAAGAUA---
AEKR01154328.1/10424-10501  UCUGGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----U--GUUGGGUCCUGCAGUACUGGCUUACCAUAGUA
AALT01643156.1/444-367      UCCAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----U--ACGAGGUCCUGCAGUACGGGCUUAGGGGAGCA
AFYH01089550.1/2099-2023    -CAAGCAAGUUACCUACAGCUGAUGAGCUCCAAGAAGAGCGAAACC----U--UAUAGGUCCUGUAGUACUGGCUUGUUACCAU-
AAIY01498693.1/2014-1937    CCGAGCCG-UUGCCUGCAGCUGAUGAGCUCCAACAAGAGCGAAACC----G--AACAGGUCCUGCAGUACGGGUGGGGUCAGCAG
AADN03002802.1/91438-91372  --GAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----A--GUUAGGUCCUGCAGUACUGGCUG--------
AGCE01141575.1/4443-4377    --GAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----U--AUUAGGUCCUGCAGUACUGGCUU--------
ACIV010818800.1/185-250     --GAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAG-GCGAAACC----U--AUUAGGUCCUGCAGUACUGGCUU--------
ABQO010129822.1/1187-1253   --AGGCCG-UUACCUGCAGCUGAUGAGCUCCAAUAAGAGCGAAACC----A--AUUAGGUCCUGCAGUACUGGCUU--------
ABQF01023900.1/7348-7414    --GAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----A--GUUAGGUCCUGCAGUACUGGCUA--------
AAHX01036414.1/22499-22433  --GAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----U--GUUAGGUCCUGCAGUACUGGCUU--------
AGAI01061309.1/24394-24460  --GAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----A--GUUAGGUCCUGCAGUACUGGCUA--------
AFEY01454121.1/10166-10232  --AGGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----A--AUUAGGUCCUGCAGUACUGGCUU--------
AGTP01043633.1/33547-33613  --GAGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----G--AUAAGGUCCUGCAGUACUGGCUU--------
AL773539.18/161561-161627   --UGGCCG-UUACCUGCAGCUGAUGAGCUCCAAAAAGAGCGAAACC----U--GUUGGGUCCUGCAGUACUGGCUU--------
SS_cons                     :::(((((.----((((((,,,,,,,<<<<______>>>>,,,<<<...._..____>>>,))))))---))))):::::::::.
```

Fig. 43. *Hammerhead_HH9* `Rfam` family alignment visualisation, the number of alignment entries can be set via option. The displayed column indices allow association with the corresponding nodes in the model. The consensus secondary structure is shown in the last line.

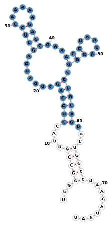

Fig. 44. Consensus secondary structure visualisation for Hammerhead HH9 with `forna`. Nucleotides linked to Hammerhead_1 family are highlighted by color.

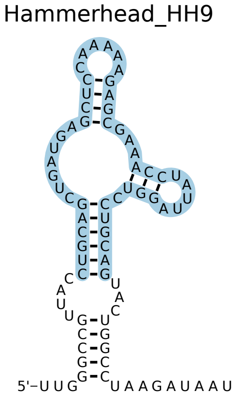

Fig. 45. Consensus secondary structure visualisation for Hammerhead HH9 with `R2R`. Nucleotides linked to Hammerhead_1 family are highlighted by color.

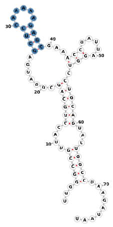

Fig. 46. Consensus secondary structure visualisation for Hammerhead HH9 with `forna`. Nucleotides linked to Hammerhead_3 family are highlighted by color.

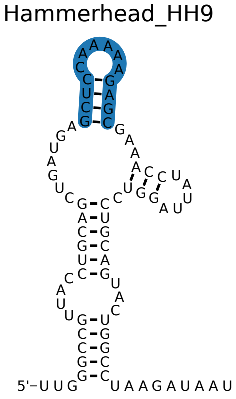

Fig. 47. Consensus secondary structure visualisation for Hammerhead HH9 with `R2R`. Nucleotides linked to Hammerhead_3 family are highlighted by color.

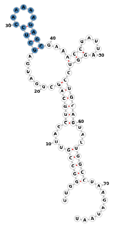

Fig. 48. Consensus secondary structure visualisation for Hammerhead HH9 with `forna`. Nucleotides linked to Hammerhead HH10 family are highlighted by color.

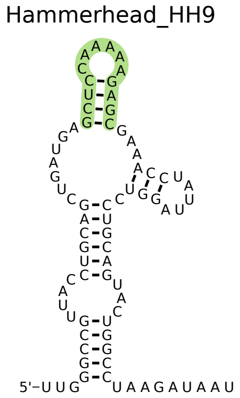

Fig. 49. Consensus secondary structure visualisation for Hammerhead HH9 with `R2R`. Nucleotides linked to Hammerhead HH10 family are highlighted by color.