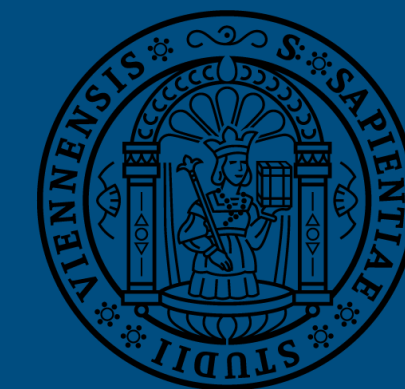


Co-transcriptional simulator to analyze ALU element interactions

Fuzzyfold workspace in Rust

Supervisor: Dr. Stefan Badelt

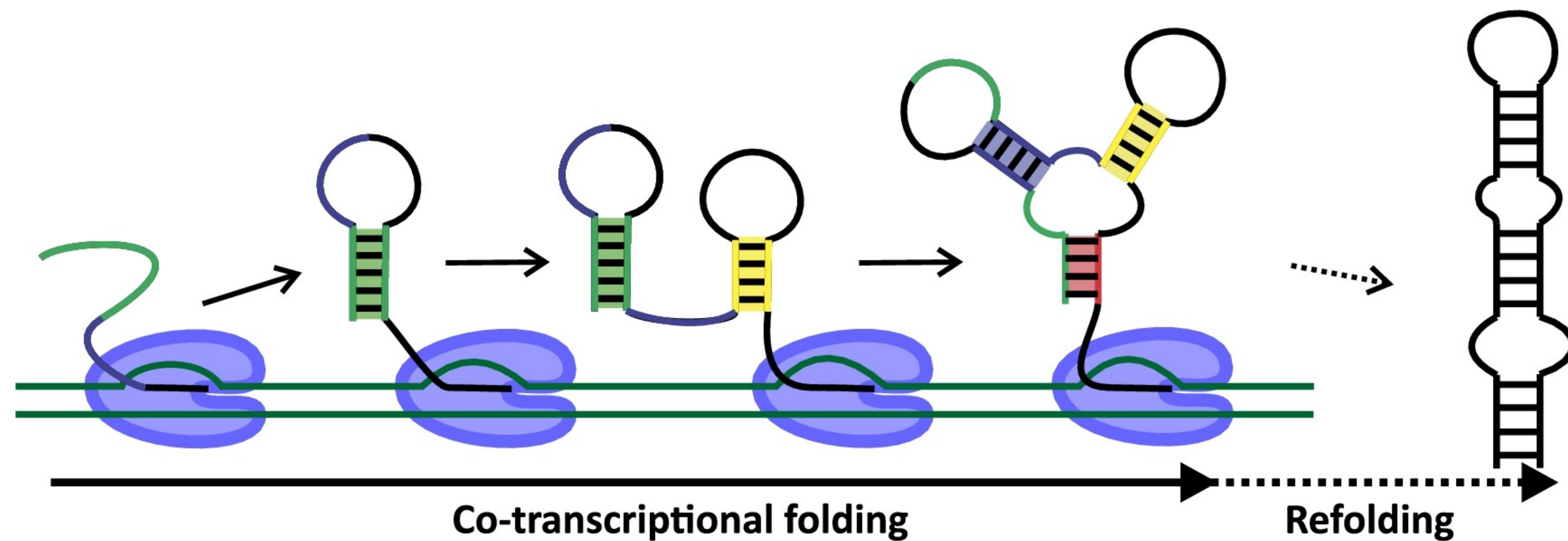
Hannah Hartung, 10.02.2026



universität
wien

Co-transcriptional Folding

- Nucleotides of the already synthesized RNA can form base pairs during transcription

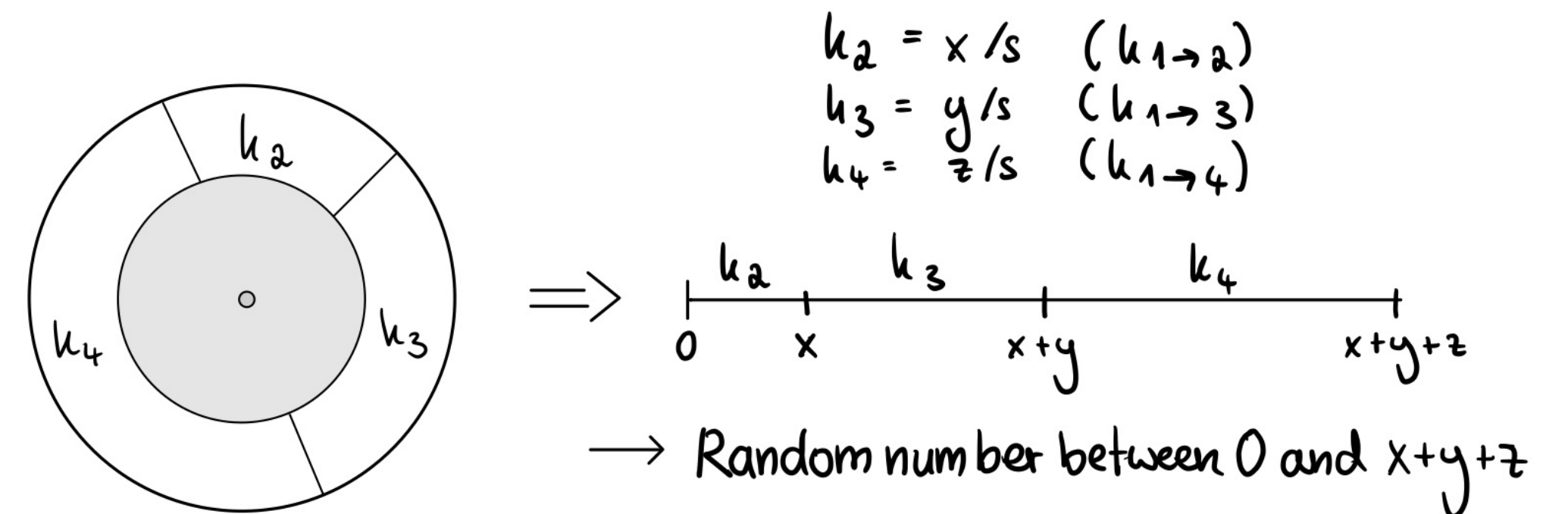
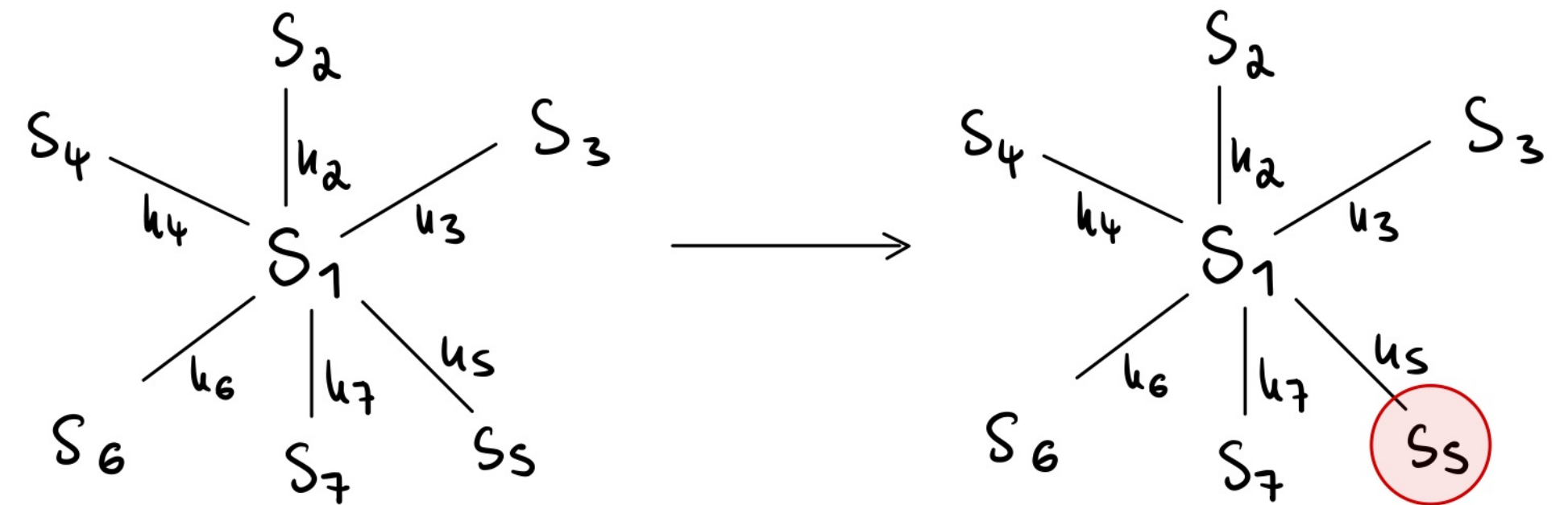


Lei Jin, Shi-Jie Chen (2025): „Computation modeling of cotranscriptional RNA folding“

Gillespie-type Algorithm for RNA

Stochastic folding kinetics

- Elementary moves: insertion/ deletion of base pairs
- Rates: Metropolis-rate model
- Selects move randomly weighted by rate
- Which event happens and when it happens



RNA folding trajectory from stochastic simulation

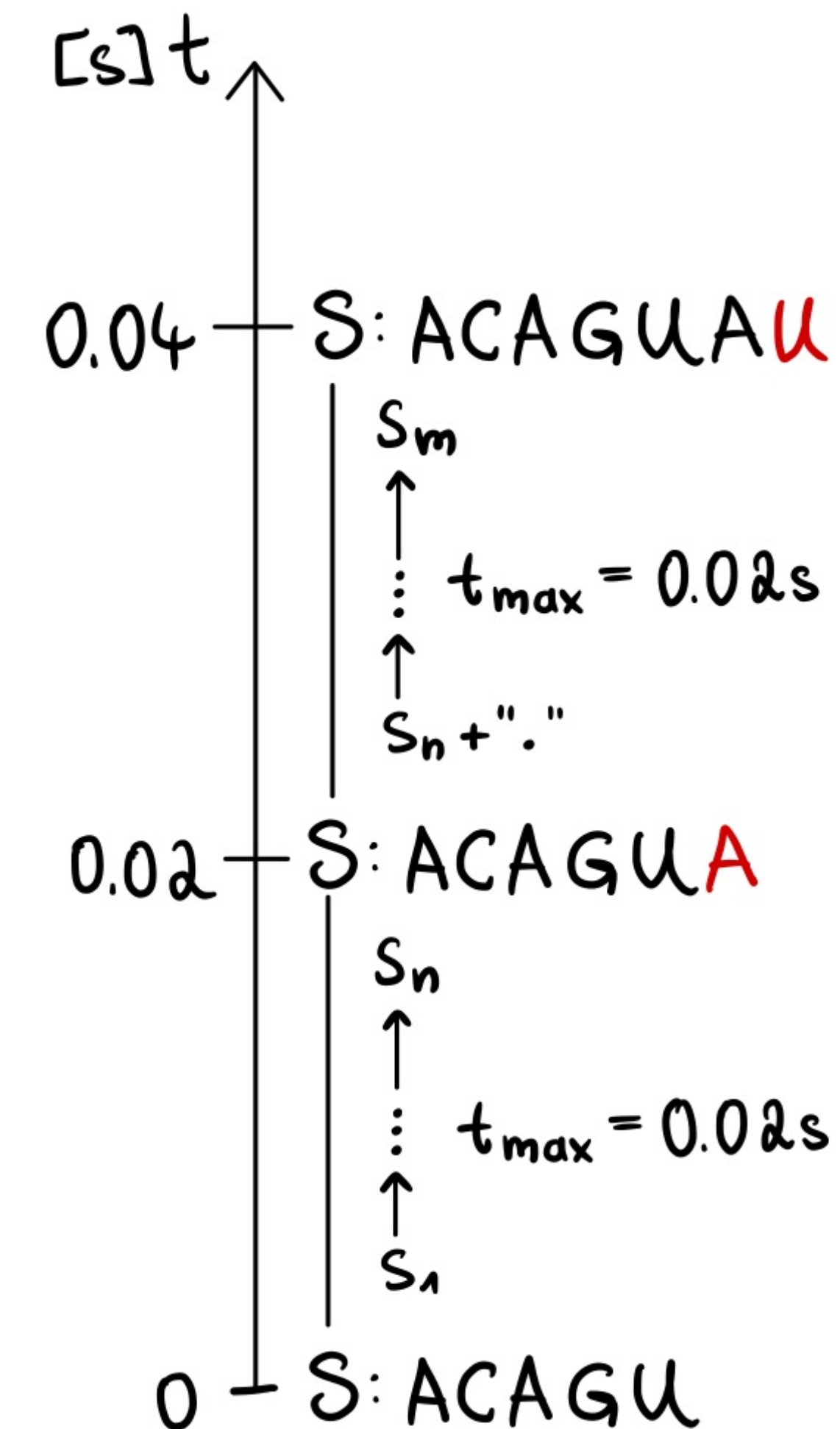
Example Output

GCGUUUCCAGGGUUUAGACGGACGGGUGUGACUCGCCCAGCCCCGACCUC	energy	arrival time	waiting time
.....	0.00	0.00000000e0	5.48838308e-1
.....(.....)	2.10	5.48838308e-1	7.42186429e-1
.....(.....)(.....)	4.50	1.29102474e0	6.62519714e-1
.....(.....)	2.40	1.95354445e0	8.70308936e-3
.....	0.00	1.96224754e0	2.24827455e0
.....(.....)	1.90	4.21052209e0	1.08942365e0
.....((.....))	0.10	5.29994574e0	3.93454939e-1
.....(.((.....)).)	-0.20	5.69340068e0	1.06769149e-1
.....(.((.....)).)	1.80	5.80016983e0	4.33243095e-1
.....(((.....)))	-2.40	6.23341293e0	1.28813977e0
.....((((.....))))	-1.60	7.52155270e0	2.45415452e-1
.....((((.....))))	-1.50	7.76696815e0	6.94202383e-2
.....((((.....))))	-5.60	7.83638839e0	3.47571920e0
.....((((.....))))	-2.90	1.13121076e1	1.55874453e0
.....((((.....))))	-5.60	1.28708521e1	2.36328447e0
.....((((.....))))(.....)	-2.10	1.52341366e1	7.41356896e-3
.....((((.....))))((.....))	-4.70	1.52415502e1	2.00829892e1
..((((.....))))((.....))	-0.50	3.53245394e1	1.26546682e0
.....((((.....))))((.....))	-4.70	3.65900062e1	4.58067121e1

Implementation of stochastic co-transcriptional folding

Transcription rate: 50 nucleotides/second

- simulate for 0.02 seconds per nucleotide
- Extension: append exterior loop by “.”, only recompute energy and neighbors for exterior loop

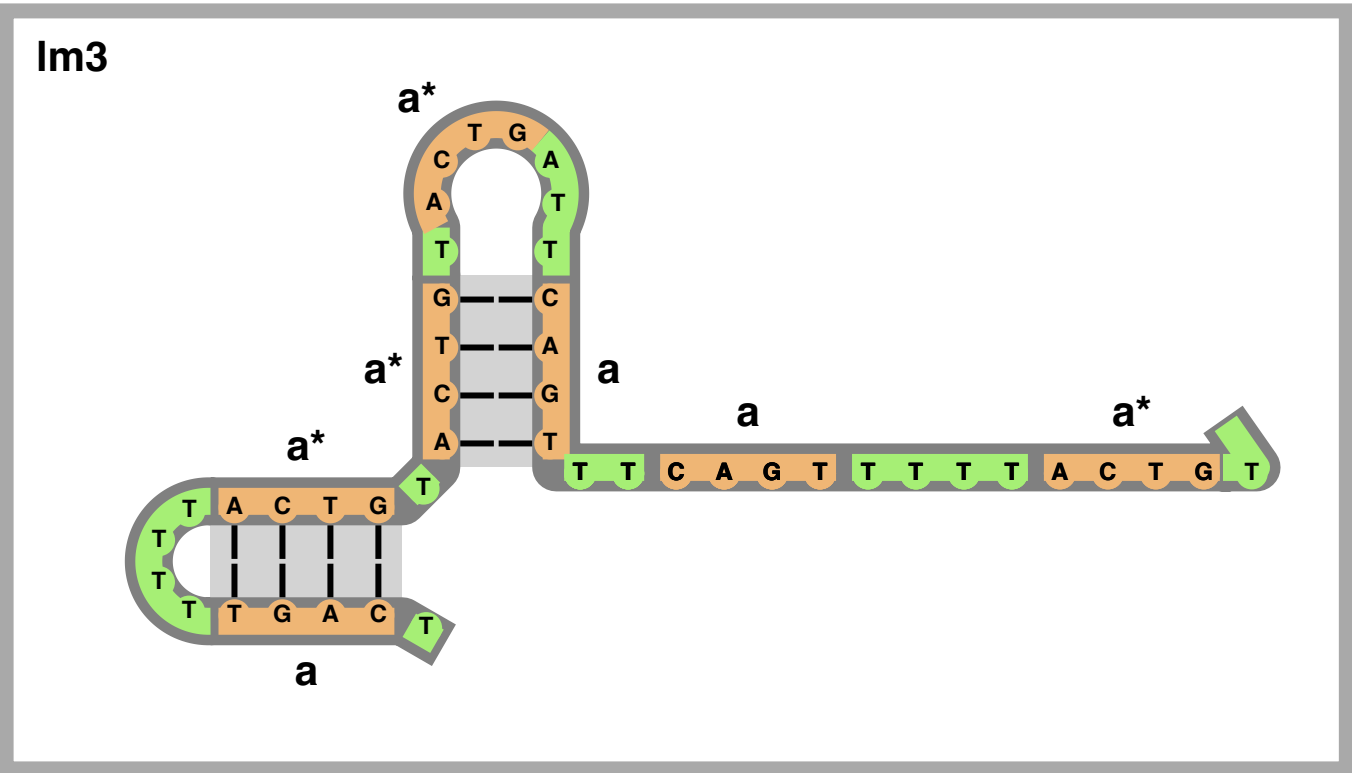
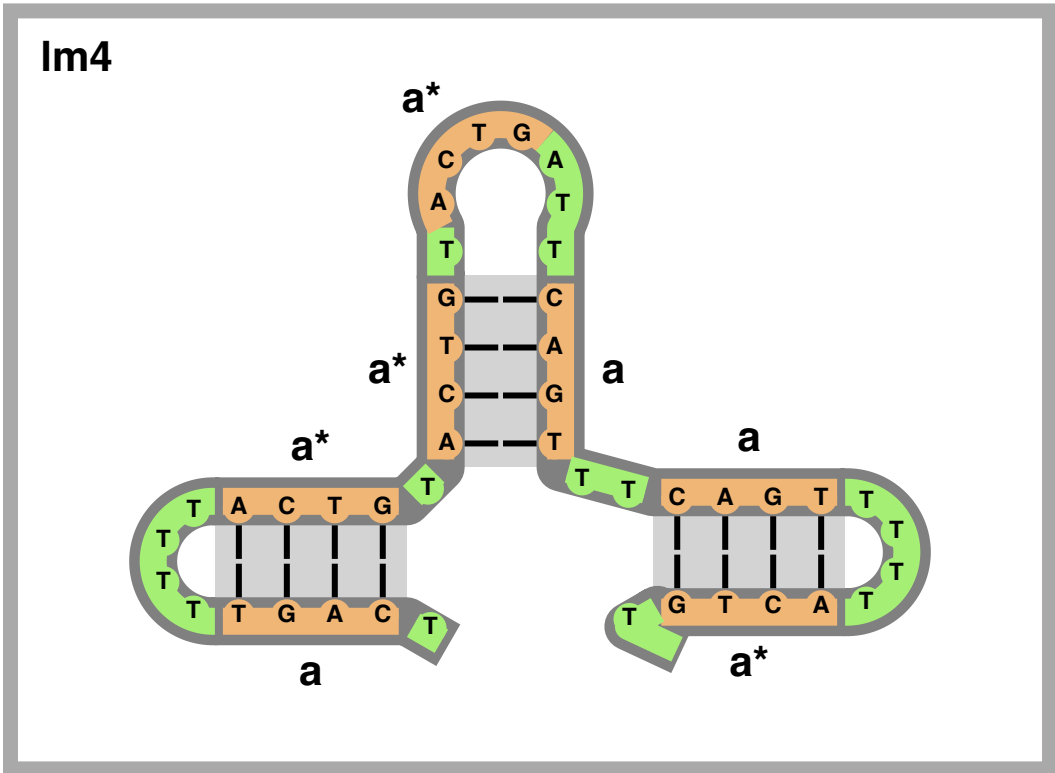
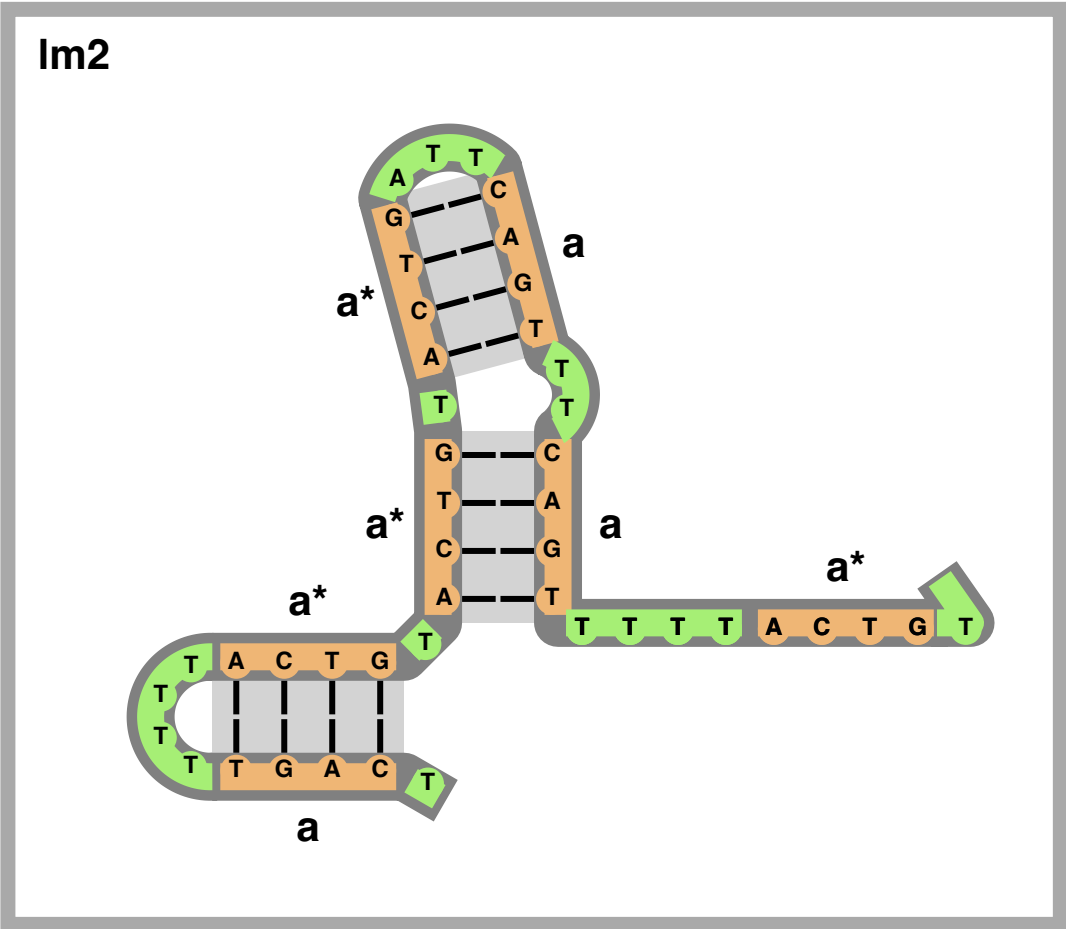
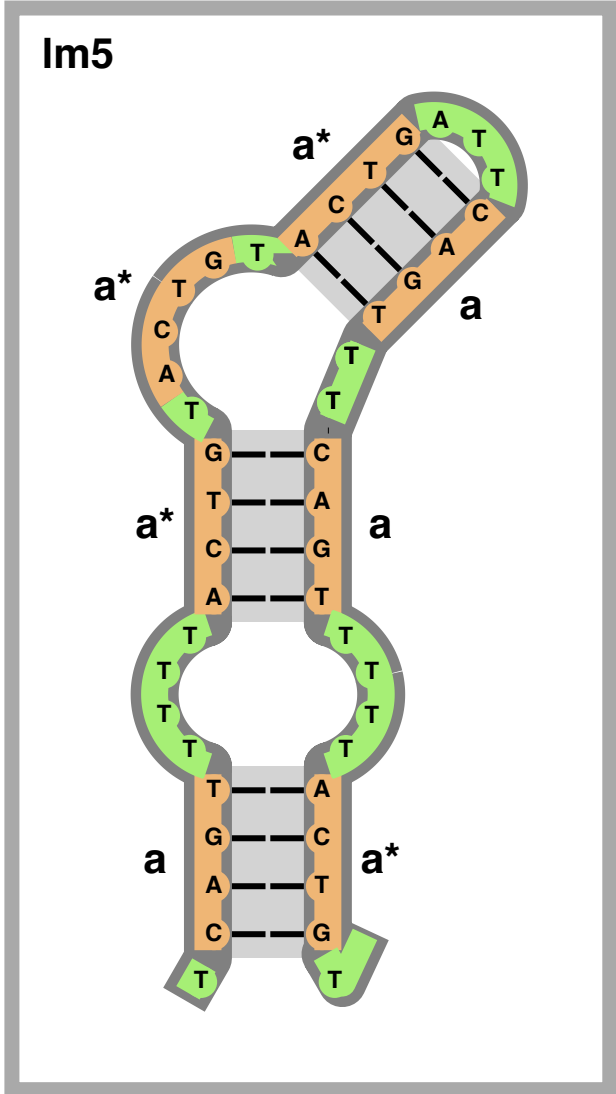
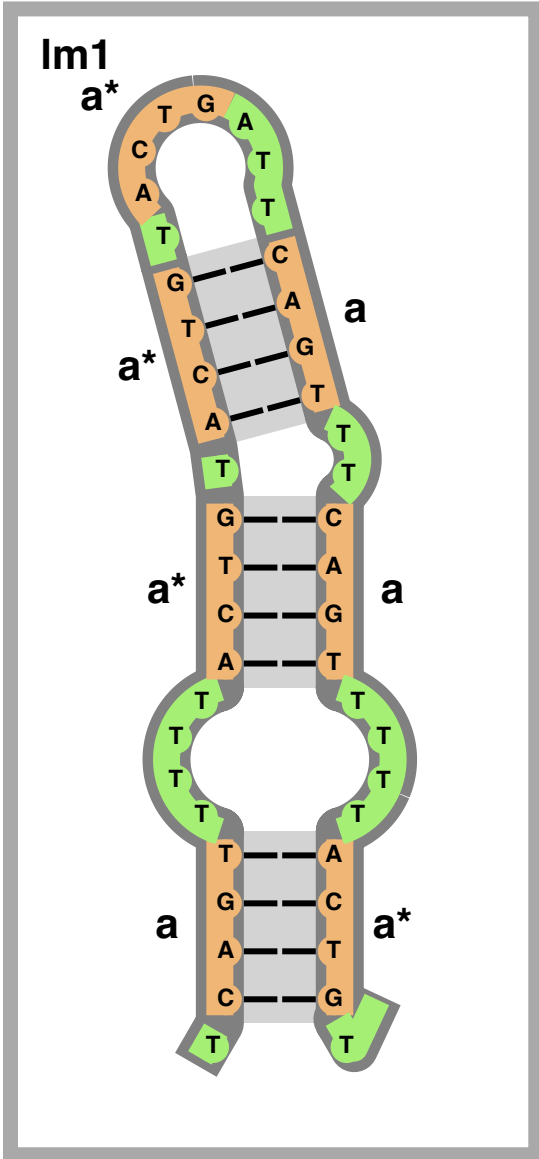


Command line tools

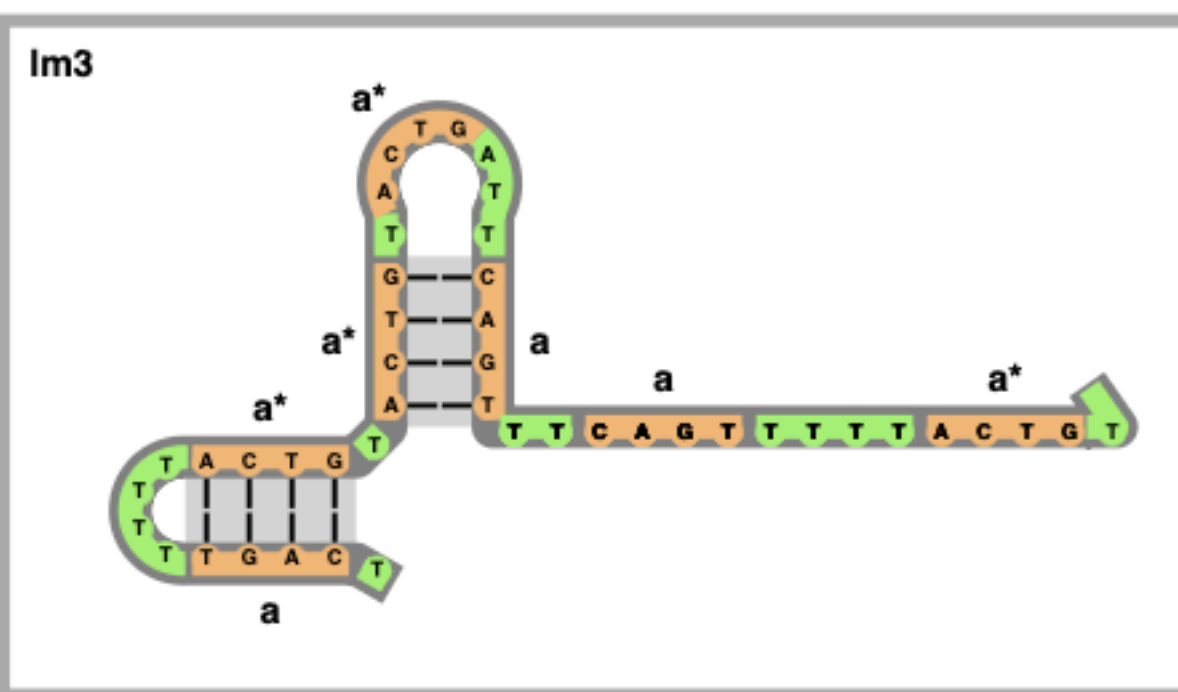
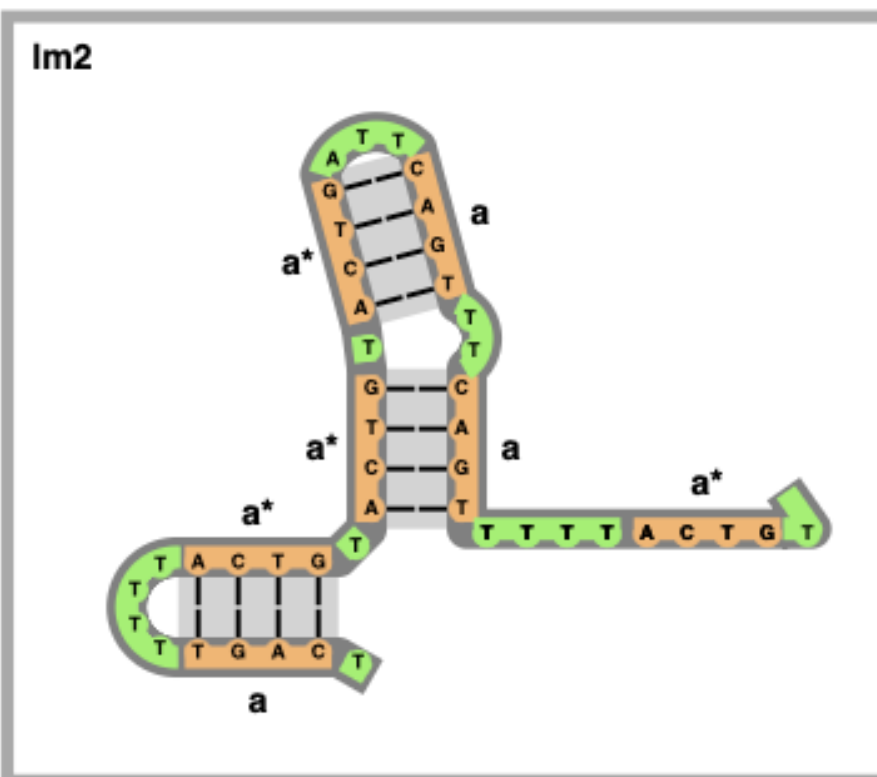
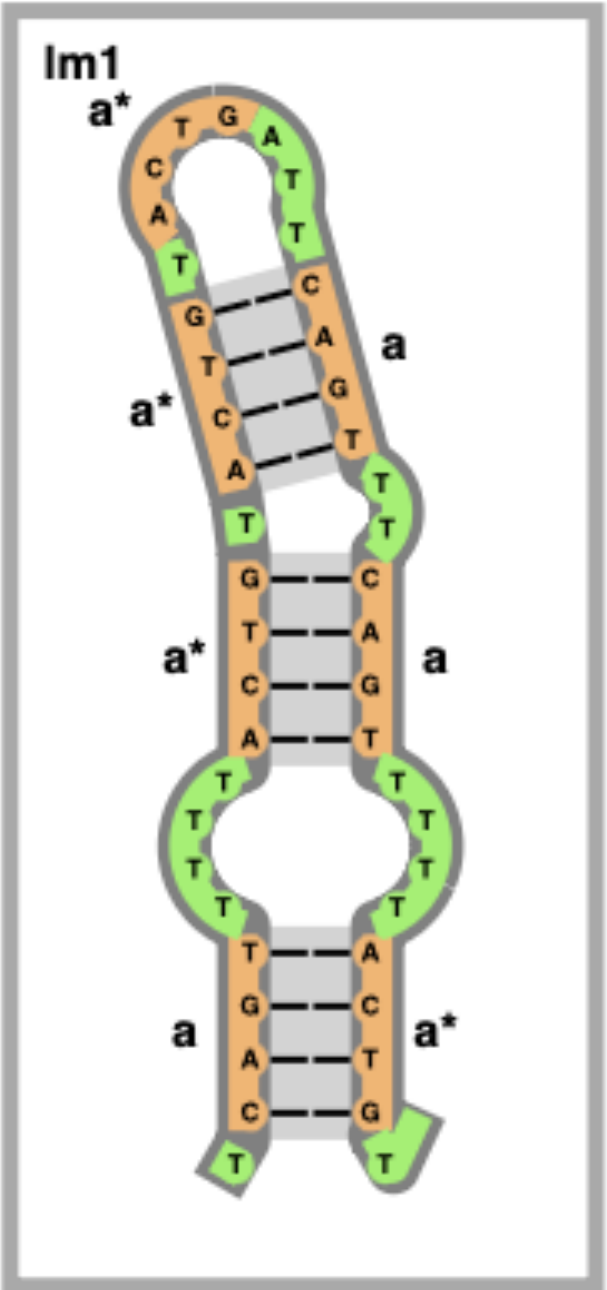
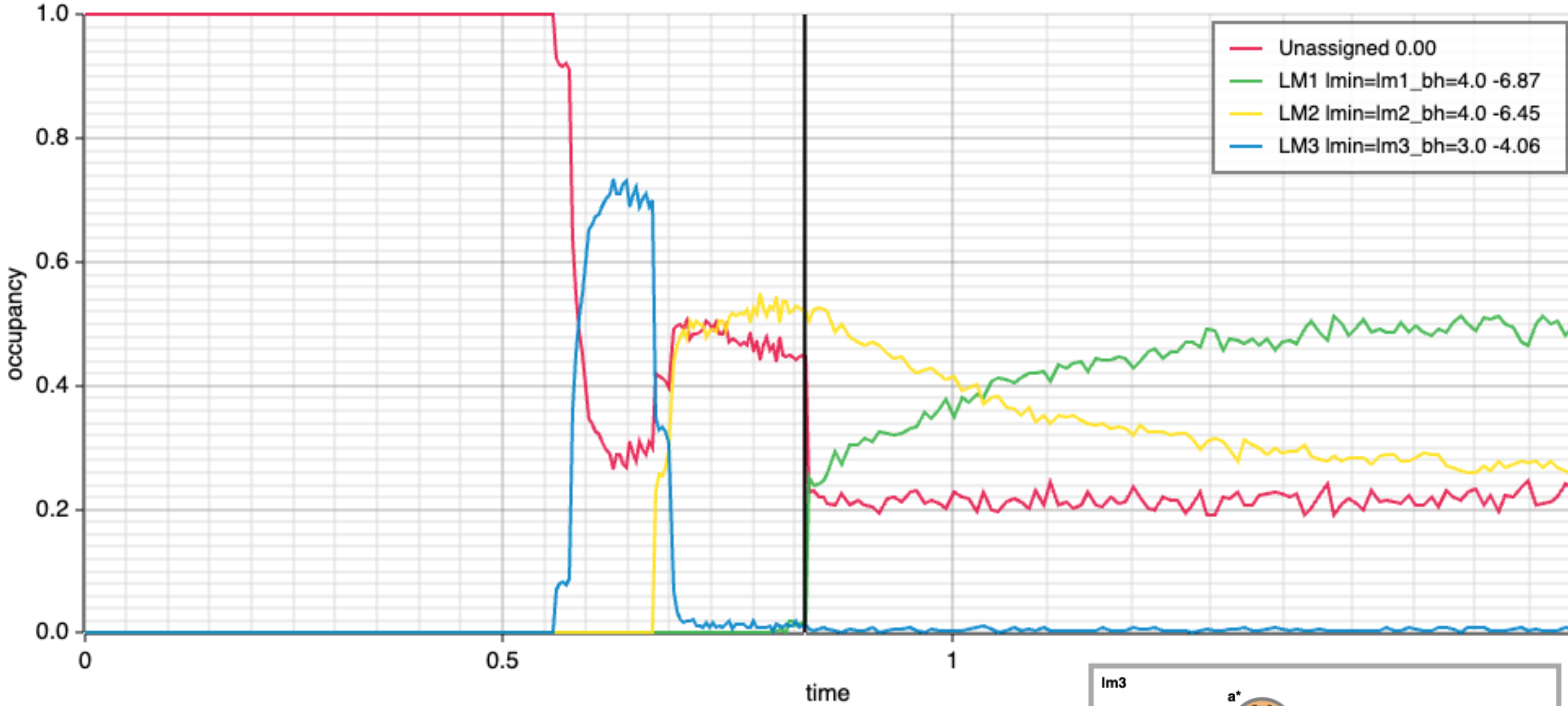
- Trajectory and time course
- Start structure ($\Rightarrow$ start length)
- Extension time
- Pausing sites
- Post transcriptional folding time

Macrostates

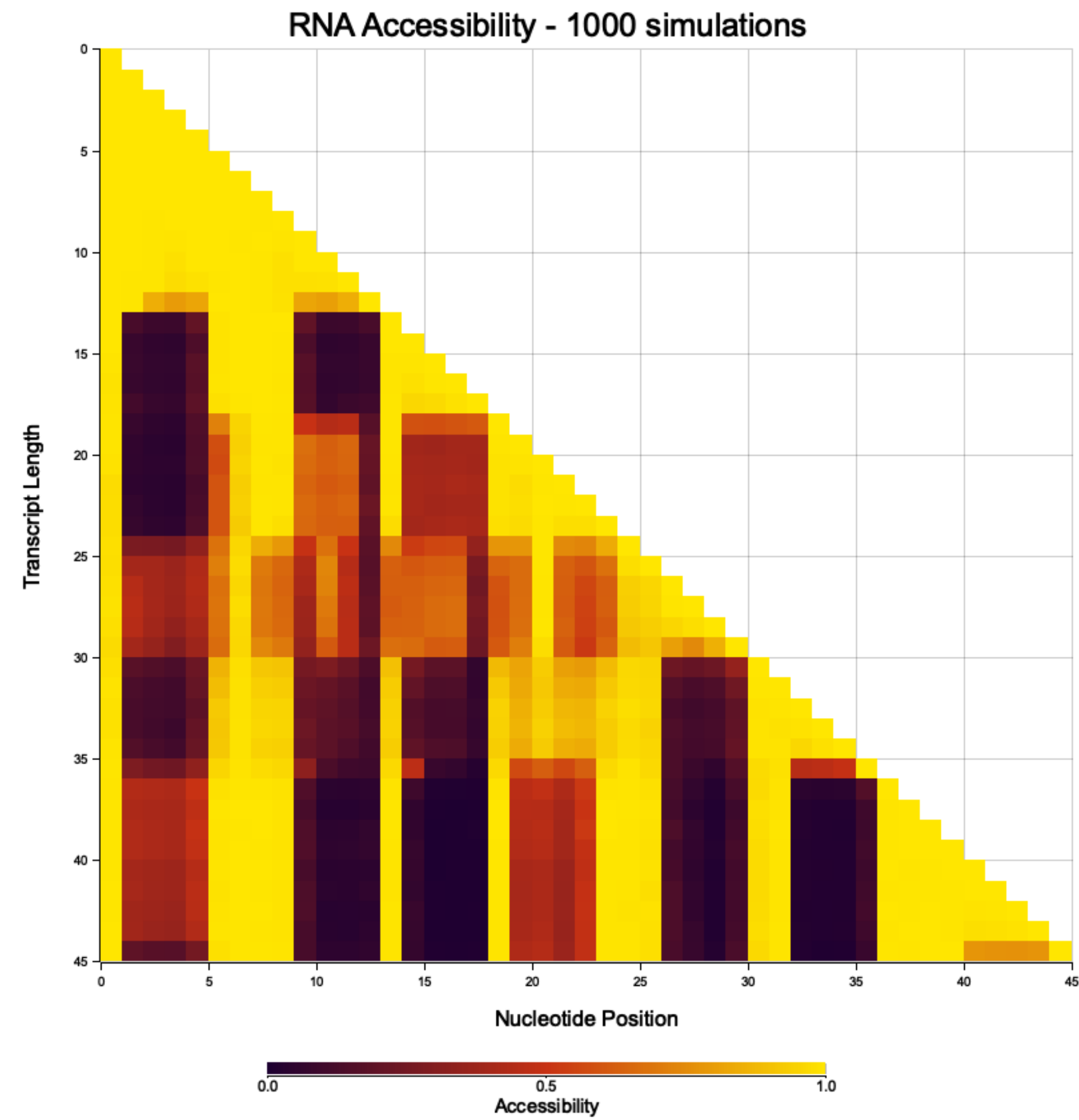
UCAGUCUUCGCUGCGCUGUAUCGAUUCGGUUUCAGUUUUUAUUGC



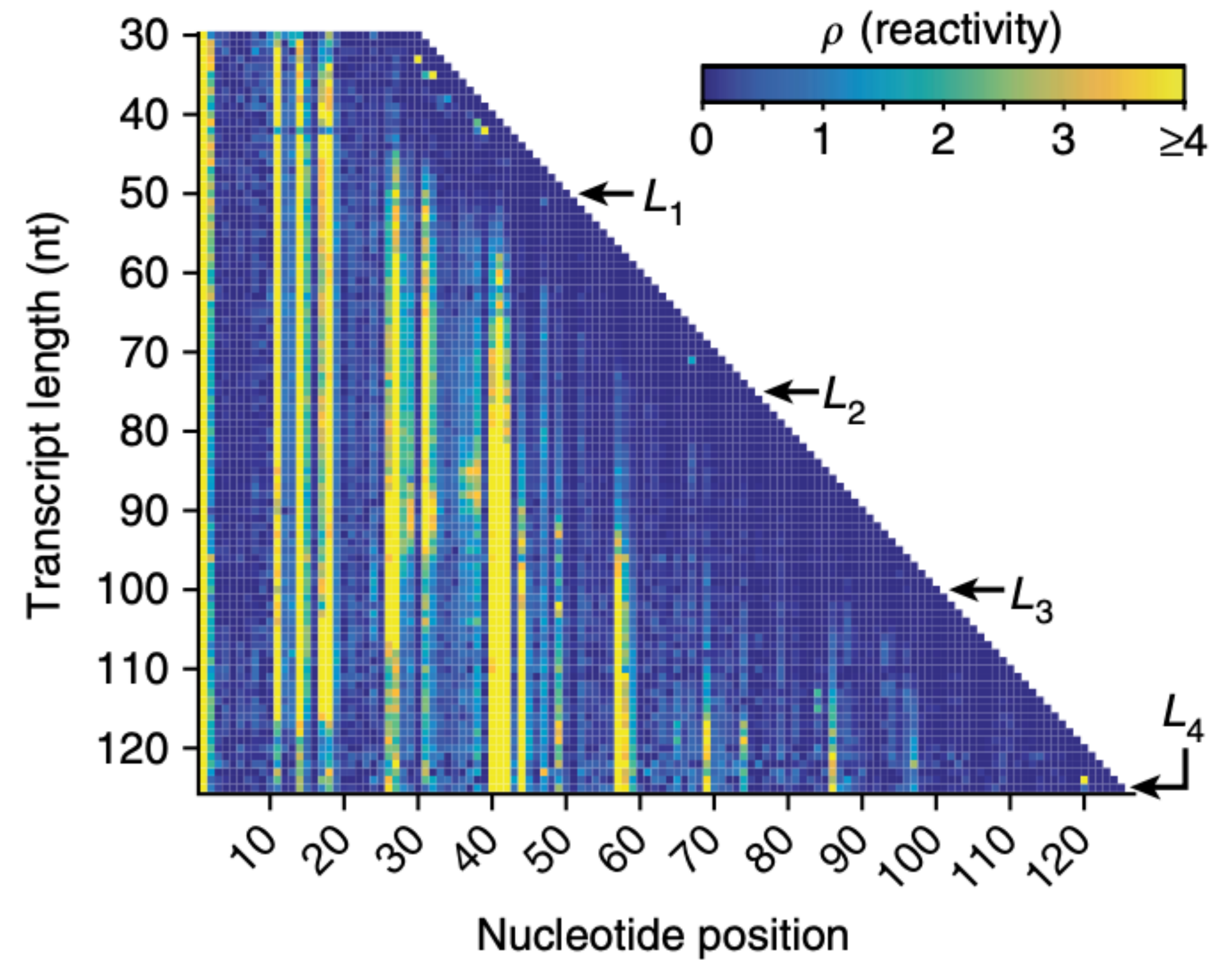
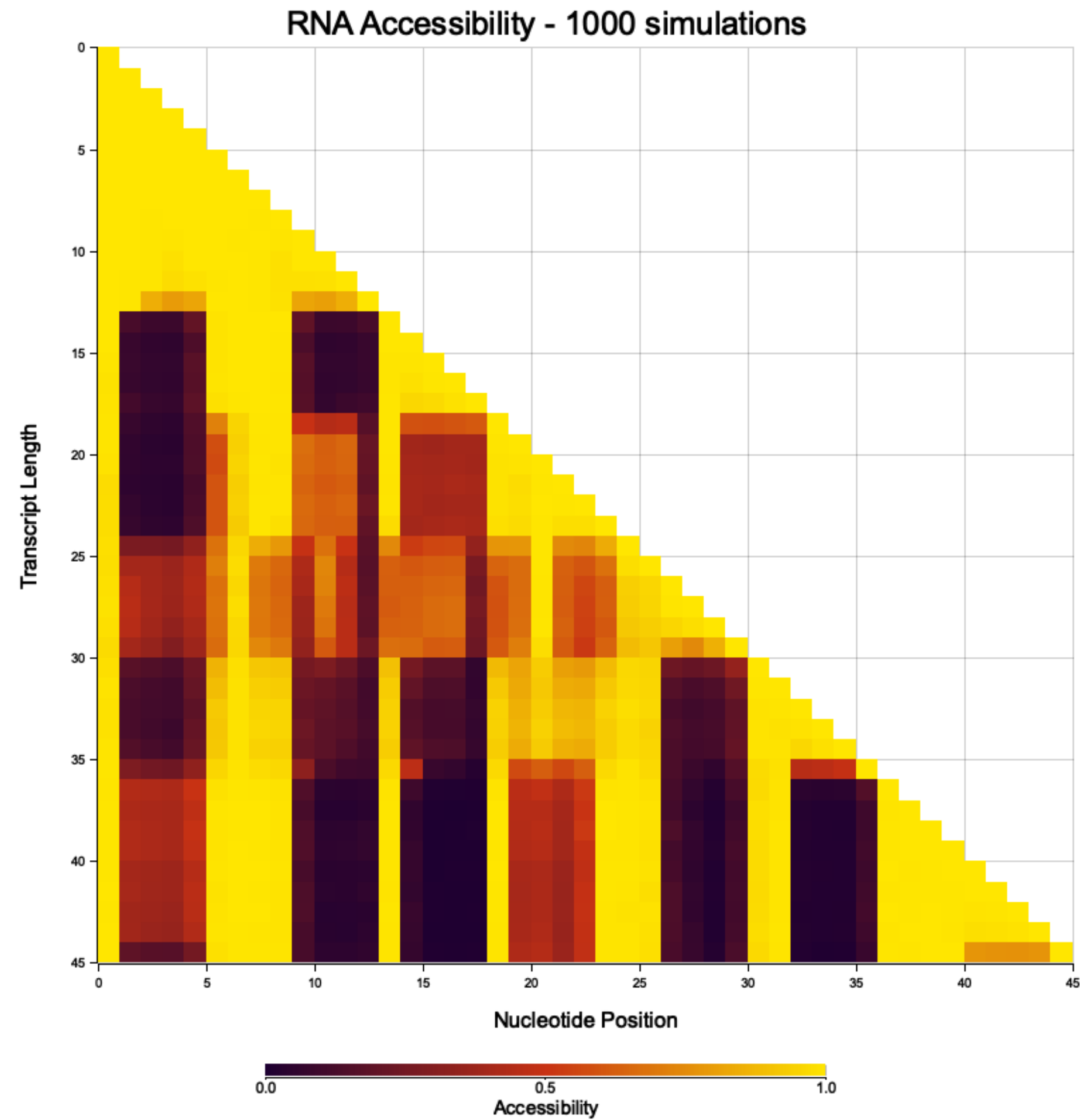
ff-co_simulate (1000 simulations)



Visualization



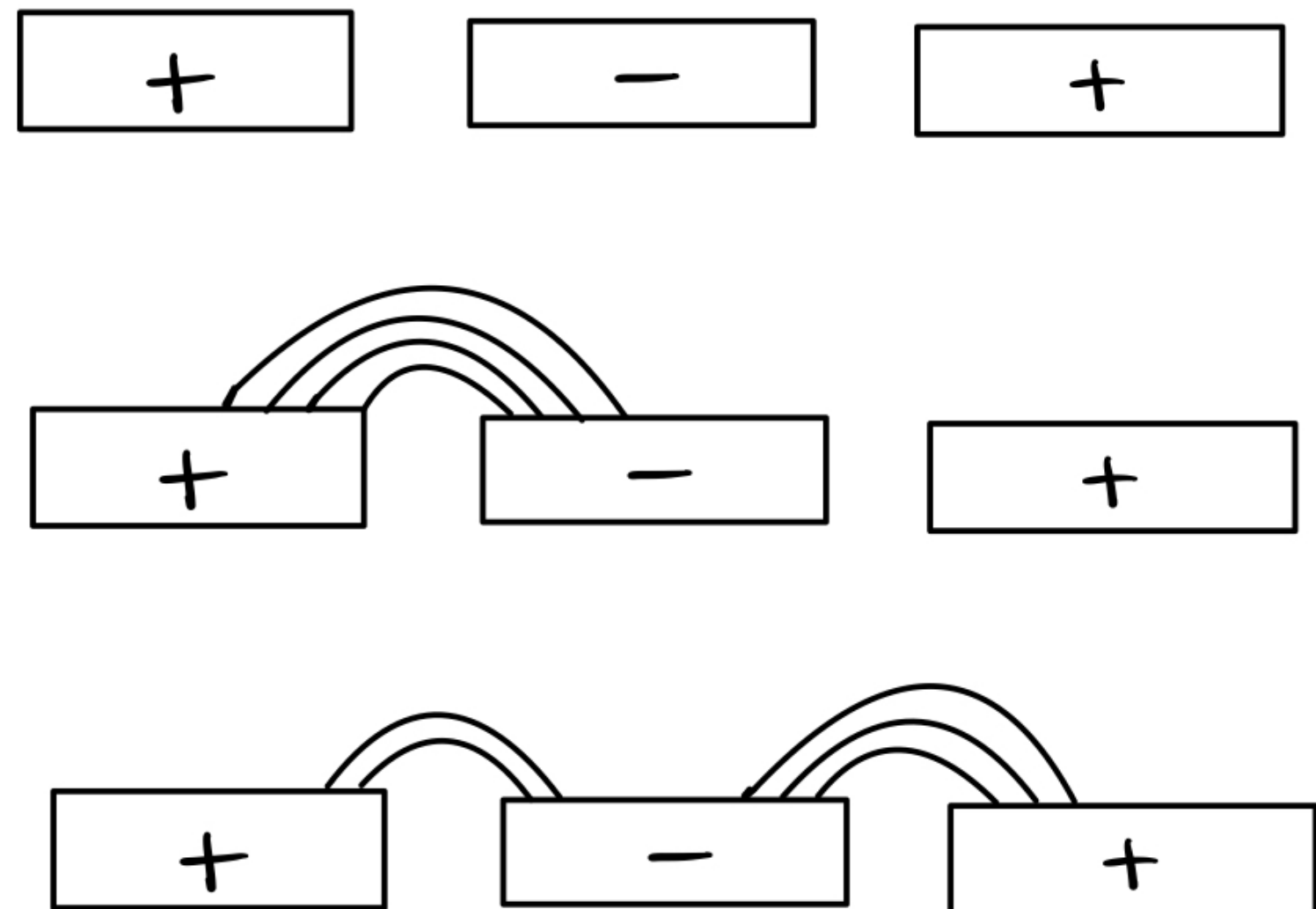
Visualization



Watters, K., Strobel, E., Yu, A. *et al.* Cotranscriptional folding of a riboswitch at nucleotide resolution. *Nat Struct Mol Biol* **23**, 1124–1131 (2016). <https://doi.org/10.1038/nsmb.3316>

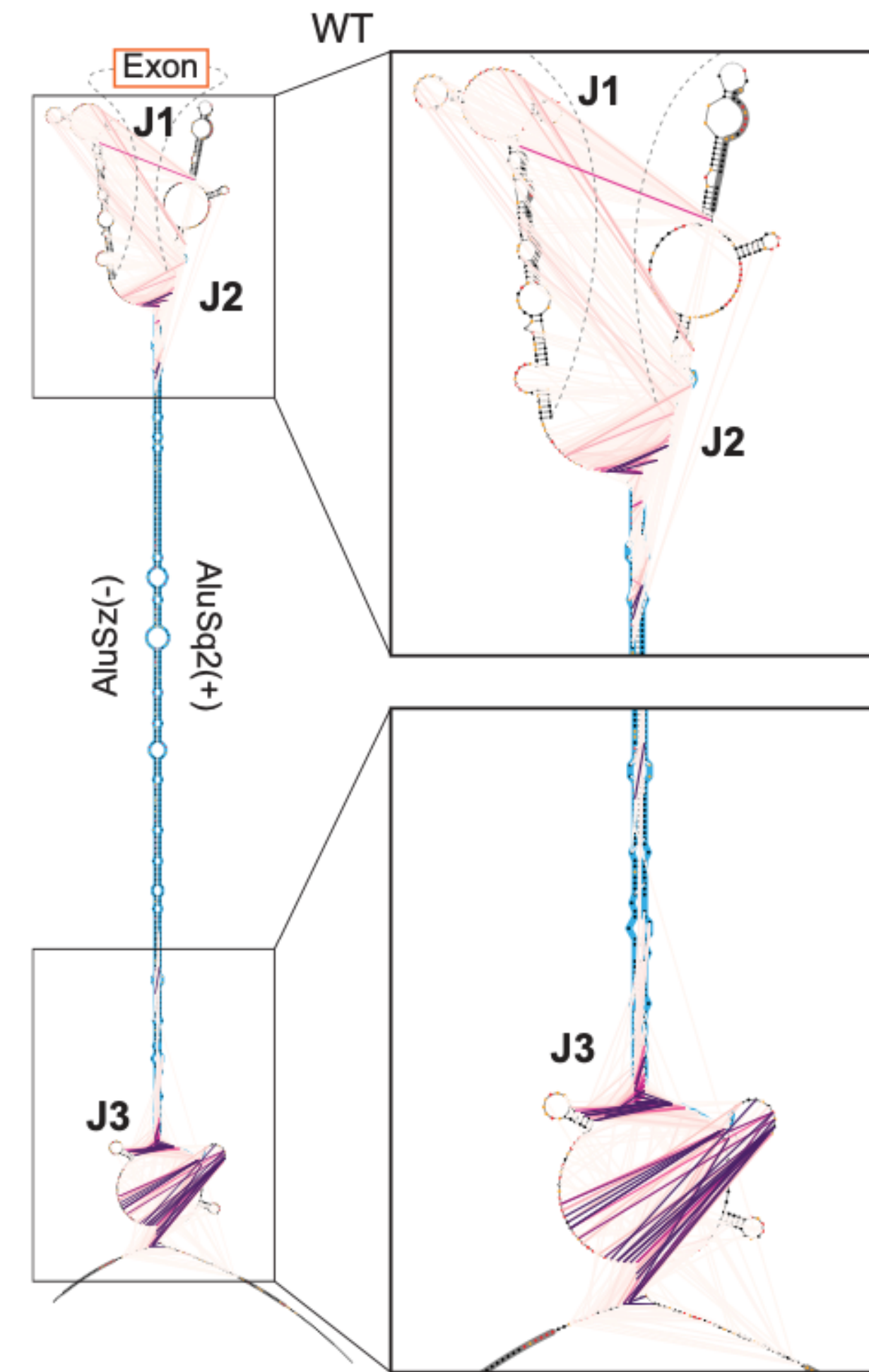
Alu-Elements

- Non-autonomous retrotransposons
- Sequence similarity between any two Alu elements $> 80\%$
=> Two inverted repeat Alu elements: high degree of complementarity



Cotranscriptional Folding of ALU elements

- Sequences between 2 - 3 kB
- Integration of SHAPE data



Waldern Justin M. et al. (2025): „Structural determinants of inverted Alu-mediated backspacing revealed by -MaP and JuMP“.

Special thanks to



Prof. Alain Laederach



Dr. Stefan Badelt

Questions?