Visualizing structural models for long(er) RNAs

Yann Ponty
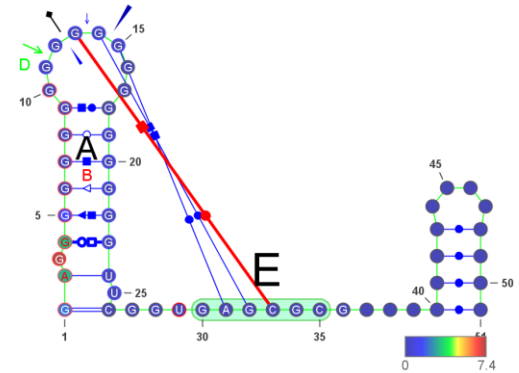
AMIBio team
LIX, UMR 7161

RNA viz dogma

► Modularity

► Robustness

► Clarity

► Realism

► Aesthetics

VARNA: main features

► Multiple layouts

► Annotations: reactivities, regions, glyphs…

► Basic pseudoknots

► Support for multiple input formats (inc. RNAML)
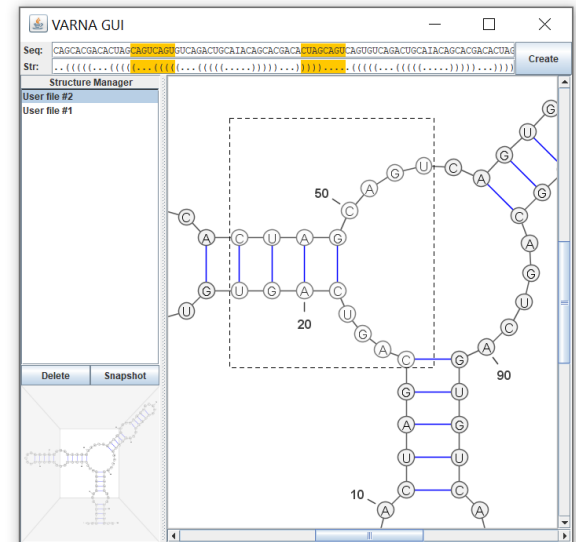
► Under (discrete) development since 2008

► Interactive editor
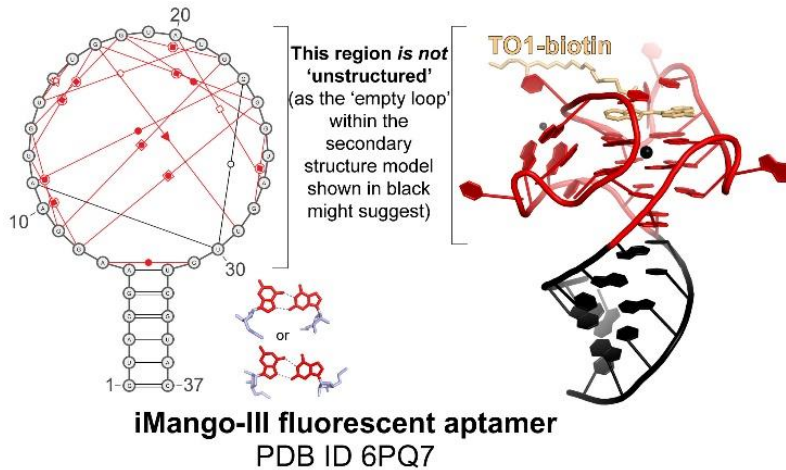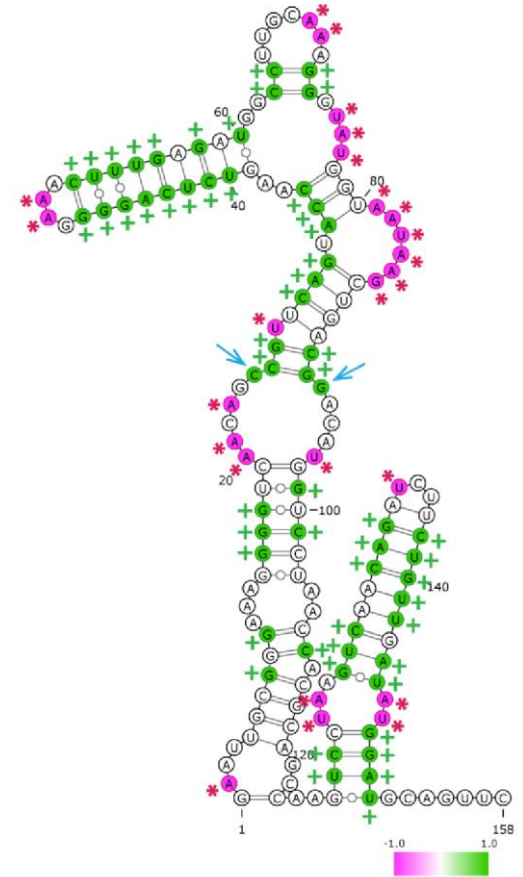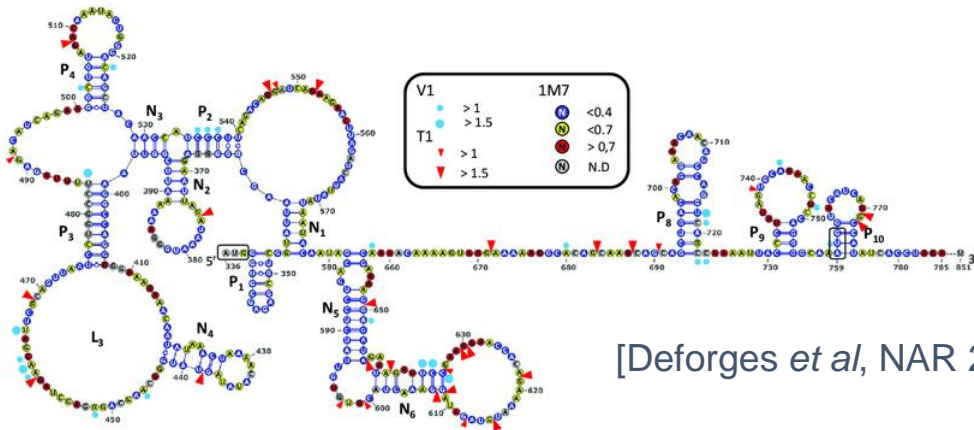
► Jupyter-friendly Python API

Thanks to Hua-Ting Yao

http://varna.lri.fr/
https://htyao.gitlab.io/varna-api/

Some examples by others*

[Deforges *et al*, NAR 2017]

This region *is not* 'unstructured' (as the 'empty loop' within the secondary structure model shown in black might suggest)

TO1-biotin

iMango-III fluorescent aptamer
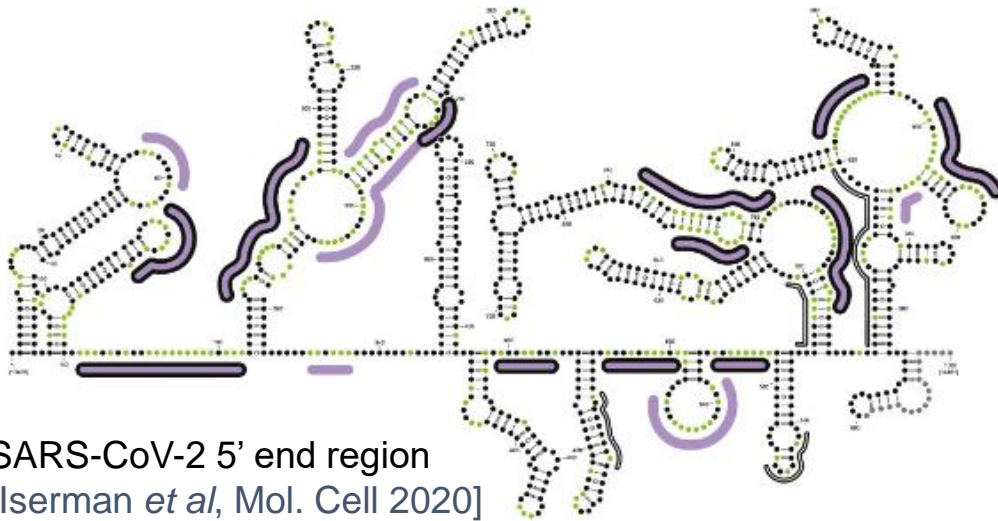PDB ID 6PQ7

[Sau *et al*, RNA 2018]

Generally speaking, no drawing tool has really established itself beyond the laboratory it originated from, except perhaps Varna and R2R... 😎
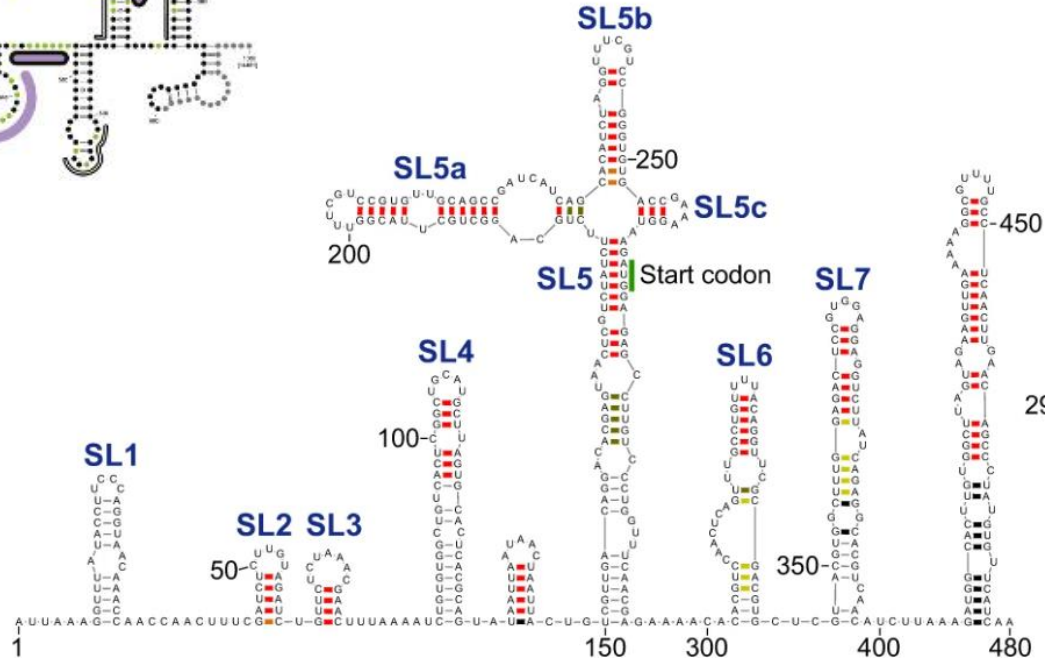[Vicens & Kieft, PNAS 2022]
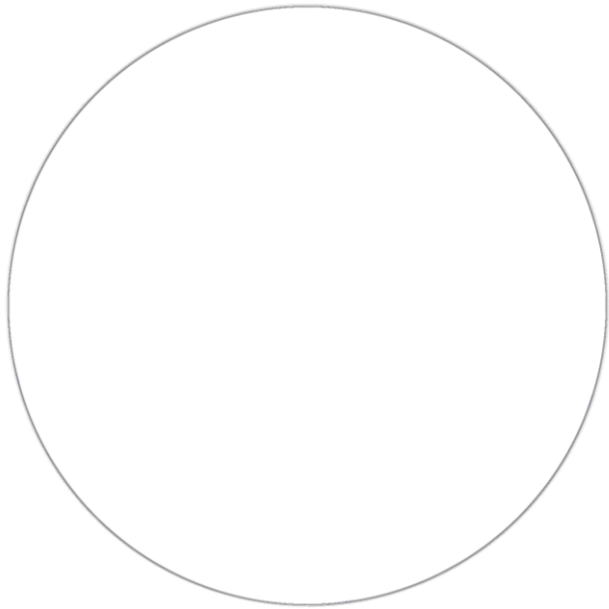
Popular option for structured viral RNAs

SARS-CoV-2 5' end region
[Iserman *et al*, Mol. Cell 2020]

RIC-SEQ
[Cao et al, Nature Comm 2021]

Genome-wide ssRNA models

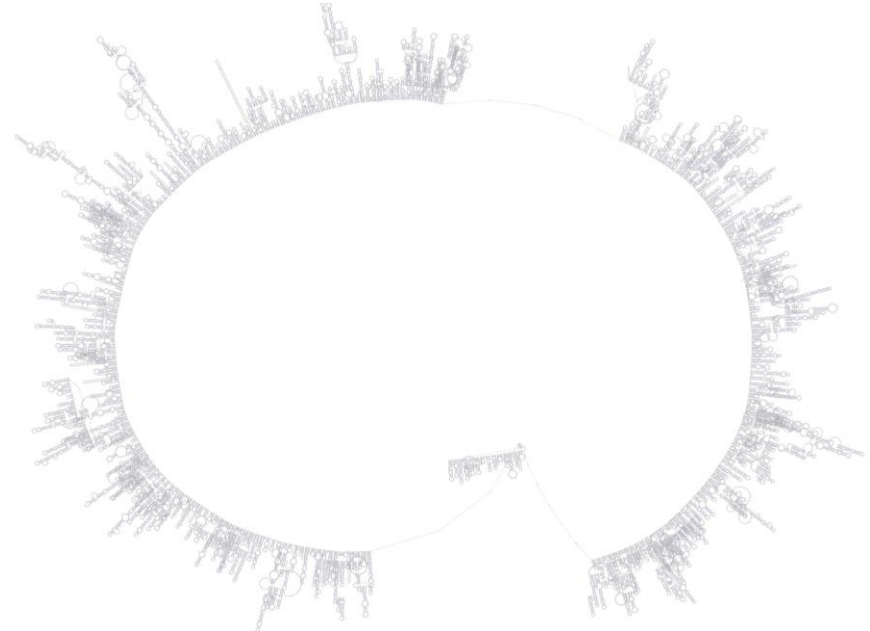HIV-1 NL4-3 genome [Watts *et al*, Nature 2009]

SARS-CoV-2 RIC-SEQ [Cao *et al*, Nature Comm 2021]

Automated layouts lack in grace

In vivo SHAPE model (bounded BP span) [Manfredonia et al, NAR 2020]
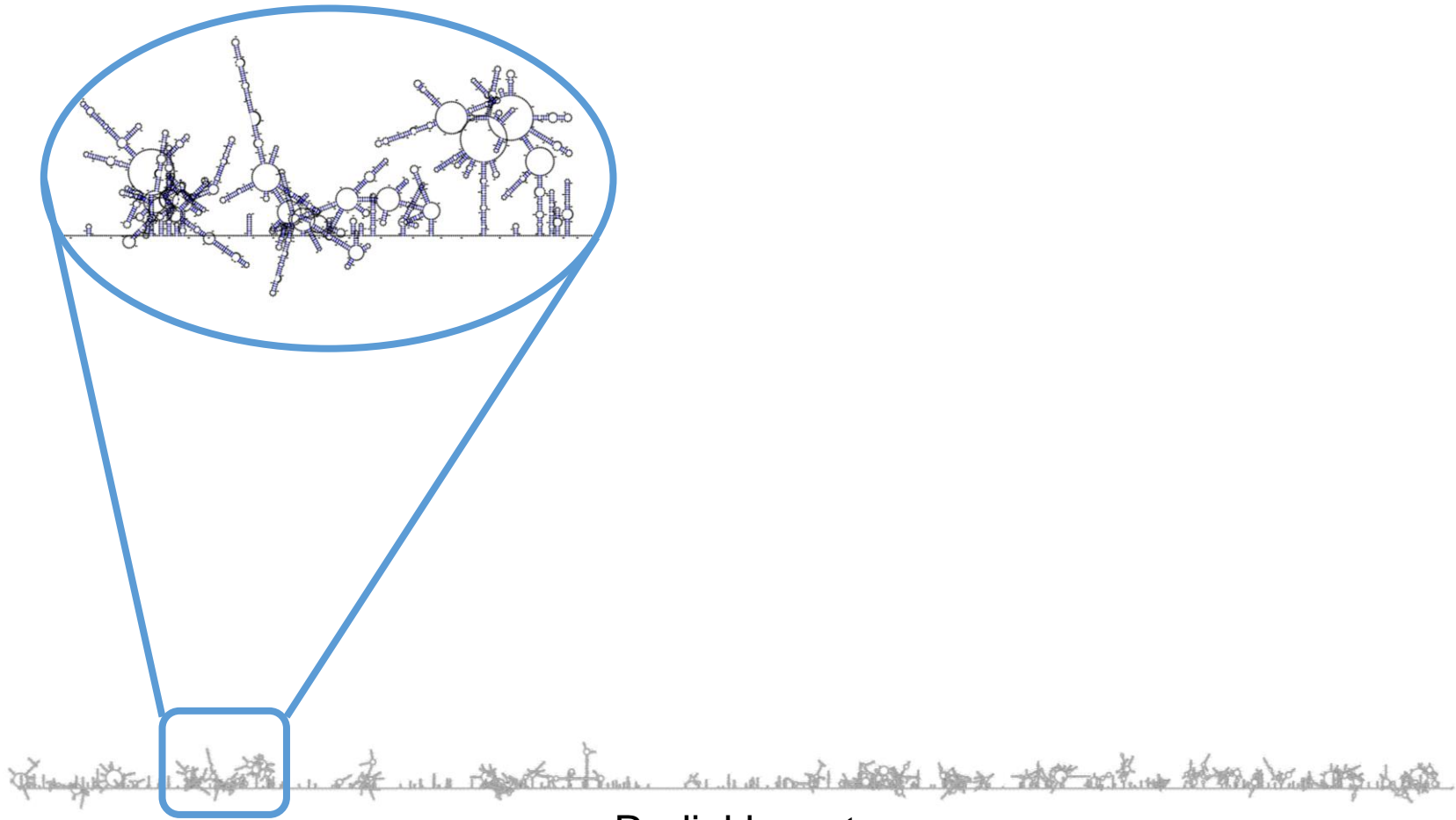

Circle layout

NAView

Arc diagram

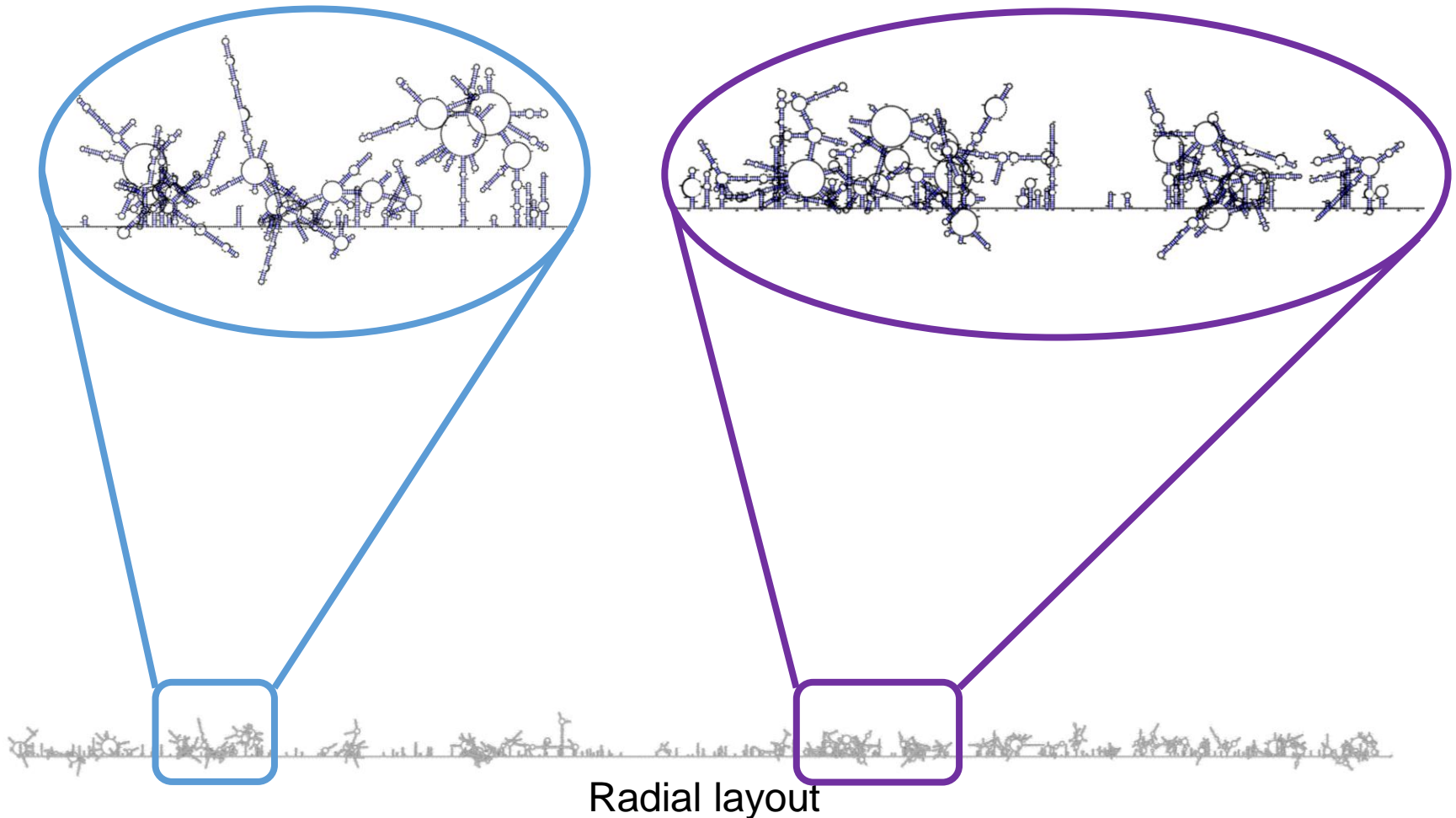Radial layout

SARS-CoV-2 genome-wide architectures

In vivo SHAPE model (bounded BP span) [Manfredonia et al, NAR 2020]
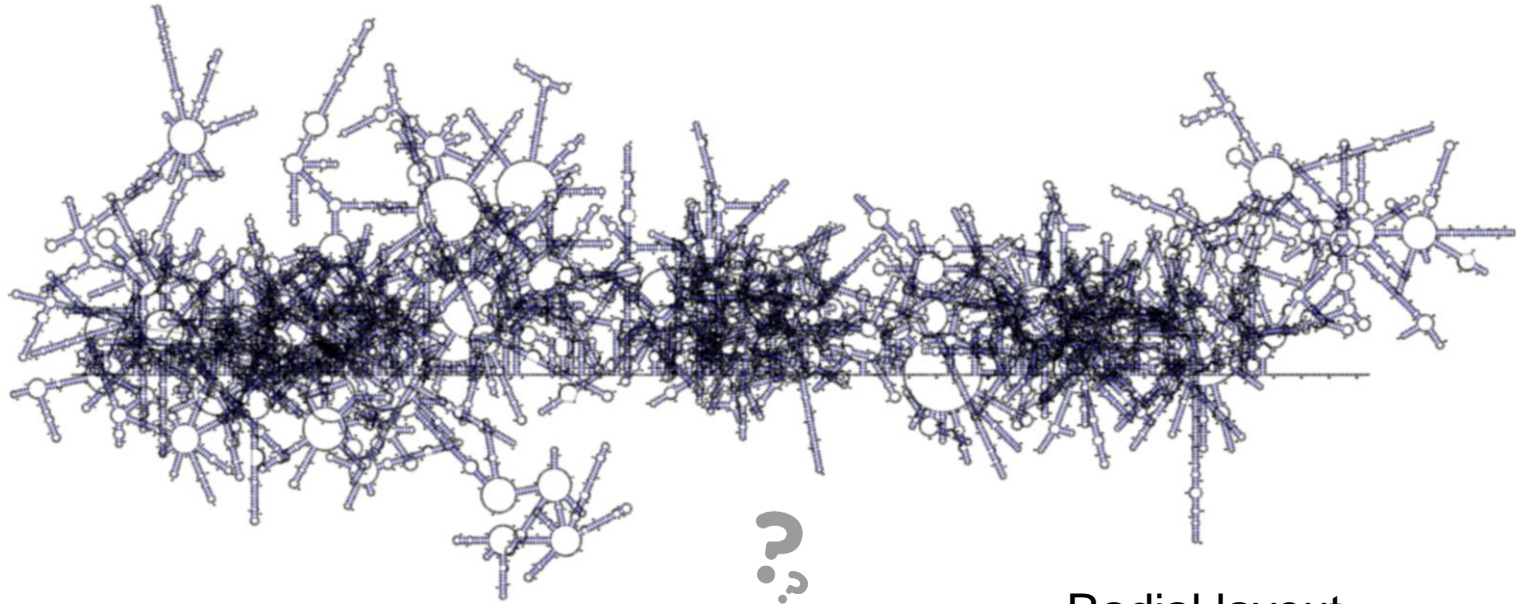

Radial layout

SARS-CoV-2 genome-wide architectures

In vivo SHAPE model (bounded BP span) [Manfredonia et al, NAR 2020]

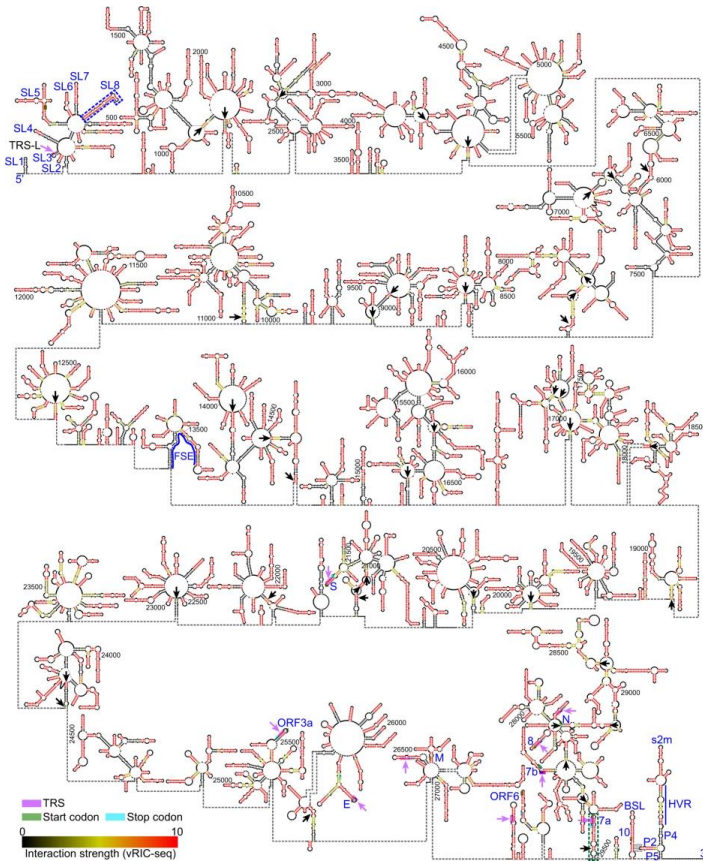Radial layout

SARS-CoV-2 genome-wide architectures

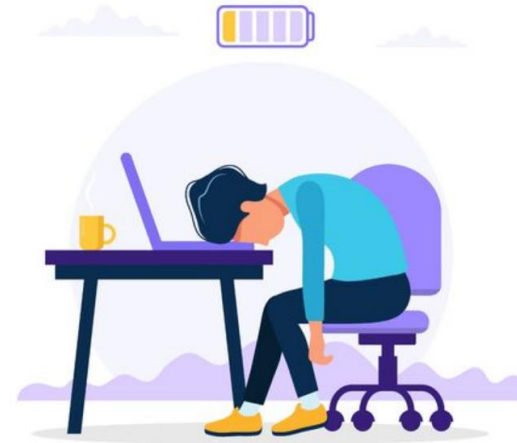SHAPE + (limited) long range interactions [Cao *et al*, Nature Comm. 2021]

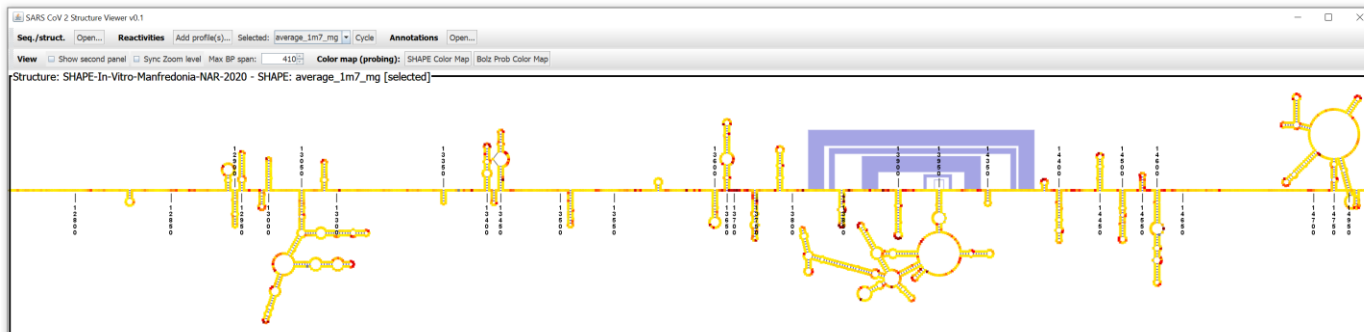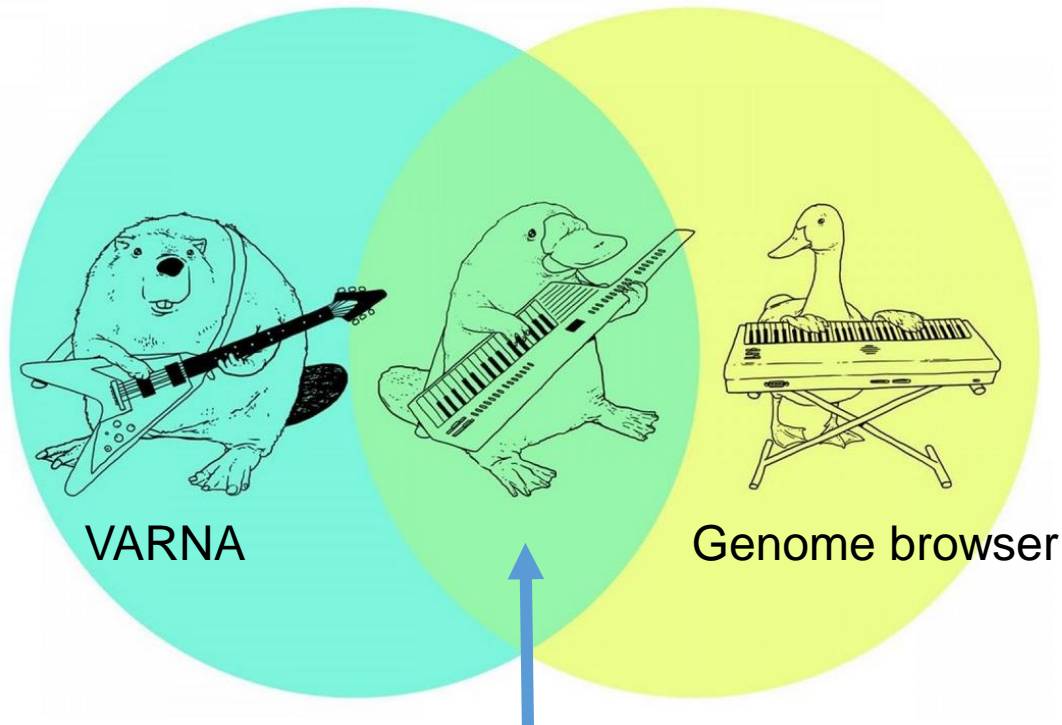Radial layout

The trouble with larger RNAs

RIC-SEQ [Cao et al, Nature Comm 2021]

► VARNA is **not** designed for 30knts RNAs

► Long range BPs induce entanglements

► Domains (probably) drawn/fixed/assembled by innocent ~~slaves~~ junior collaborators

► Interactive exploration simply unreasonable

The big picture

VARNA

Genome browser

Wishlist for the visualization of larger RNAs

► Showcase structure

► Keep reasonable information density

► Linear representation, suggesting genomic coordinates

► Performances enabling real-time exploration

► Rich annotations (react., regions, long range interactions…)

► Quick visual comparison of competing models

► Avoid overlaps + interactions to edit drawing/model

► Export to editable vector/bitmap formats

Live demo

Wishlist for the visualization of larger RNAs

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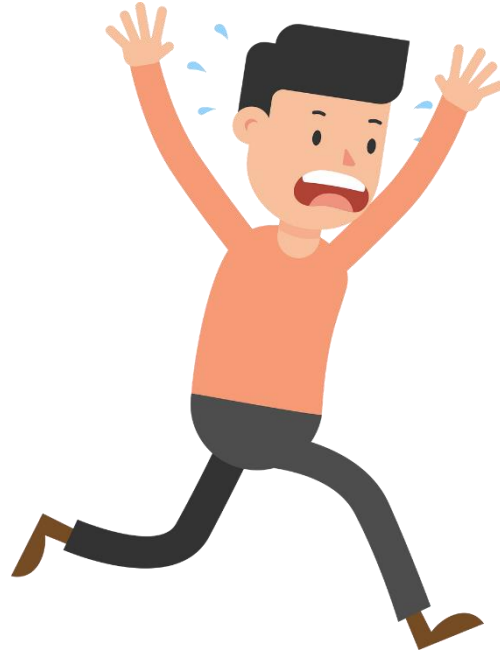
► Performances enabling real-time exploration

► Rich annotations (react., regions, long range interactions…)
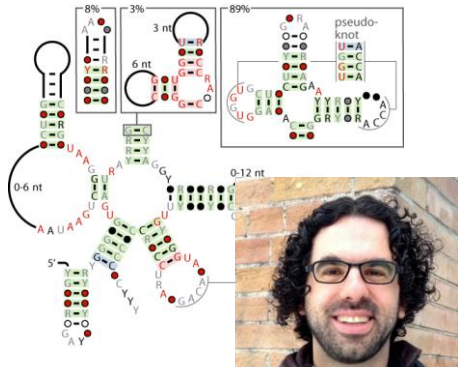
► Quick visual comparison of competing models

► Avoid overlaps + interactions to edit drawing/model
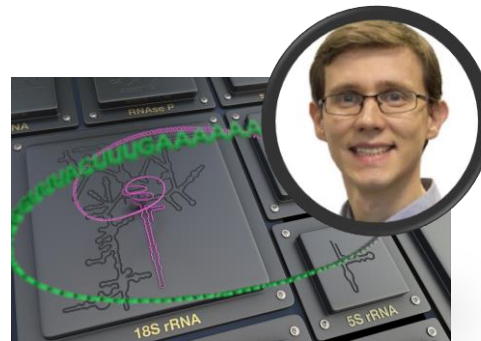
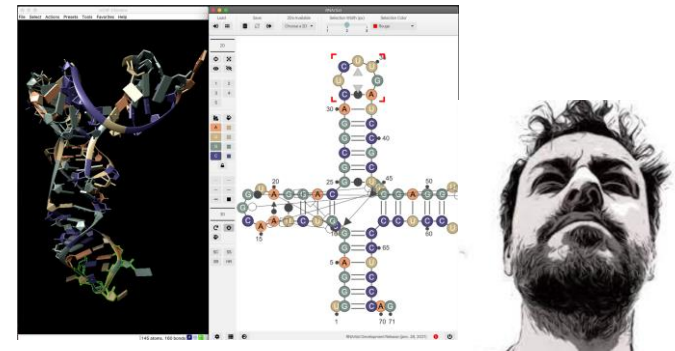► Export to editable vector/bitmap formats

► More ???

Acknowledgements

► Alain Denise (Univ. Paris Saclay)

► Hua-Ting Yao (TBI Vienna)

► VARNA users for 10+ years of great feedback/suggestions

► RNA vizualisation enthusiasts

R2R by Zasha Weinberg
Univ. Leipzig

R2DT by Anton Petrov
(coming next…)

RNArtist by Fabrice Jossinet
Univ. Strasbourg

And many others…