

JUST WHAT THE DOCTOR ORDERED

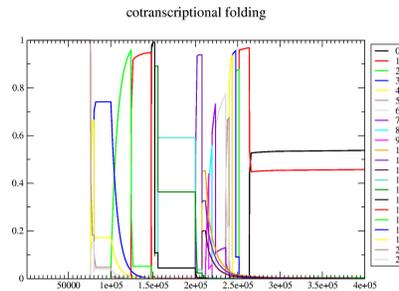
EXPLORING COTRANSCRIPTIONAL RNA FOLDING USING DR. TRANSFORMER AND DR. FORNA

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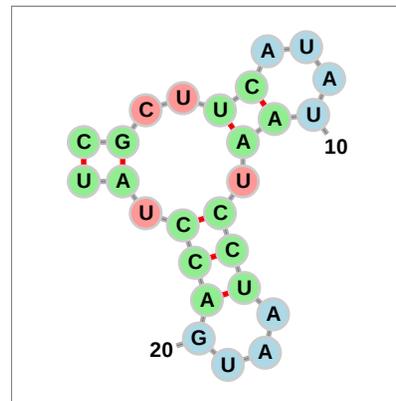
TBI

A STORY WITH TWO PLOTS

Cotranscriptional folding

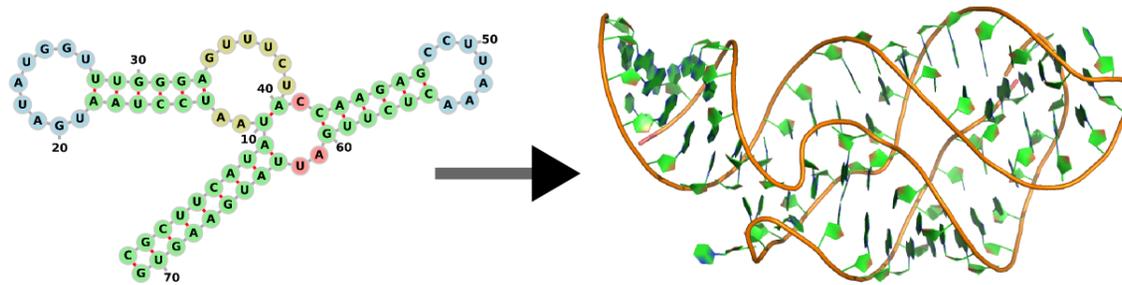


RNA Secondary Structure Display



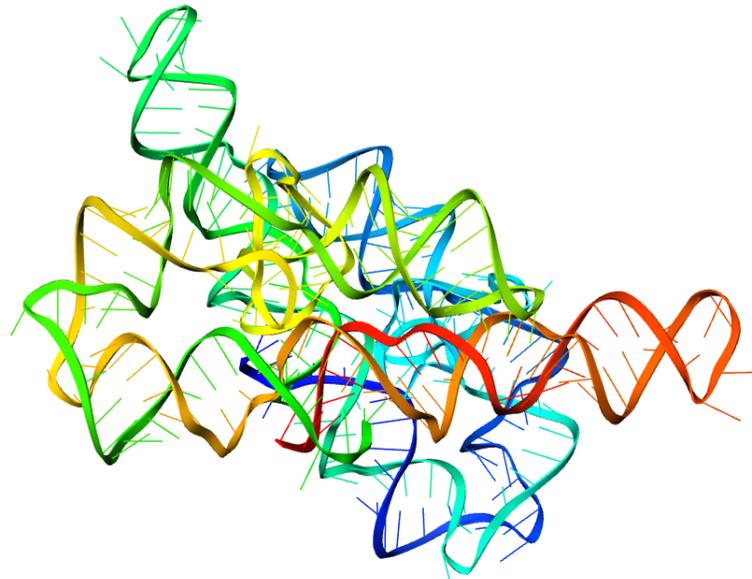
IT ALL BEGAN WITH...

RNA tertiary structure prediction...

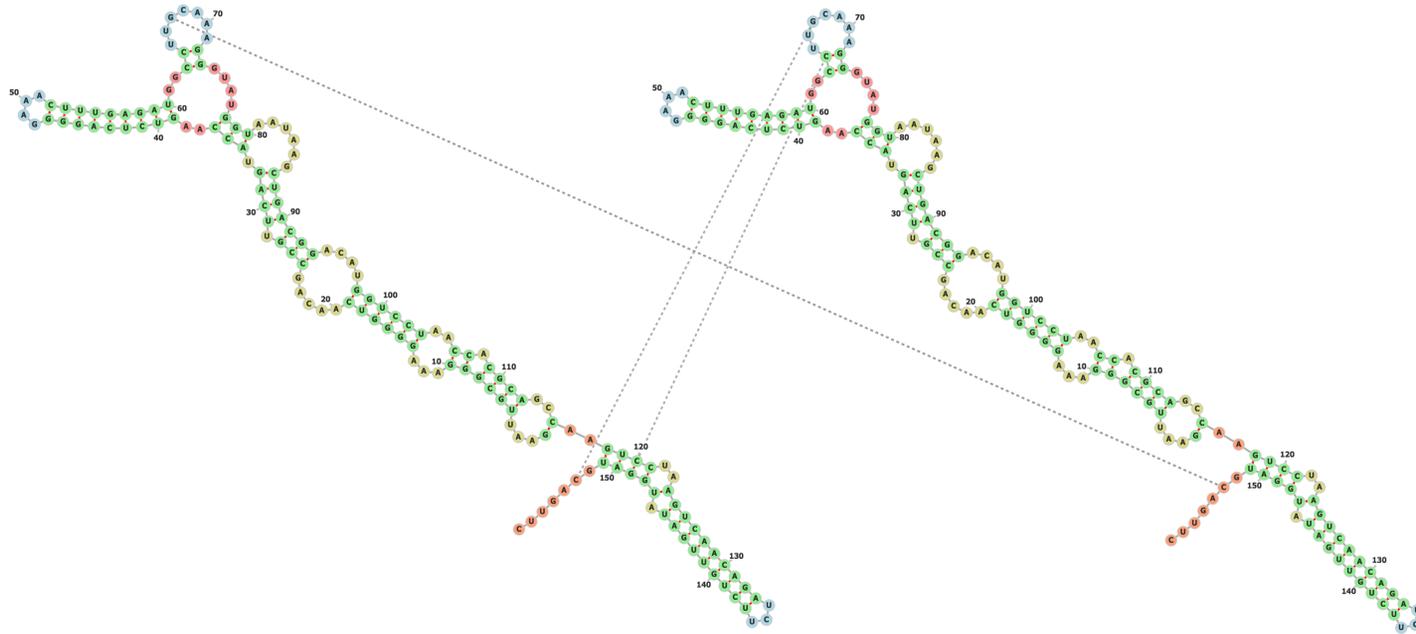


WHICH REQUIRED...

Simplifying known tertiary structures

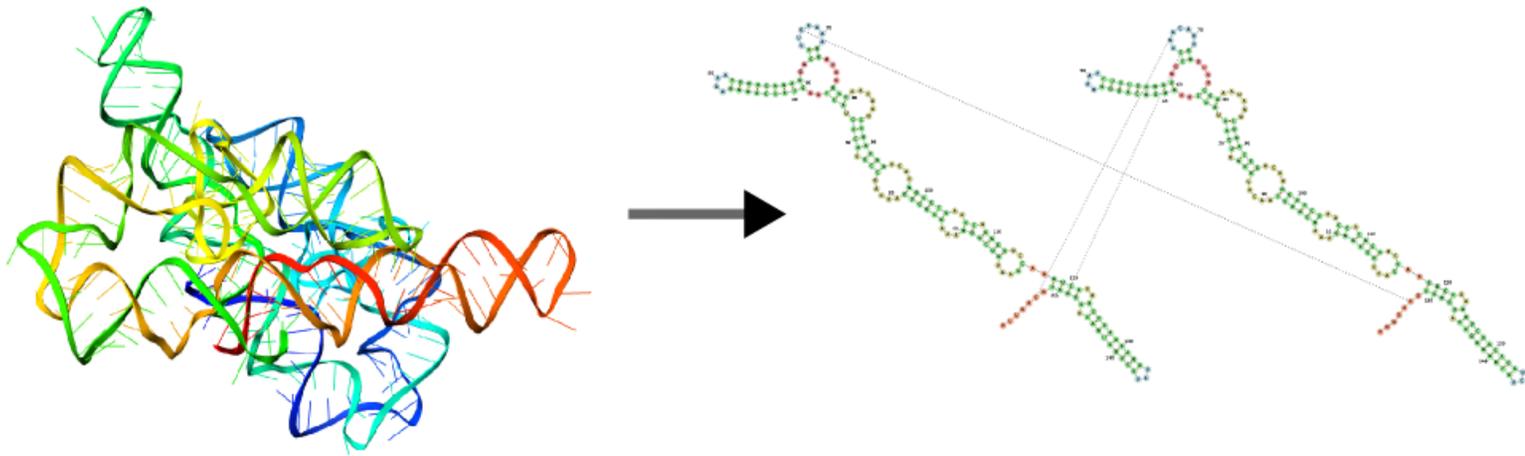


Back to secondary structures



SO WE MADE A TOOL

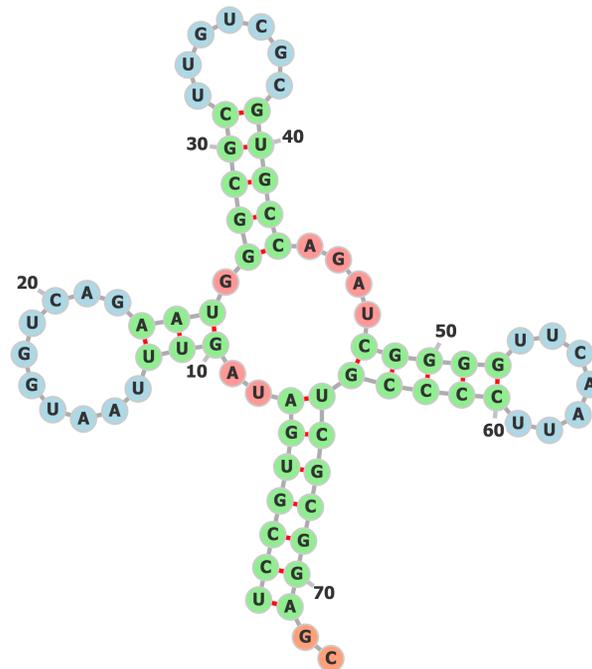
To convert 3D structures to 2D



AND...

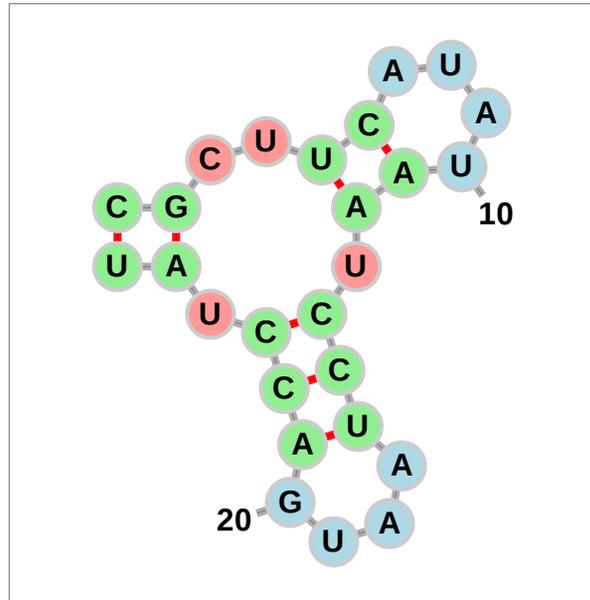
To convert 1D structures to 2D

```
>2TRA_A
UCCGUGAUAGUUUAAUGGUCAGAAUGGGCGCUUGUCGCGUGCCAGAUCGGGGUUCAAUUCCCGUCGCGGA
GC
(((((((..(((.....))))).((((.....))))). .... ((((((.....)))))))))
..
```



AND...

To share structures online:

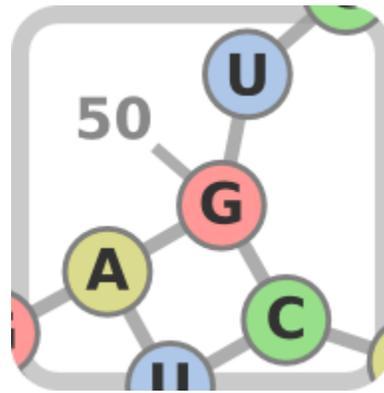


Using a few lines of javascript:

```
var container1 = new FornaContainer("#rna_ss1",
    {'applyForce': false, 'allowPanningAndZooming': true});
var options = {'structure': '((...((.....)).(((.....)))..))',
    'sequence': 'CGCUUCAUAUAUCCUAAUGACCUAU'
};
container1.addRNA(options.structure, options);
```

AND...

We called it **forna**



And you can use it freely at:

<http://rna.tbi.univie.ac.at/~forna>

MEANWHILE...

A QUESTION BURNED...

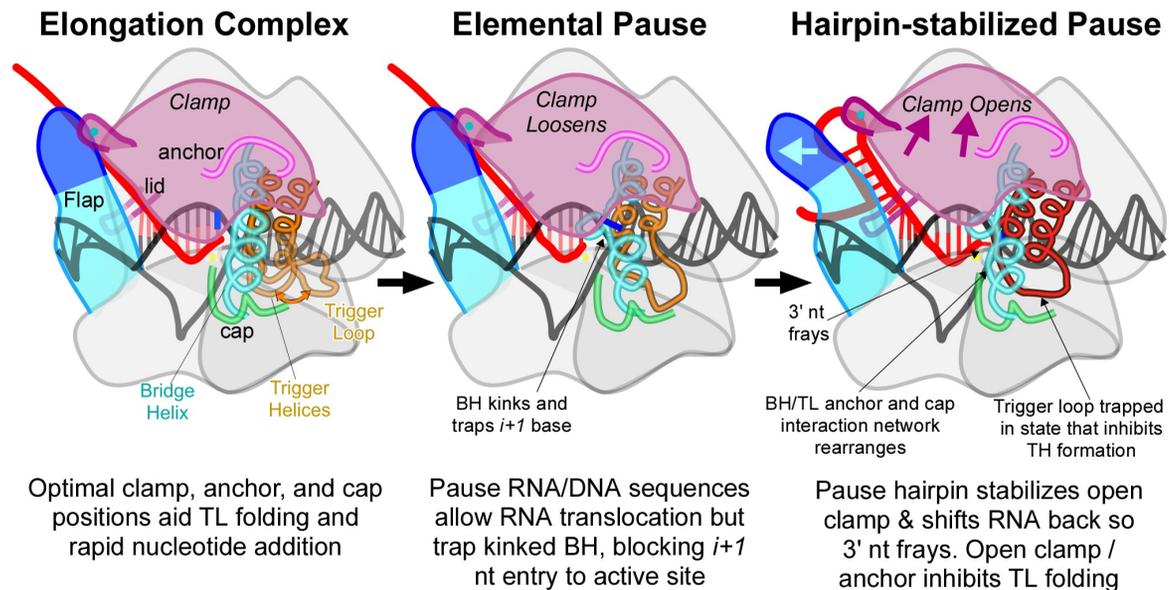
What happens to the structure of an RNA as it's being transcribed?

DOES IT FOLD AFTER TRANSCRIPTION?

OR DURING TRANSCRIPTION?

MOST WOULD AGREE

Folding begins during transcription



<http://landick.wisc.edu/research.htm>

WHAT DOES IT LOOK LIKE?

Enter Dr Transformer

A tool for modeling cotranscriptional folding.

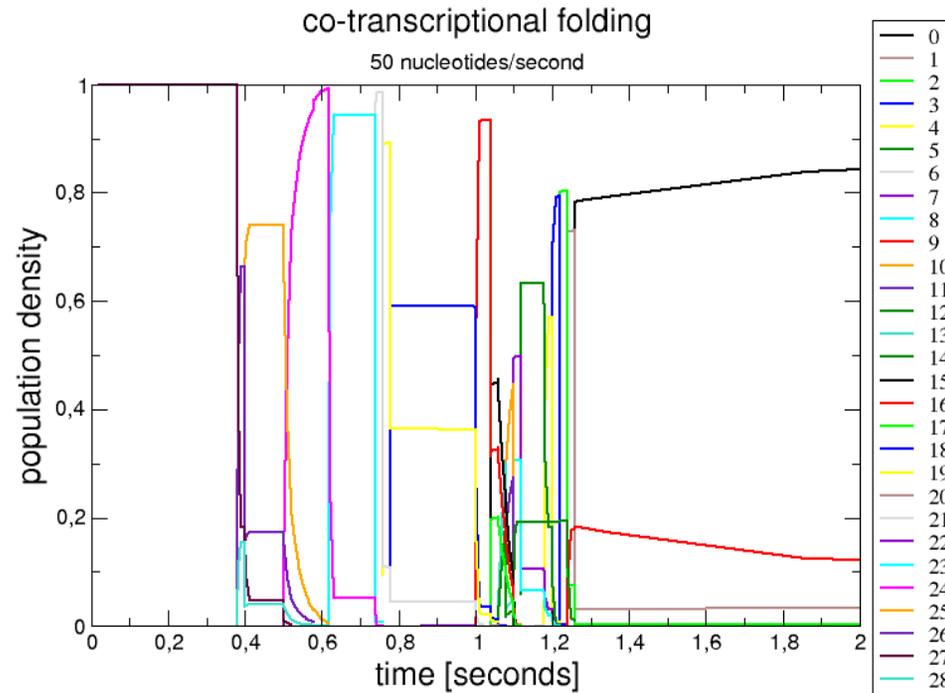
DR TRANSFORMER

Provides a time series of concentration information about the various RNA structures that appear during transcription.

id	time	concentration	structure	energy
1	0.380000	1.000000	0.00
2	0.3800005	3.396416e-04	.((((((.....))))).))	-0.80
1	0.3800005	9.996583e-01	0.00
3	0.3800005	2.029009e-06	...((((.....)))...)	0.10
2	0.3800036947695	2.424217e-03	.((((((.....))))).))	-0.80
1	0.3800036947695	9.974787e-01	0.00
3	0.3800036947695	9.708779e-05	...((((.....)))...)	0.10
2	0.380027302645	1.592437e-02	.((((((.....))))).))	-0.80

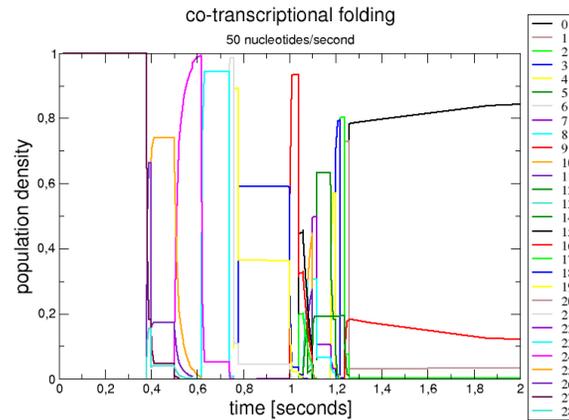
Calculated by solving a system of differential equations, parameterized on the energies of the predicted sub-optimal structures at each step of transcription

A DIFFERENT VIEW



Great! So what's wrong?

WHAT'S THE PROBLEM?

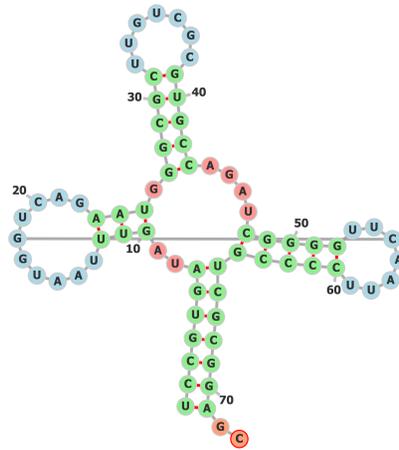


- Confusion
- Too much data
- Not enough data

Can we do better?

WHAT IF?

We combine the the raw data from **Dr Transformer** with the RNA plotting capabilities of **forna**?



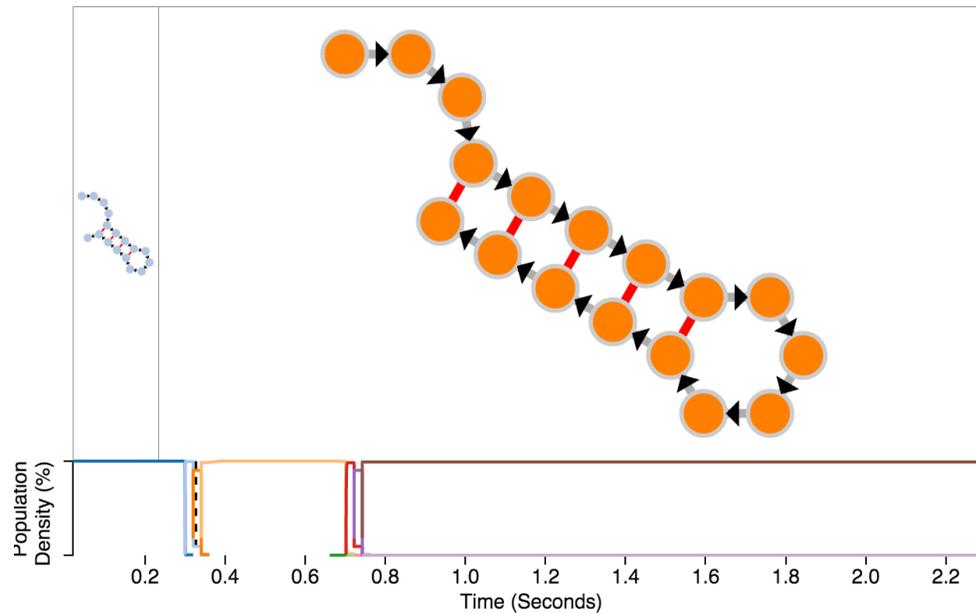
A VISUAL EXPLORATION OF COTRANSCRIPTIONAL FOLDING (DR. FORNA)



NEXT:

A web server...

PROBLEM:



When are two structures actually different?

I have no idea...

Help appreciated!

SO WHAT'S THE POINT?

To summarize

- We can easily draw RNA structures online using **forna**
- We can model cotranscriptional folding using **Dr Transfomer**
- We can combine these two disparate projects to present data in a novel, informative format to help understand biological processes
- We can apply this approach to other projects including RNA regulation, riboswitch refolding, and DNA-RNA interaction.

ACKNOWLEDGEMENTS

A big thanks to...

- **Stefan Badelt** - Dr Transfomer
- **Stefan Hammer** - forna
- **Ronny Lorenz** - ViennaRNA package
- **Ivo Hofacker** - Ideas and Support
- **Everybody else at the TBI** - Good times
- **Ya'll** - Attention, advice and amusement