Modeling RNA-RNA Interaction Kinetics

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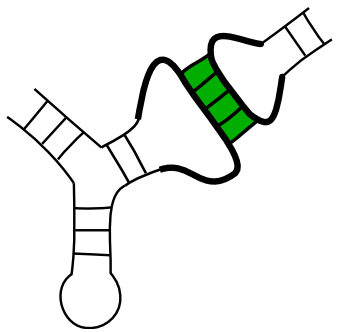
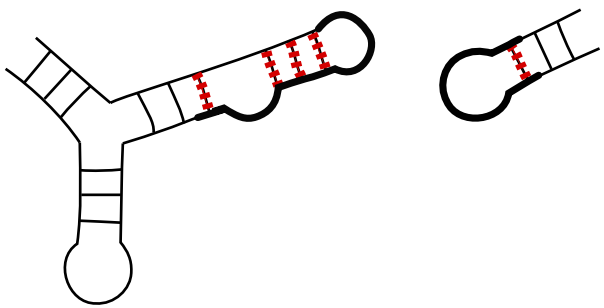
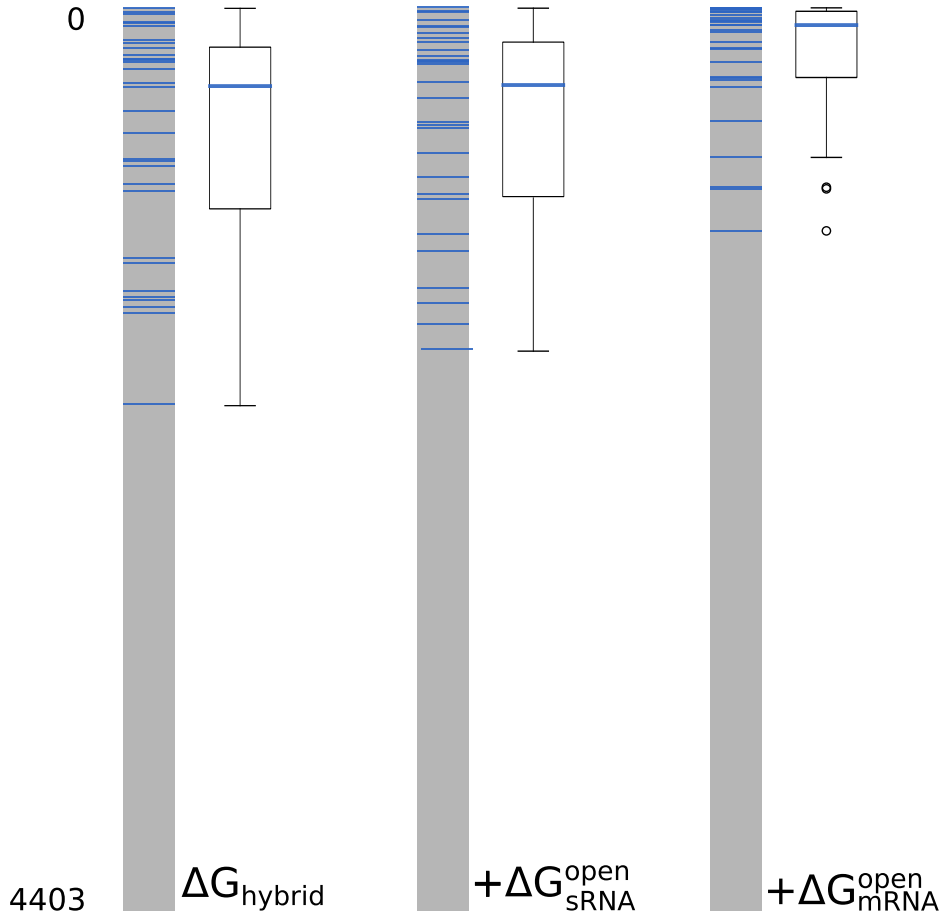
RNA-RNA interaction prediction - thermodynamic

- ΔG_{hybrid}

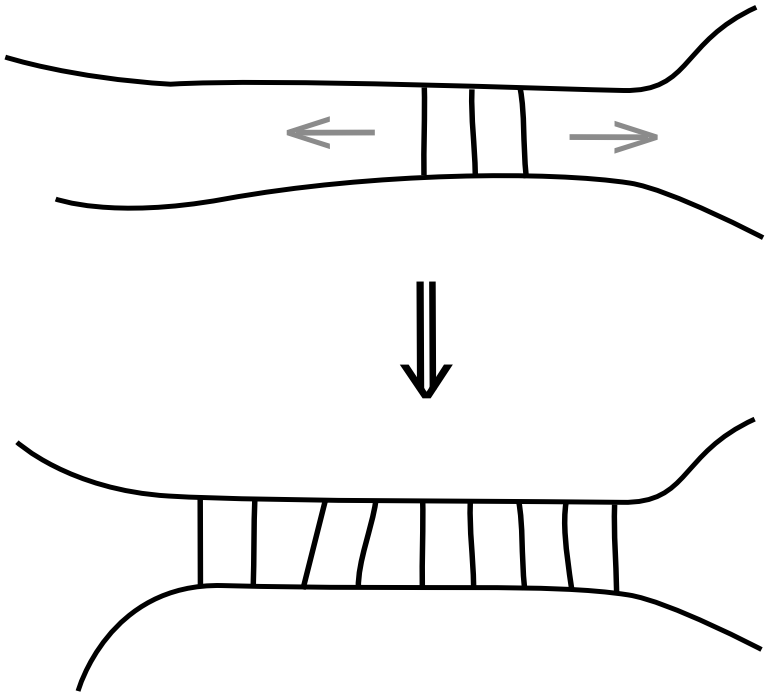


- ΔG_{open}





Interaction formation process



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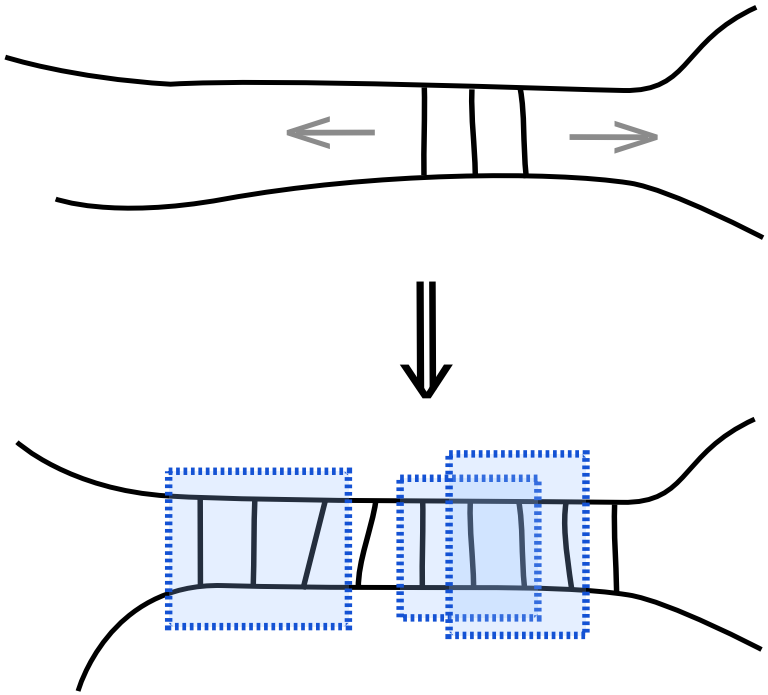

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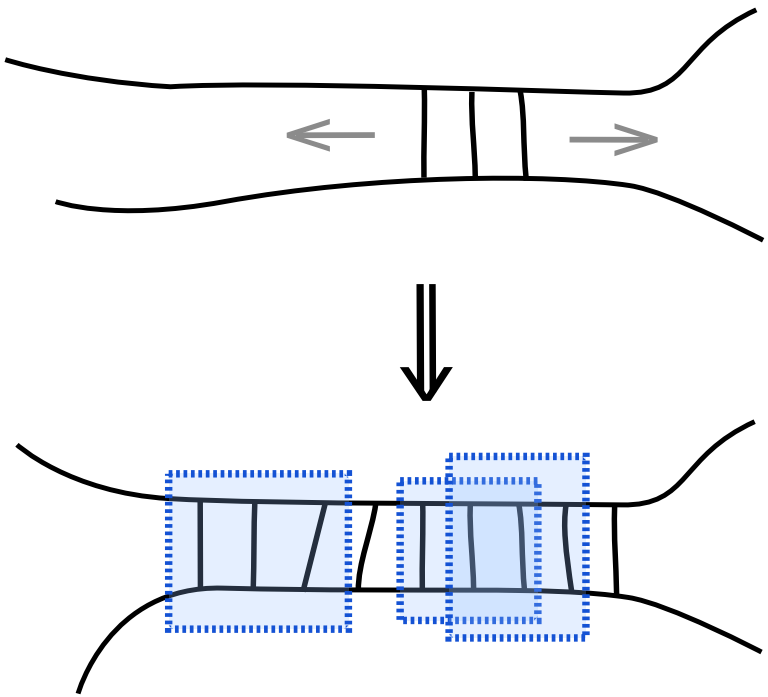
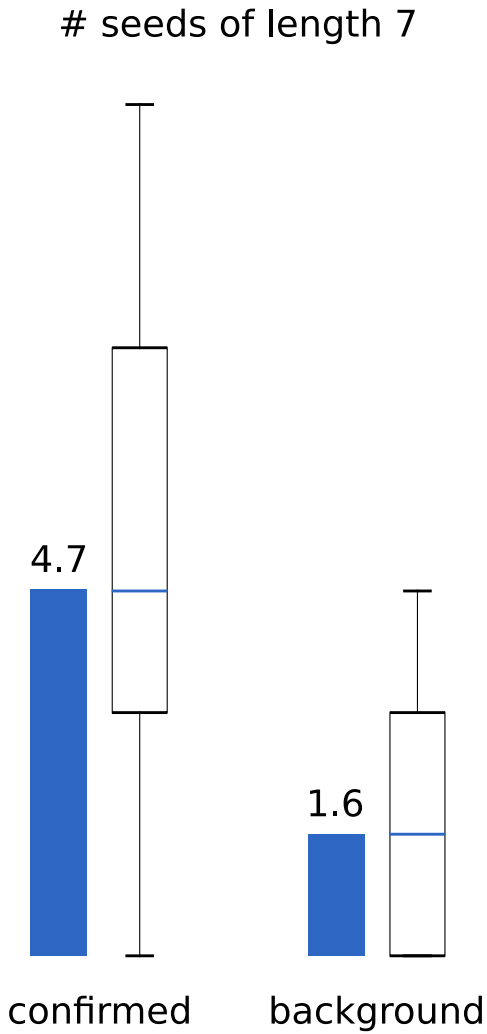
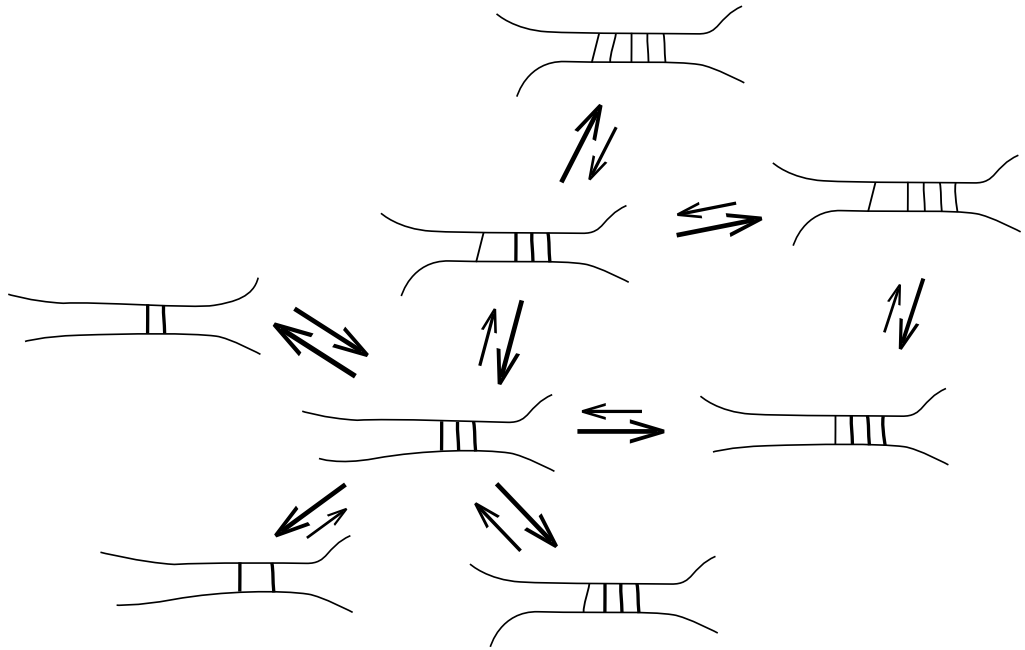


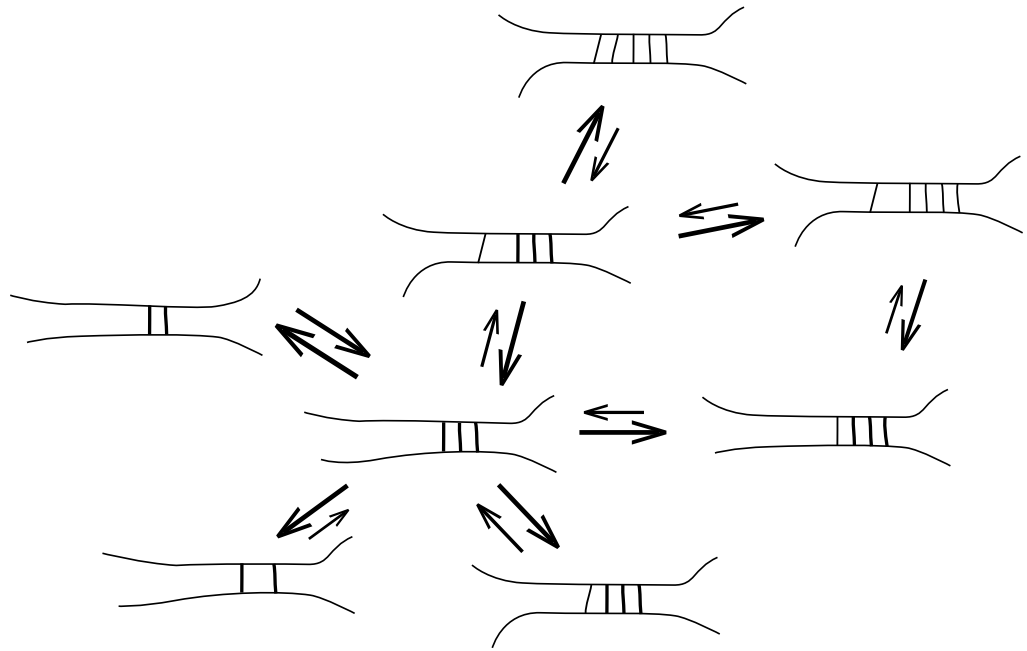


41 experimentally confirmed interactions in E. coli
20 randomized background interactions per confirmed interaction (same E_{therm})

Interaction kinetics



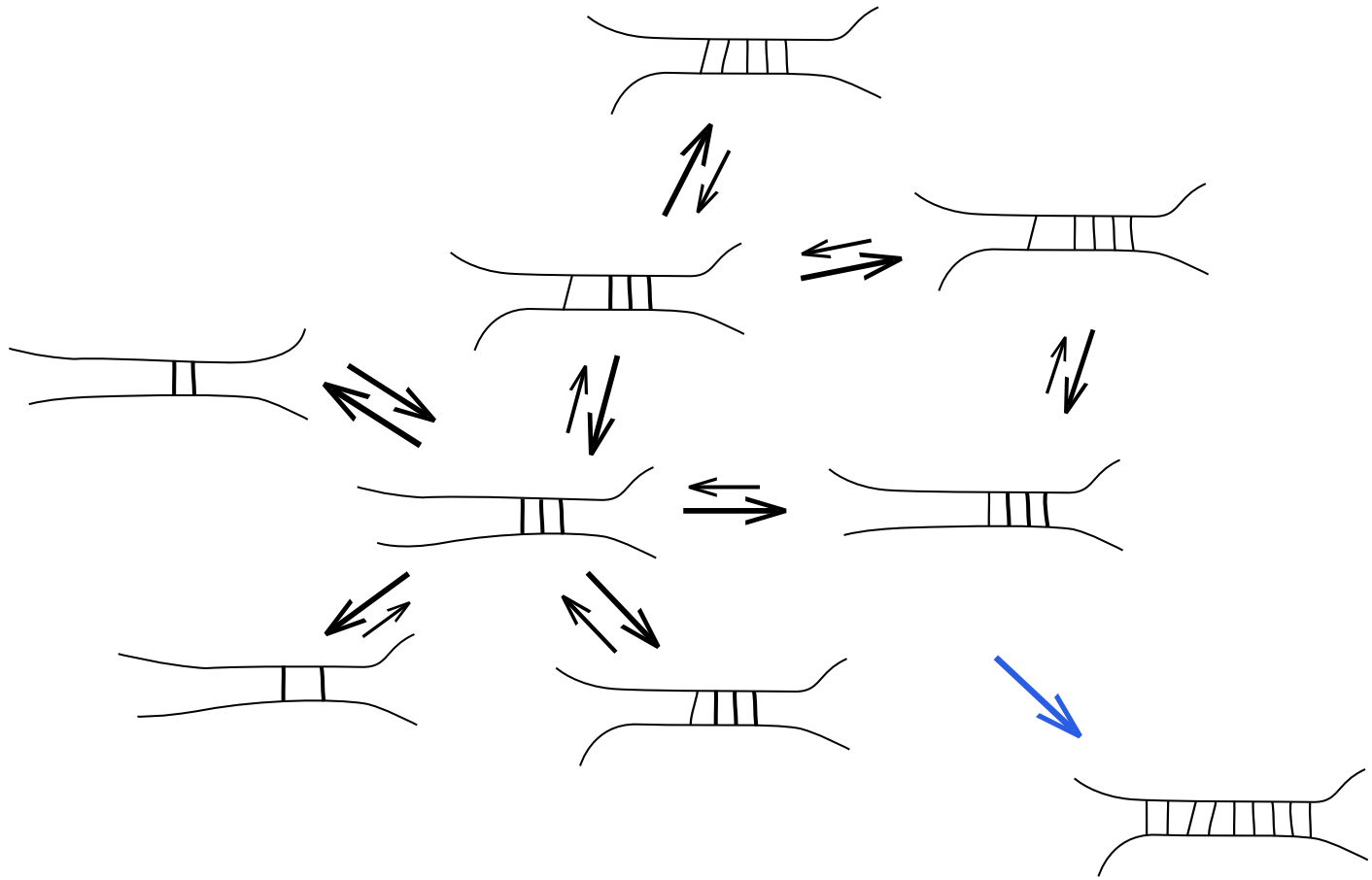
Interaction kinetics



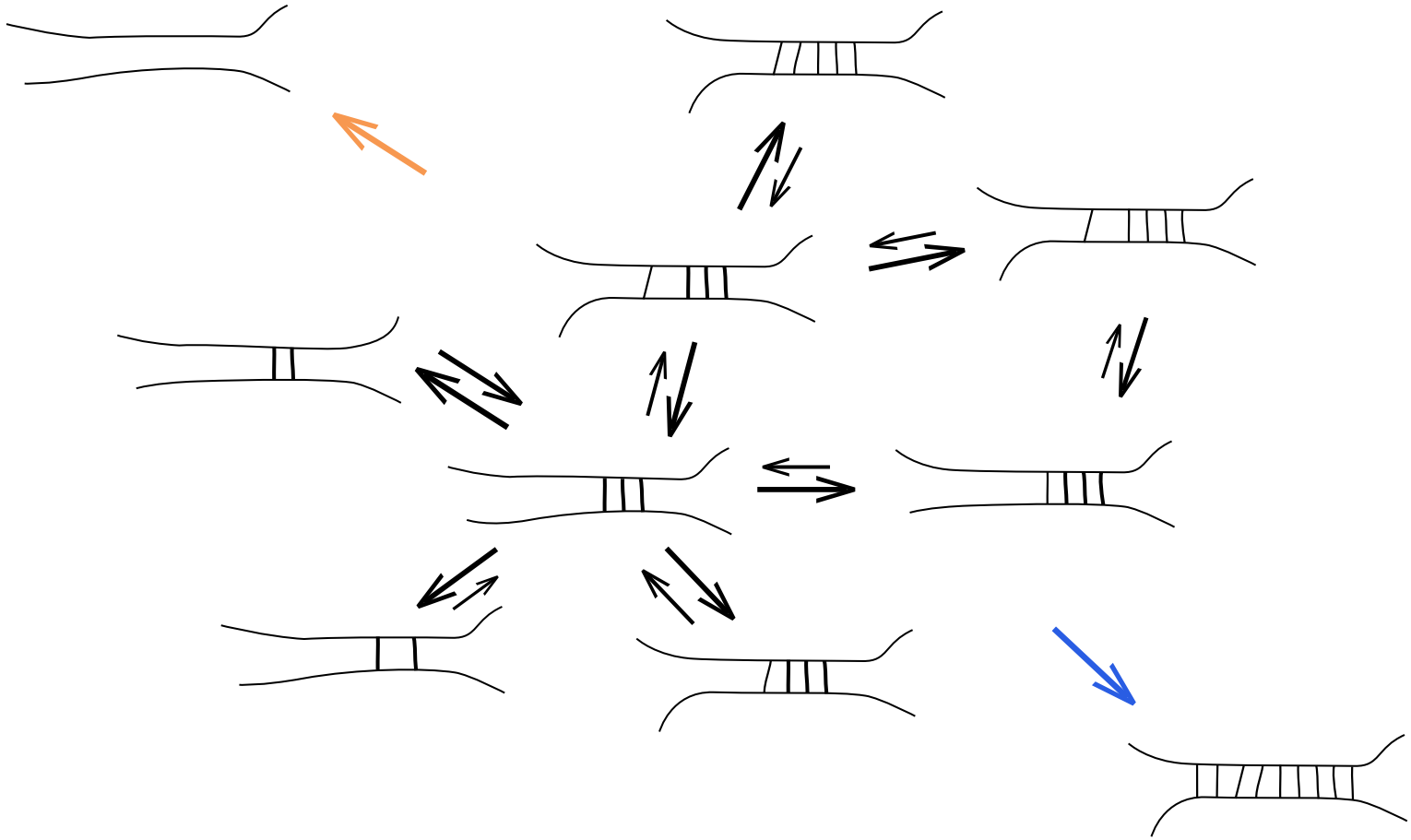
- set of structures/states Ω
- move set M
- energy function E
- $\Rightarrow$ folding rate k_{ij}

$$k_{ij} = \begin{cases} k_0 \text{ if } \Delta G^{\ddagger} \leq 0, \\ k_0 e^{\frac{-\Delta G^{\ddagger}}{RT}} \text{ otherwise} \end{cases}$$

$$\frac{P_i(t)}{dt} = \sum_{i \neq j} (P_j(t) k_{ji} - P_i(t) k_{ij})$$



How fast does the full duplex form?
Dissociation before full duplex?



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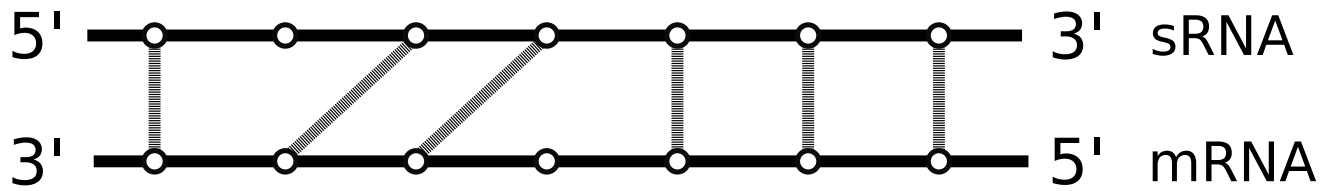
Direct folding paths



$$B_s(k,l) = \min \begin{cases} \max \begin{cases} E(k,l) \\ B_s(k+1,l) \end{cases} & \text{if } k < s \\ \max \begin{cases} E(k,l) \\ B_s(k,l-1) \end{cases} & \text{if } l > s \\ E(s,s) & \text{if } s = k = l \end{cases}$$

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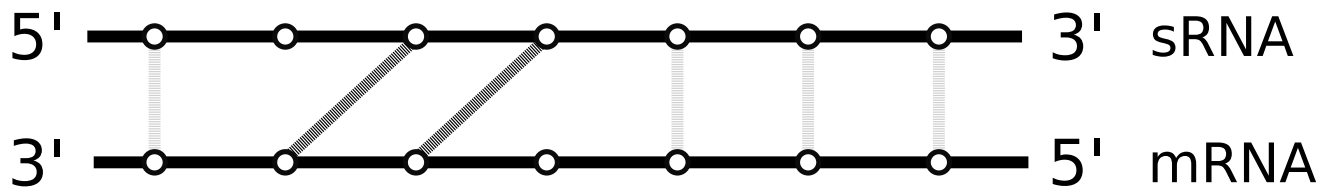

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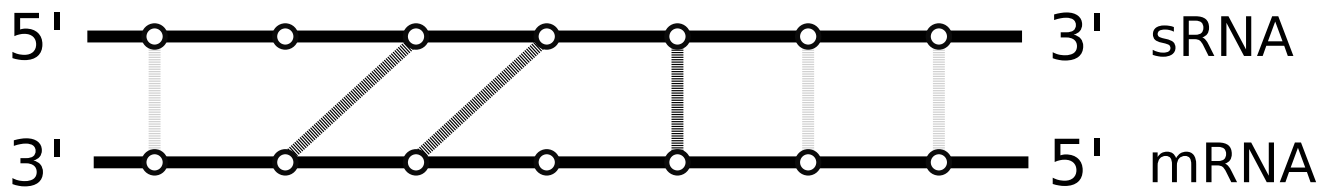

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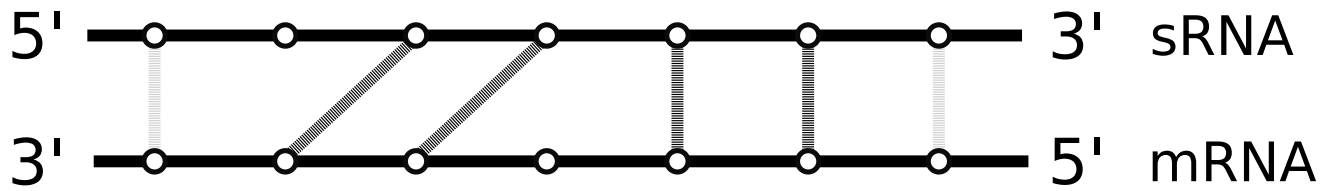

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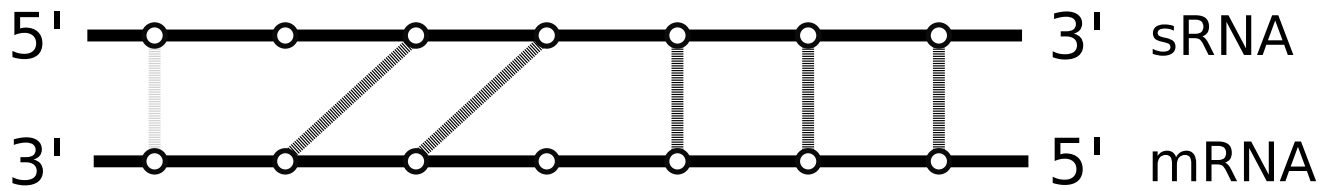

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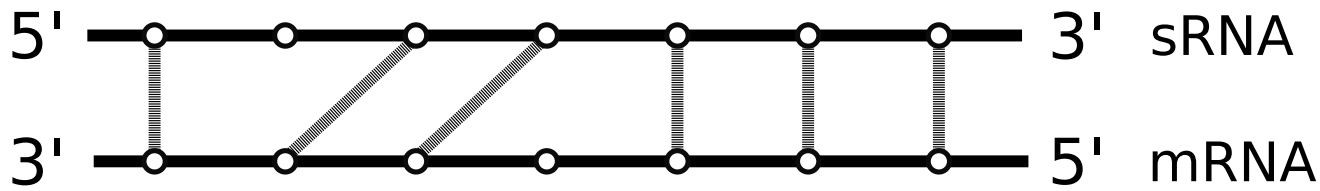

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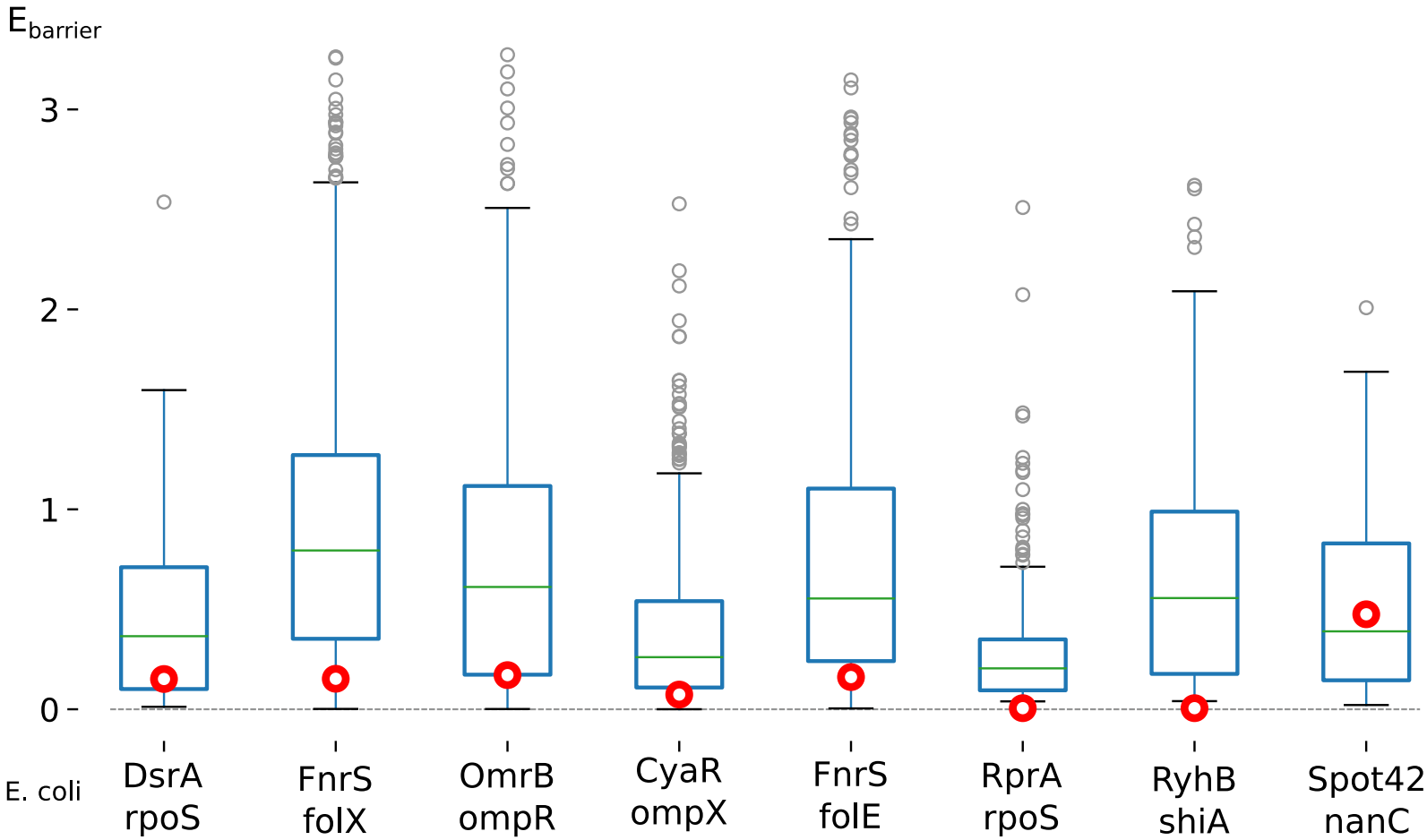
Energy barrier:
confirmed interactions vs. randomized background



Exact kinetics on reduced state space

mRNA: ptsG

```
5'-A     C        GA    U-3'
    GCACC AUACUCAG  GCAC
    :|||| ||||||||  :|||
    UGUGG UAUGAGUC  UGUG
3'-A     U        AG    U-5'
```

sRNA: SgrS

Exact kinetics on reduced state space

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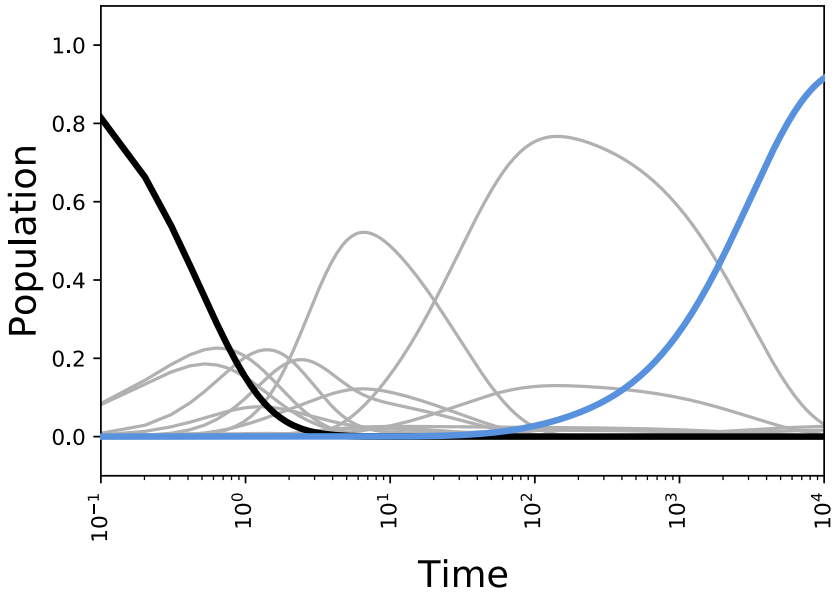

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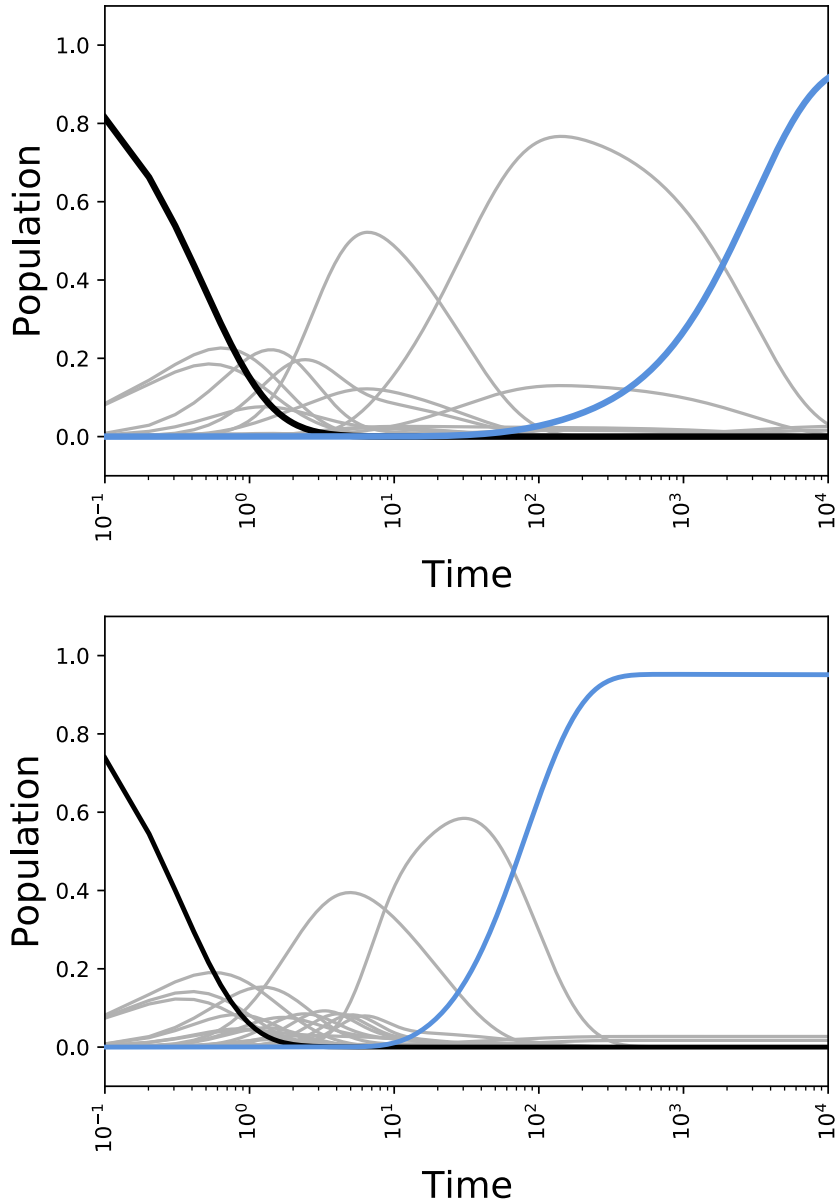
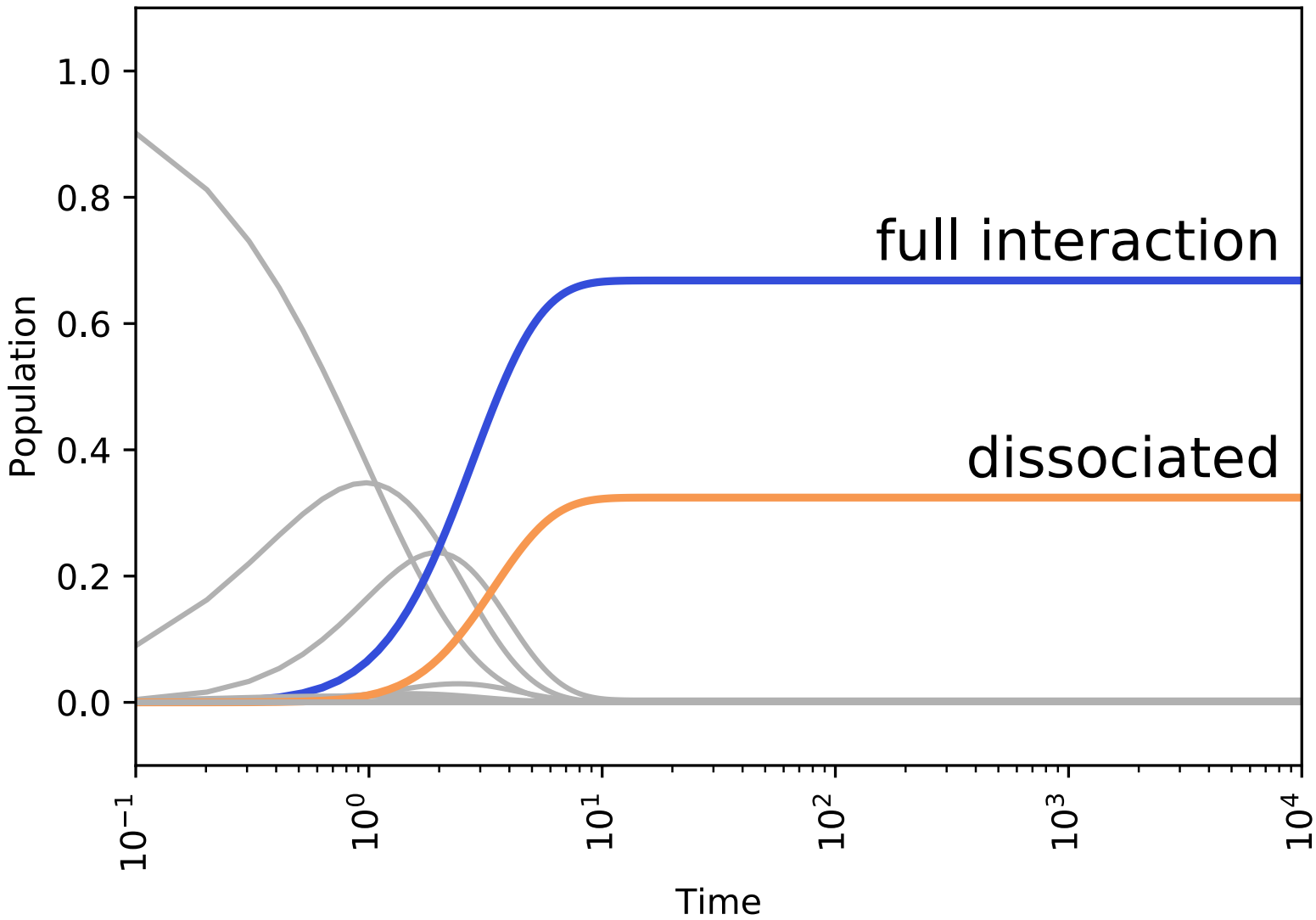
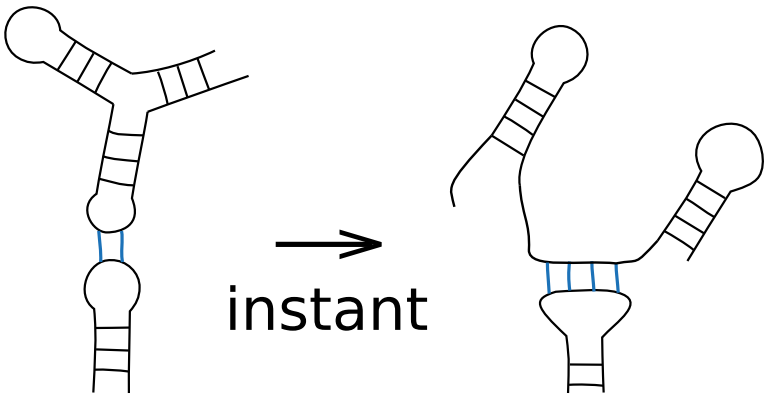


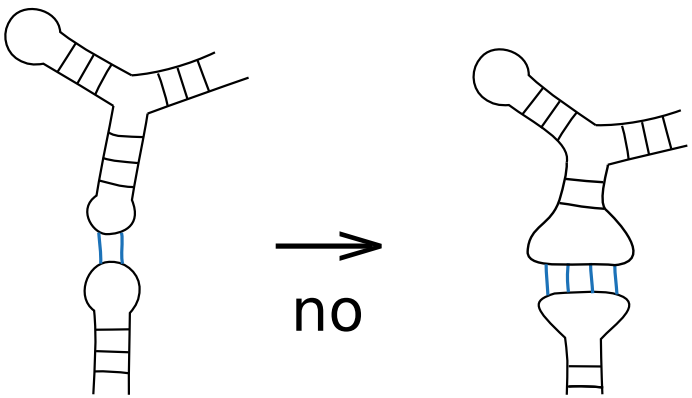
Probability of dissociation before full interaction is formed



FnrS, folX, seed 1

Energy model - intramolecular refolding





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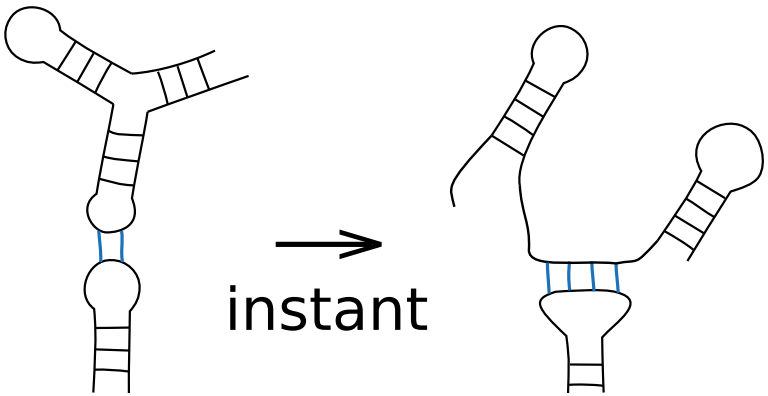

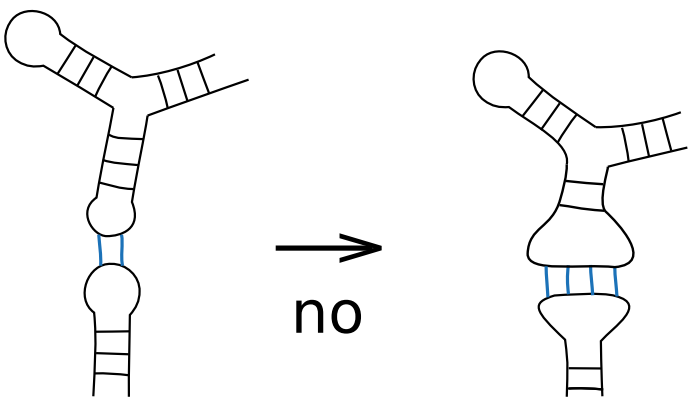

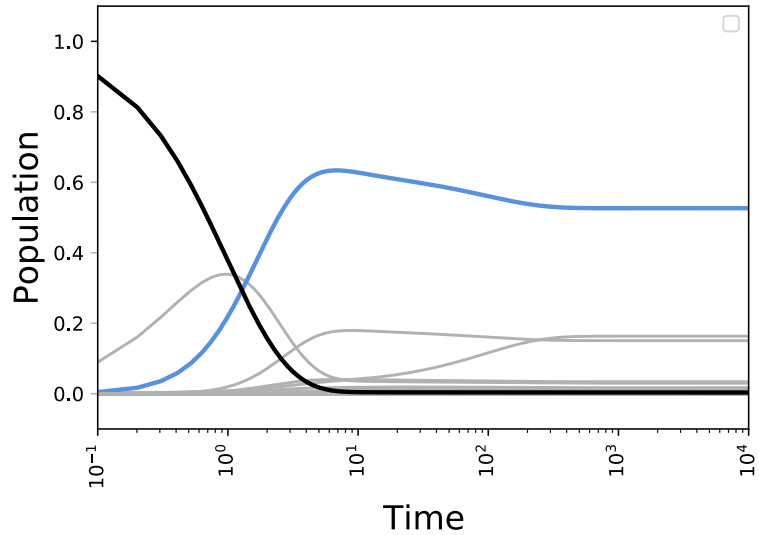

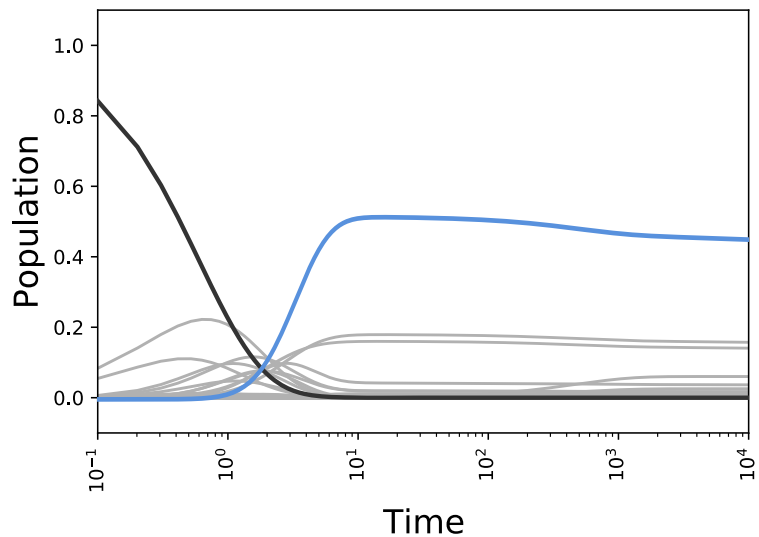

ArcZ, rpoS, seed 1

RNA-RNA interaction formation process

- mechanistic hypothesises
- identify kinetic features
- benchmark data set and background models
- efficient computation methods for kinetic features
- extend and improve interaction prediction method

THANKS TO ...

- Irene, Sebastian, Ivo
- TBI team
- Martin Raden, Rolf Backofen
- **You**!

Funding: FWF (I 2874-N28 and DK RNA Biology)

Direct Paths Recursion

$$B_s(k,l) = \min \begin{cases} \max \begin{cases} E(k,l) \\ B_s(k+1,l) \end{cases} & \text{if } k < s \\ \max \begin{cases} E(k,l) \\ B_s(k,l-1) \end{cases} & \text{if } l > s \\ E(s,s) & \text{if } s = k = l \end{cases}$$

$$E(k,l) = E^{\text{hybrid}}(k,l) + E^{\text{unpaired}}(k,l)$$

$$E^{\text{hybrid}}(k,l) = \min \begin{cases} E^{\text{hybrid}}(k+1,l) + L(k,k+1) & \text{if } k < l \\ E_{\text{init}} & \text{if } k = l \end{cases}$$