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RNA design hands-on

Sven and Stefan
Bioinformatik Leipzig

Get miniconda and follow the install instructions:

<https://conda.io/miniconda.html>

Activate the bioconda repositories:

```
conda config --add channels defaults  
conda config --add channels bioconda  
conda config --add channels conda-forge
```



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```
conda create -n rnadesign  
conda activate rnadesign  
conda install viennarna rnablueprint barriers treekin=0.3.1
```

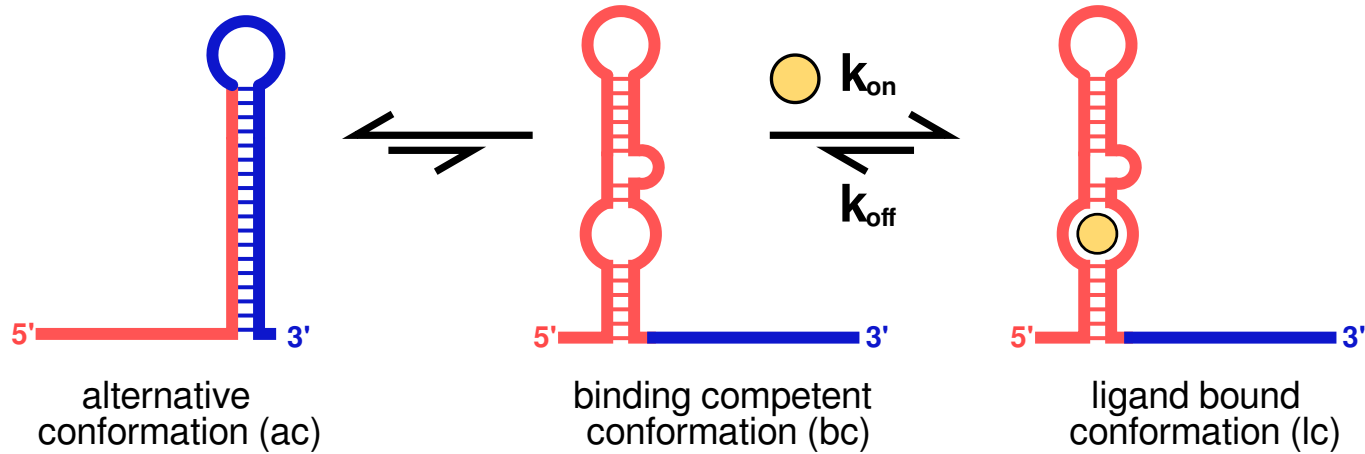
ZIP archive containing all needed files:

<https://bit.ly/2srt1Ia>



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Ligandswitch Idea

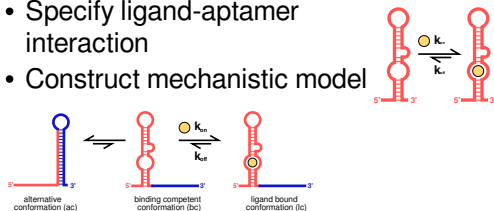




Ligandswitch Pipeline

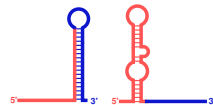
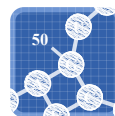
Analysis of the biological system

- Specify ligand-aptamer interaction
- Construct mechanistic model



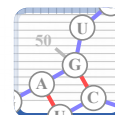
Sequence sampling

- Specify structure and sequence constraints
- Sample with *RNAblueprint*



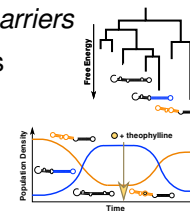
Optimization approach

- Utilize *RNA sketch*
- Adaptive walk
- Define objective function:
 - Probability of structural features
 - Apply *ViennaRNA* package



Filtering and analysis pipeline

- Energy Landscape of structural ensemble
 - Run *RNAsubopt* and *barriers*
- Kinetic folding predictions
 - Apply *treekin*
 - Structural elements
 - Coarse graining
 - Absorbing state
- Lonely base-pair evaluation





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Ligandswitch

Usage

```
$ python ligandswitch.py mfe          # mfe defect  
$ python ligandswitch.py prob        # probability defect  
$ python ligandswitch.py             # element probability defect
```

Ctrl + C to stop program!



Design a thermoswitch which folds into these two states at the given temperatures:

```
(((((.....)))))) at 28.0 degree celsius  
(((.....))).....(((.....))) at 42.0 degree celsius
```

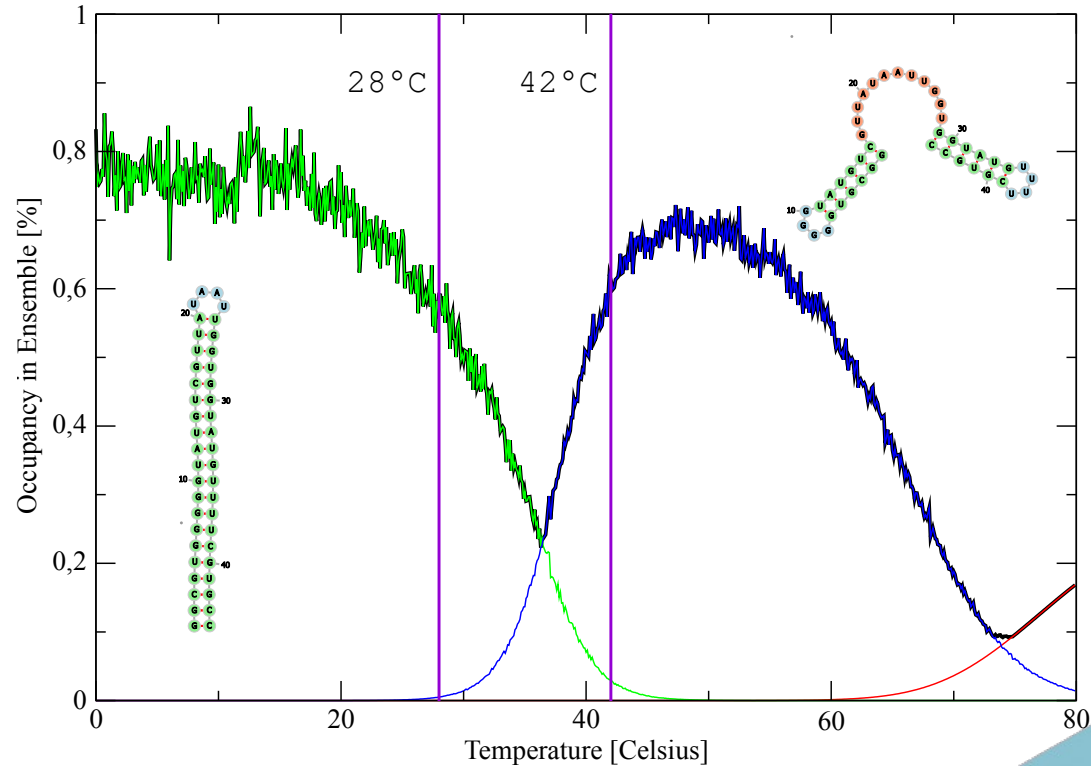
```
$ RNAfold -p -T 28  
GGCGUGGGGGUAUGUCGUUAUAUUGGUGGUAUGUUUUCGUGCC  
(((((((.....)))))))))  
  minimum free energy = -15.97 kcal/mol  
(((((((.....)))))))))  
  free energy of ensemble = -16.28 kcal/mol  
(((((((.....))))))))) {-15.97 d=0.70}  
  frequency of mfe structure in ensemble 0.591288; ensemble diversity 1.35  
  
$ RNAfold -p -T 42  
GGCGUGGGGGUAUGUCGUUAUAUUGGUGGUAUGUUUUCGUGCC  
((((.....))).....((((.....))))  
  minimum free energy = -9.13 kcal/mol  
((((.....))).....((((.....))))  
  free energy of ensemble = -9.44 kcal/mol  
((((.....))).....((((.....)))) {-9.13 d=6.10}  
  frequency of mfe structure in ensemble 0.613925; ensemble diversity 9.93
```



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Challenge Thermoswitch

GGCGUGGGGGUAUGUCGUUAUAAUUGGUGGUAUGUUUUCGUGCC





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Challenge

Thermoswitch

```
$ python thermoswitch.py prob      # probability defect  
$ python thermoswitch.py          # ensemble defect
```

Ctrl + C to stop program!