

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

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# Homologous function - homologous folding trajectories?

## RNA families

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

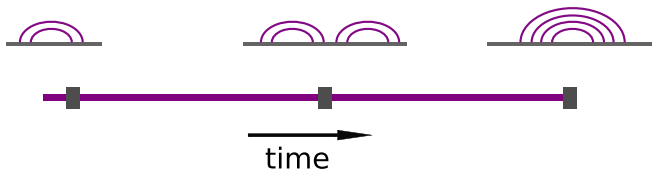
## Hypothesis

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

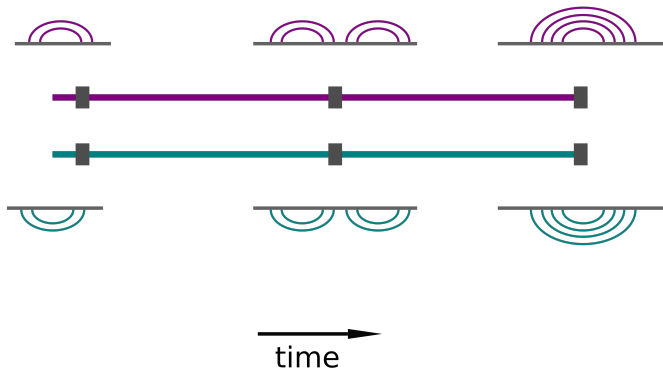
## Possible functions

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

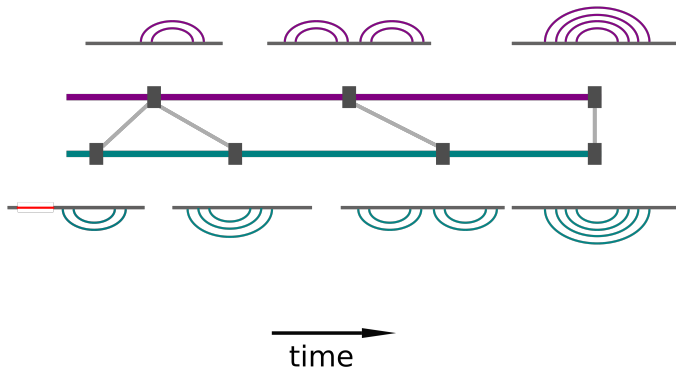
# Kinetic folding trajectories



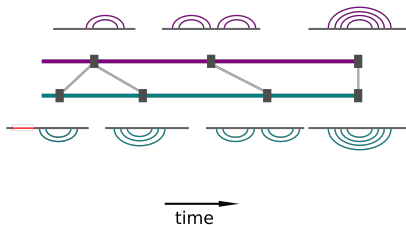
# Comparing two trajectories



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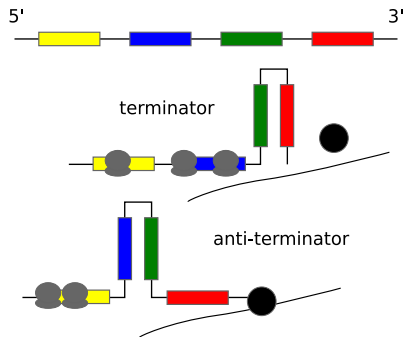
- ▶ different timescales
- ▶ sequence alignment
- ▶ scoring similarity of steps - structure
- ▶ shifted structures

# Trajectory alignment

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

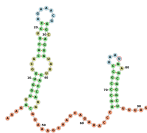
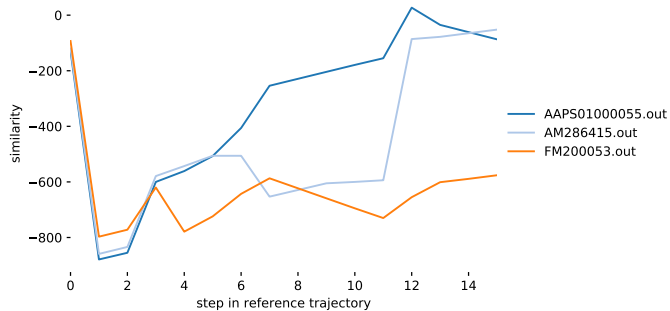
- ▶ keeps order of steps over time
- ▶ independent of time scale
- ▶  $S(i,j)$  from RNAforester - structure score
- ▶ independent of sequence alignment

# Example: TRP operon

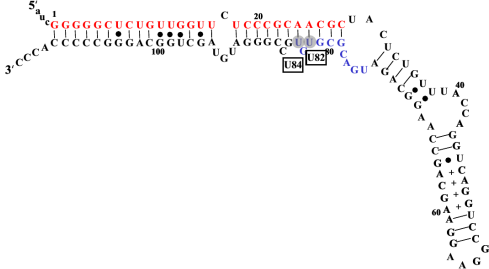




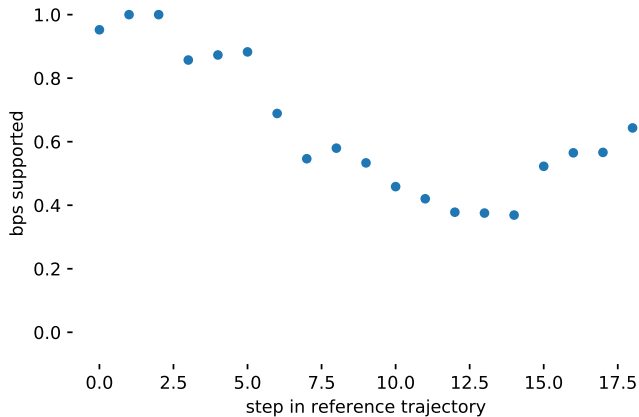
# Example: TRP operon



# Example: small bacterial SRP RNA



# Example: small bacterial SRP RNA

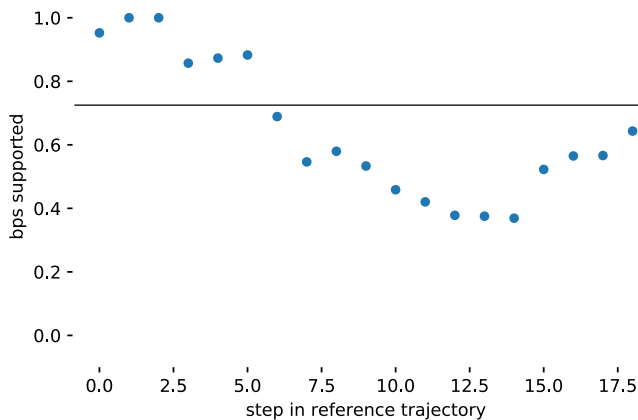


# Background model

- ▶ 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 ...

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