

RNA folding: Structural alignment of kinetic trajectories reveals conserved transient structures

Maria Waldl

Department of Theoretical Chemistry, University of Vienna
Währingerstrasse 17, 1090 Vienna, Austria
maria@tbi.univie.ac.at

Bled, February 14th, 2019

Homologous function - homologous folding trajectories?

RNA families

- | Rfam database
- | sequence + structure homologs
- | conserved function

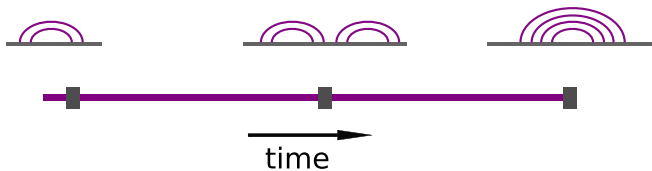
Hypothesis

- | folding trajectories are conserved
- | trajectories converge at functional intermediate states

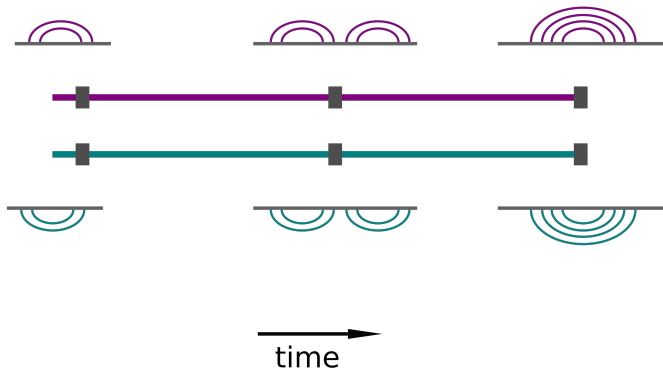
Possible functions

- | guided folding
- | interactions with ligands
- | pausing sites
- | ...

Kinetic folding trajectories



Comparing two trajectories



Comparing two trajectories

Comparing two trajectories

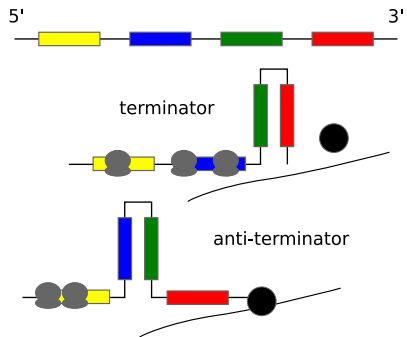
- | different timescales
- | sequence alignment
- | scoring similarity of steps - structure
- | shifted structures

Trajectory alignment

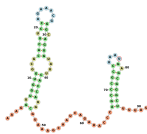
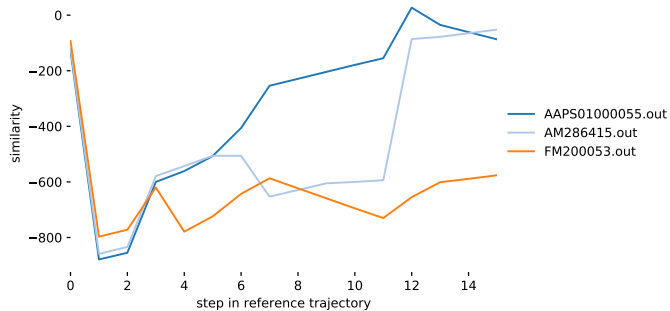
$$X(i,j) = S(i,j) + \max \begin{cases} X(i-1,j) \\ X(i,j-1) \end{cases} \quad (1)$$

- | keeps order of steps over time
- | independent of time scale
- | $S(i,j)$ from RNAforester - structure score
- | independent of sequence alignment

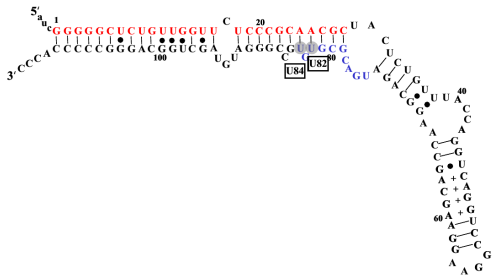
Example: TRP operon



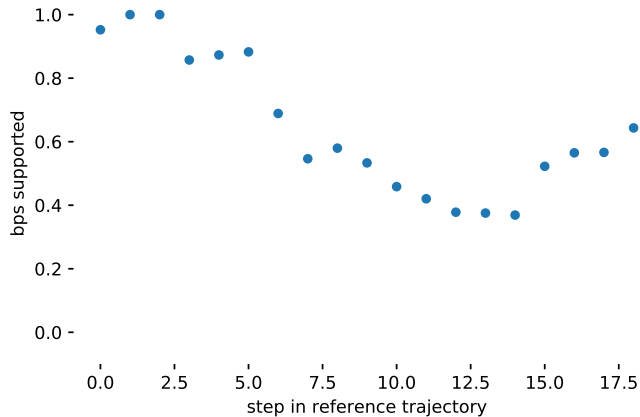
Example: TRP operon



Example: small bacterial SRP RNA



Example: small bacterial SRP RNA

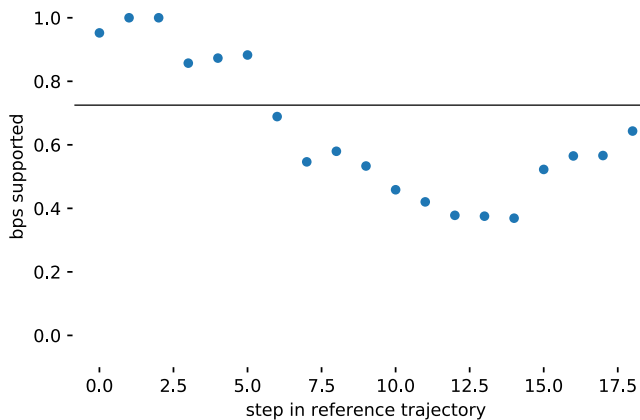


Background model

- | choose ancestor sequence that can form final functional structure
- | model evolution along phylogenetic tree of Rfam family
- | run analysis on randomized alignment

Background model

- | RNAinverse for modeling ancestor
- | Sissi for modeling evolution



THANKS TO ...

Yann Ponty
+ RNALands Team

Andrea Tanzer
Ronny Lorenz
Gregor Entzian

Ivo Hofacker
+TBI Team

Funding:

FWF-I-1804-N28, ANR-14-CE34-0011, FWF-I-2874-N28, DK RNA



universität
wien



FWF

ANR