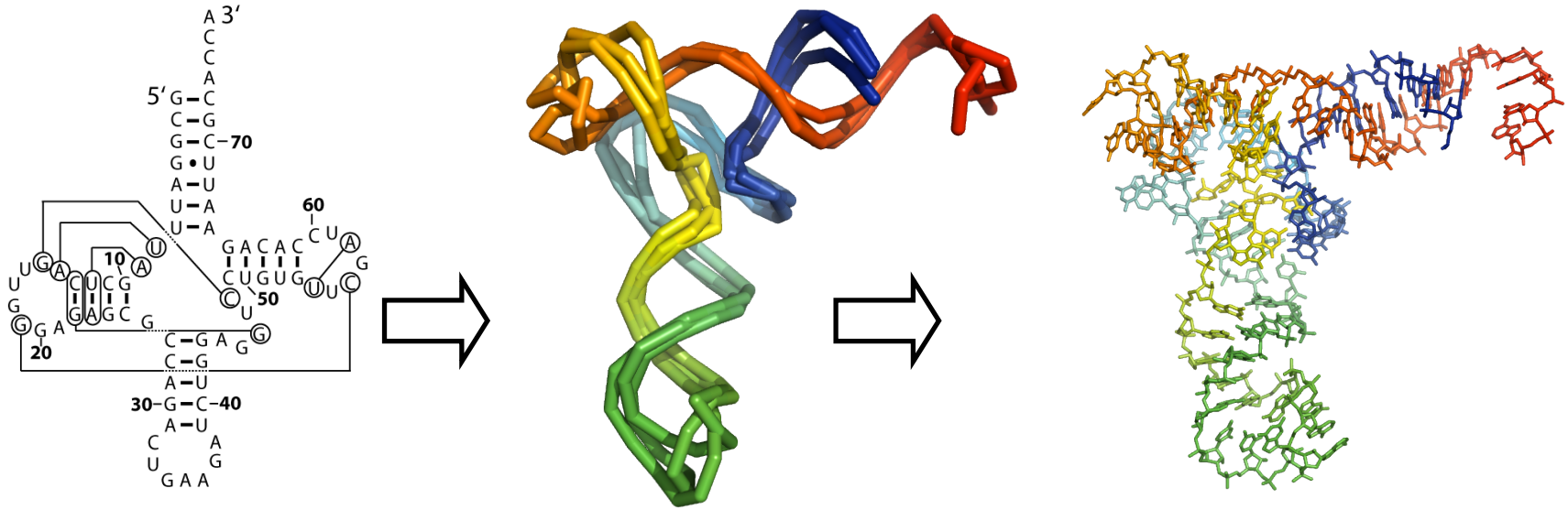
The Nucleic Acid Simulation Tool:

Coarse Grain Modeling with Atomic Refinement



Magdalena A. Jonikas

Biophysical Society Meeting

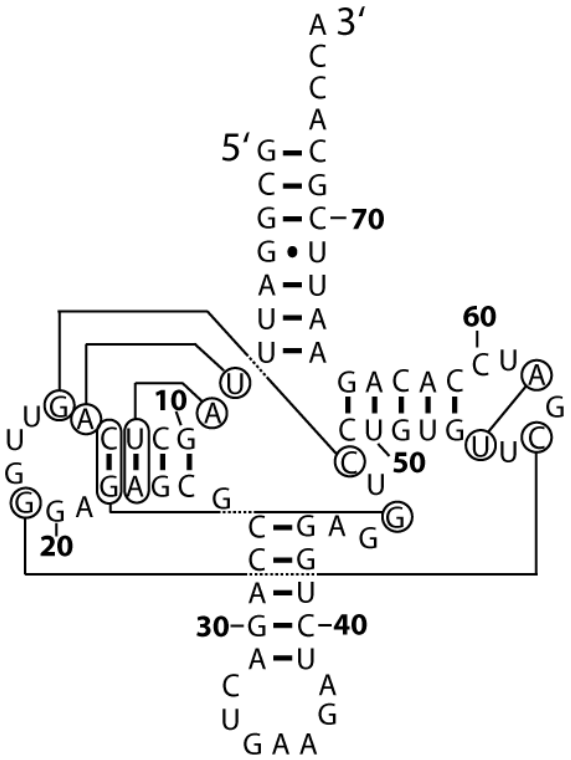
Ancillary Meeting on RNA Modeling and Simulation

February 22, 2010

STANFORD BIOENGINEERING

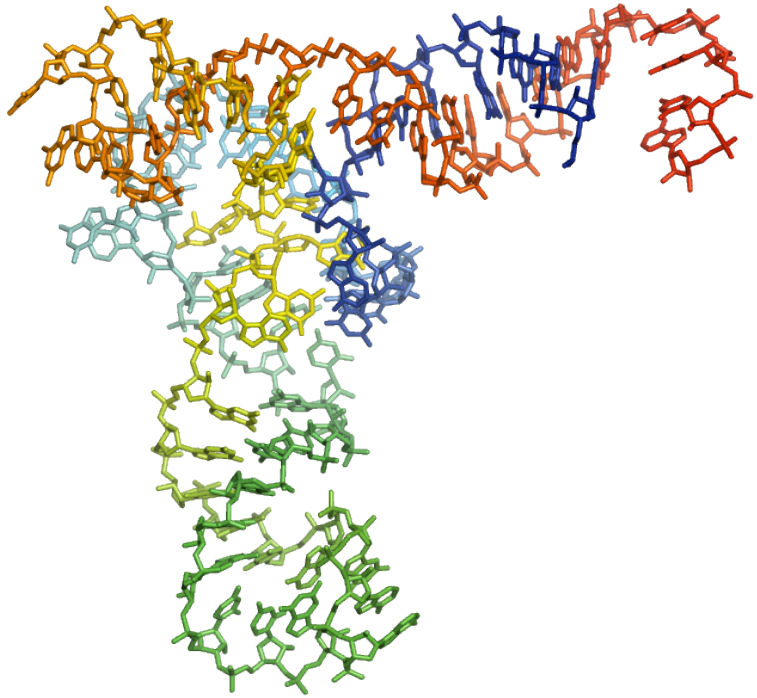
simbios

I have:



< 1 day

I want:

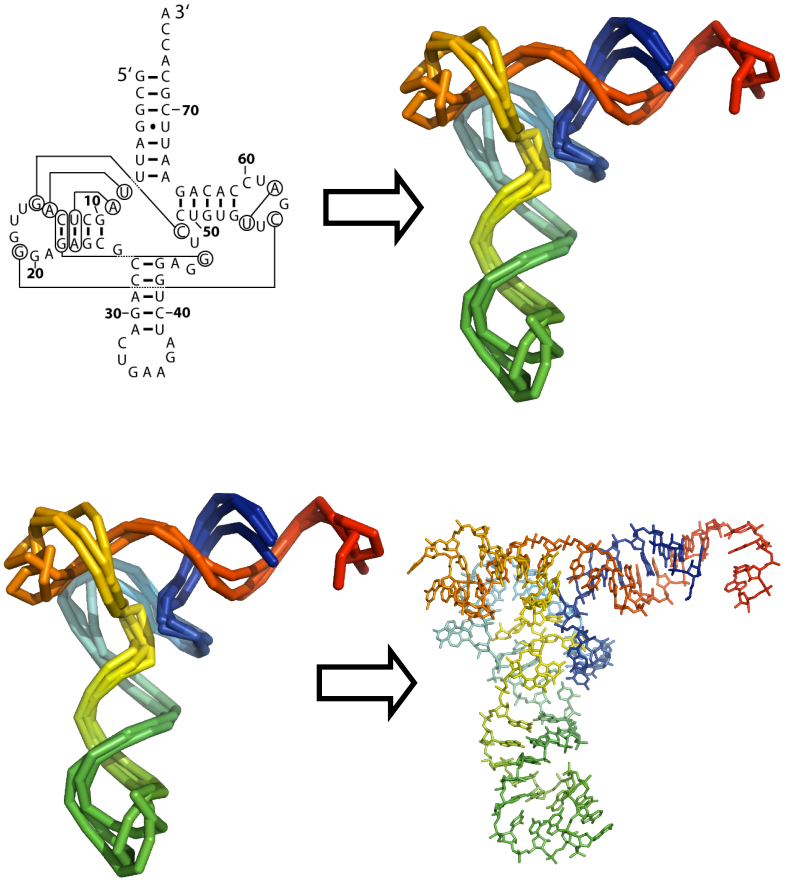


Outline

1. **Building coarse grain models (NAST).**

2. Adding full atomic detail (C2A).

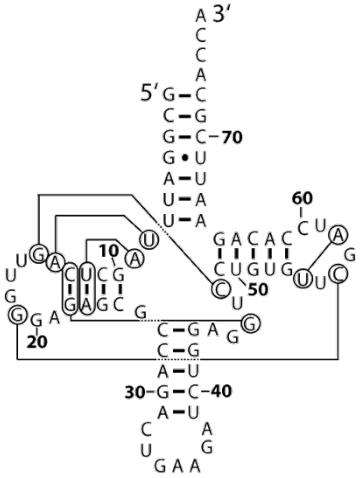
3. Minimizing the structure (Zephyr).



Building coarse grain models

Input

Primary sequence
Secondary structure
Tertiary contacts

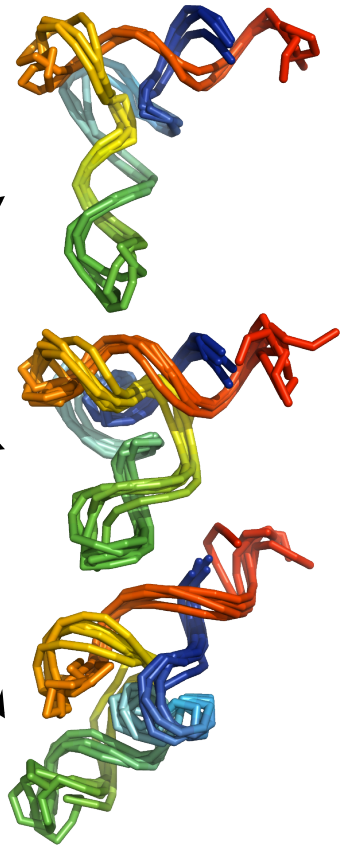


Statistics of observed geometries

The Nucleic Acid Simulation Tool (NAST)

Output

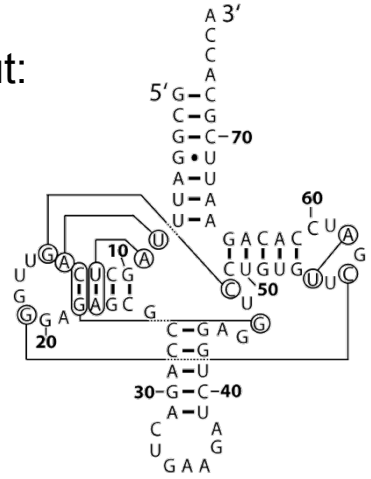
Coarse grain models

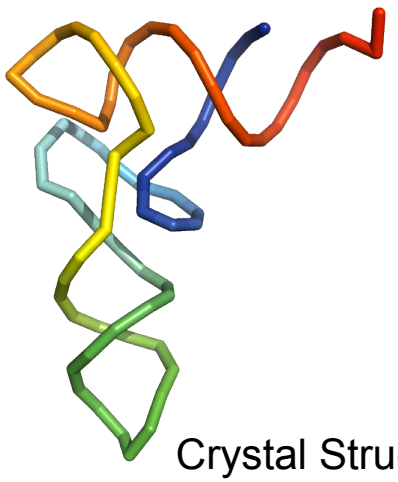


Jonikas et al., RNA 2009

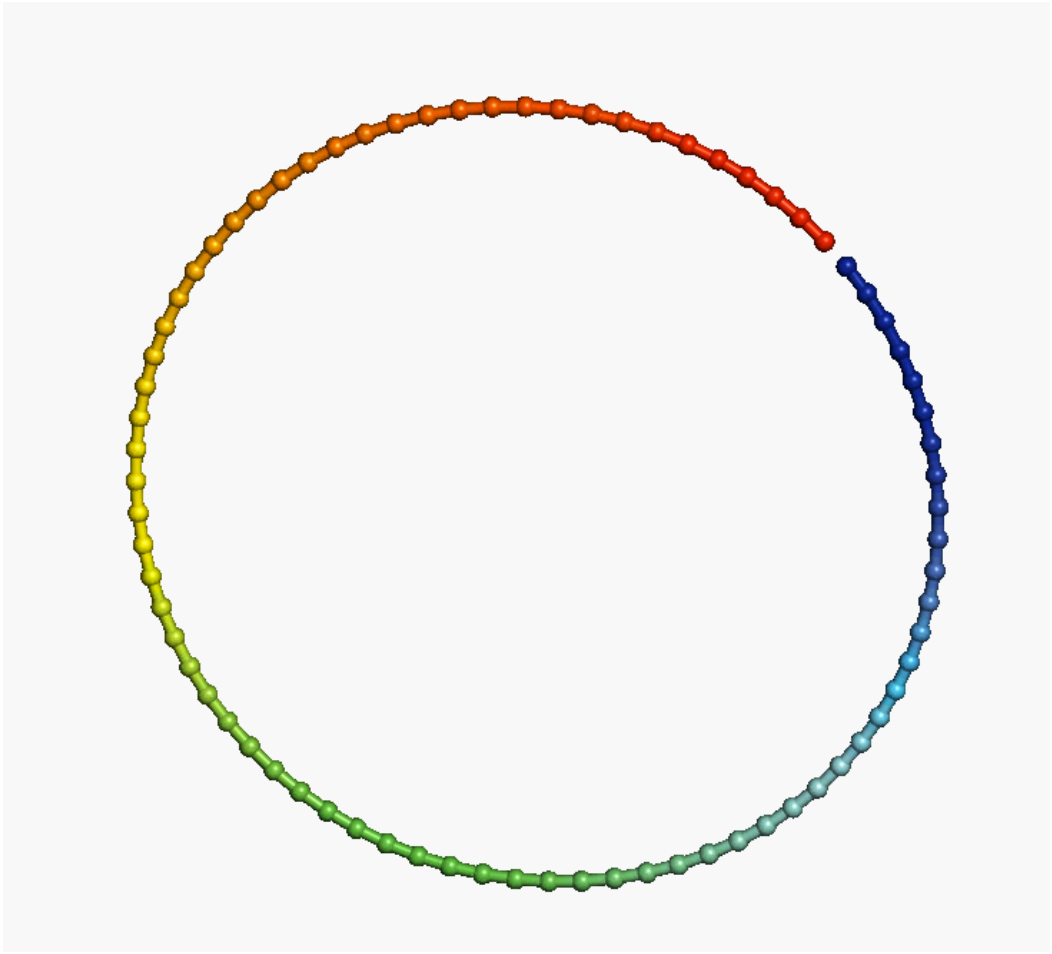
tRNA Example (< 1min)

Input:

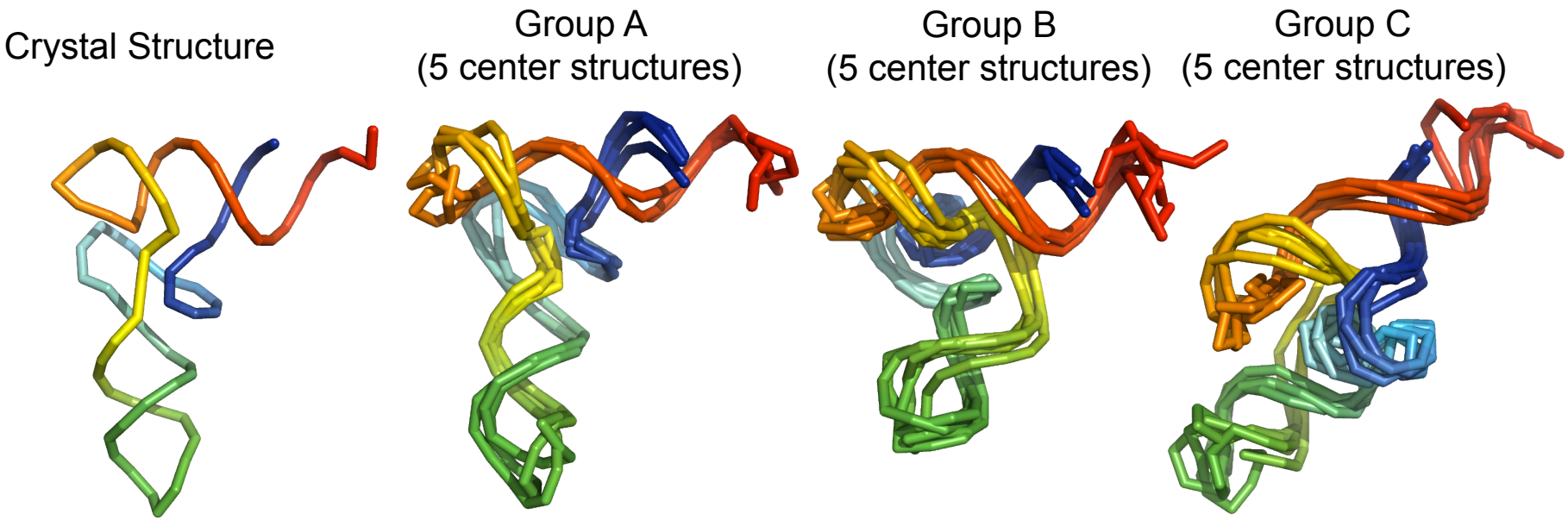




Crystal Structure



tRNA coarse grain modeling



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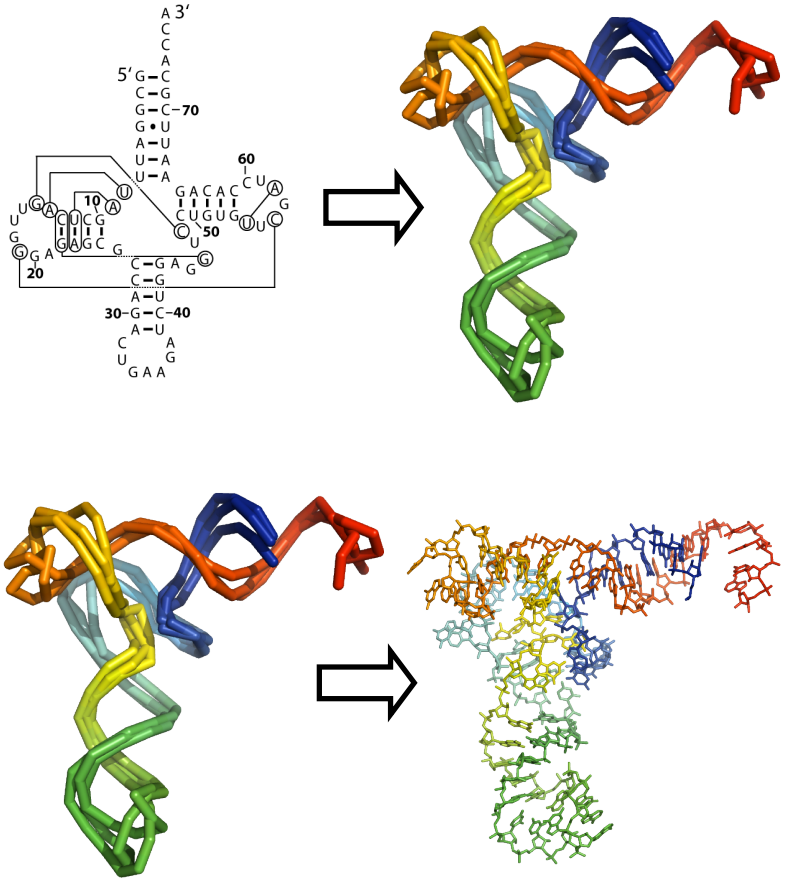
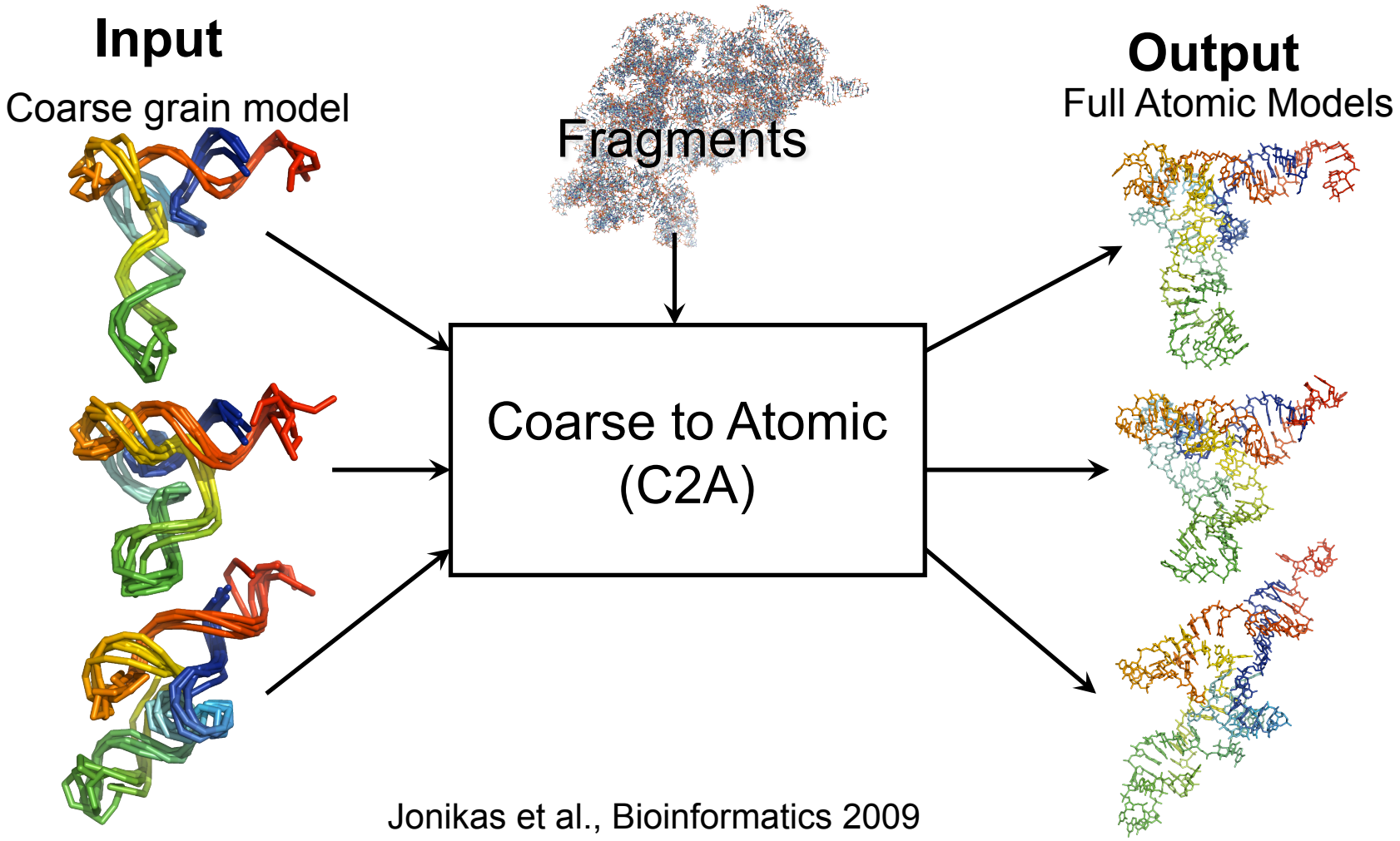
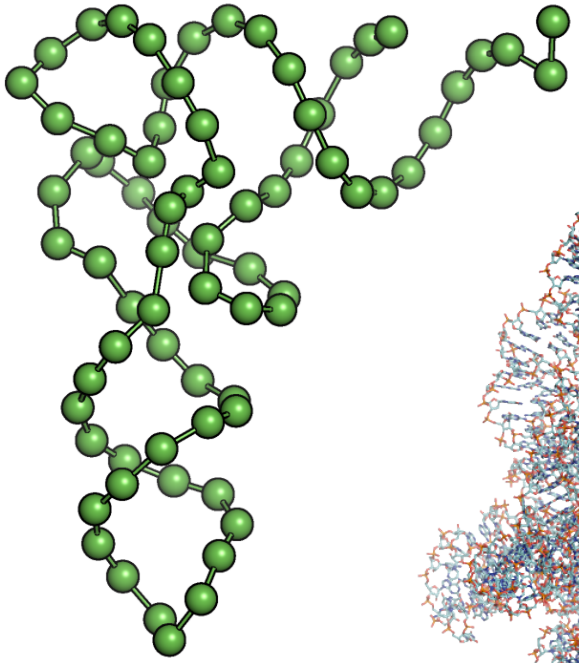


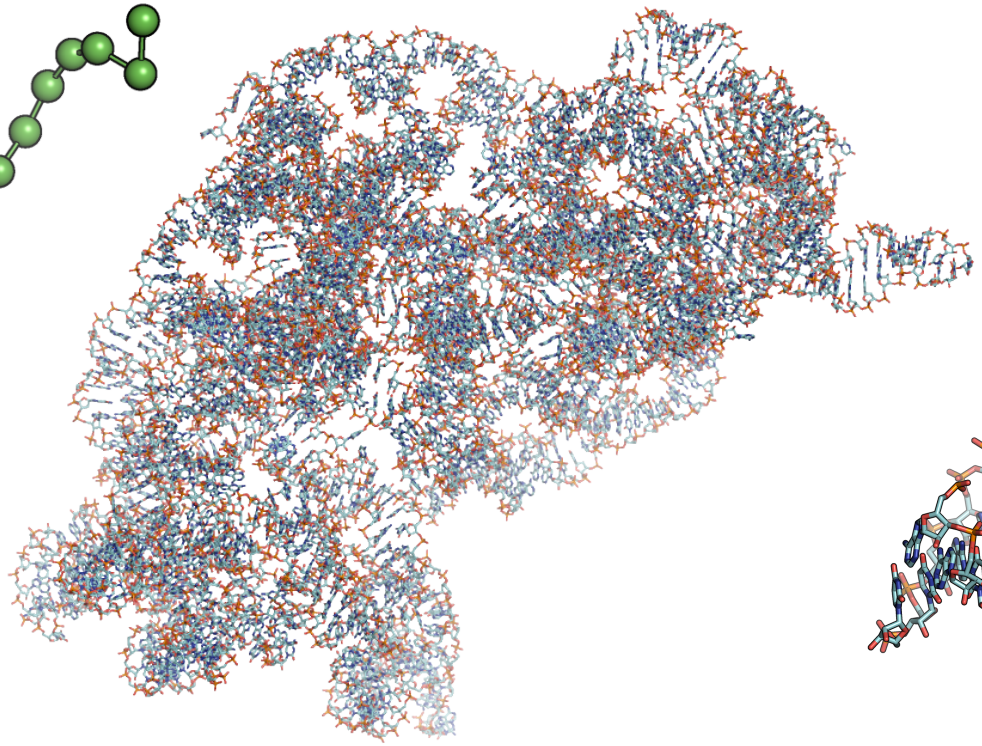
Adding full atomics detail



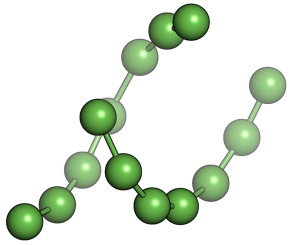
How it works



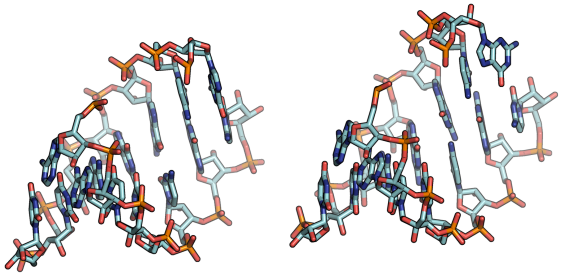
Template
Coarse-grained
Structure



Reference Full-atomic
Structure

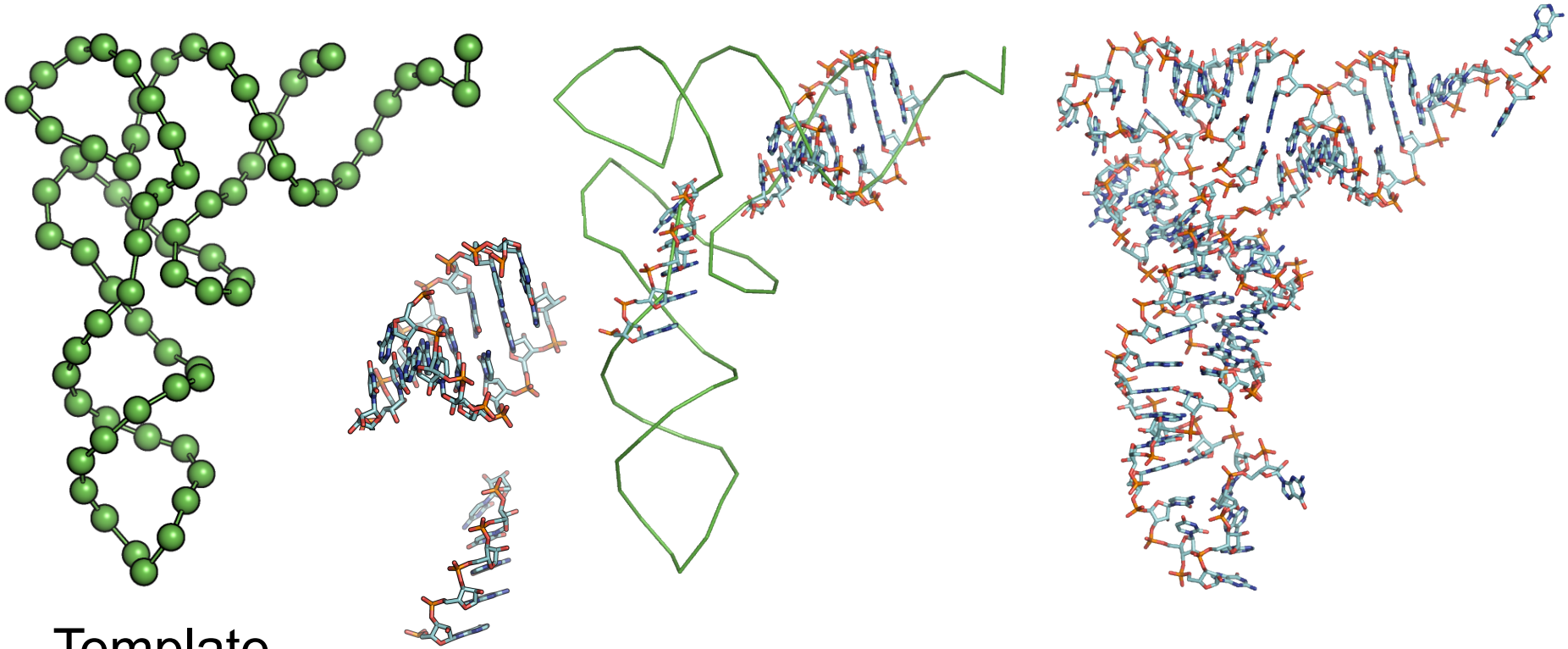


Template
Fragment



Full-atomic
Matches

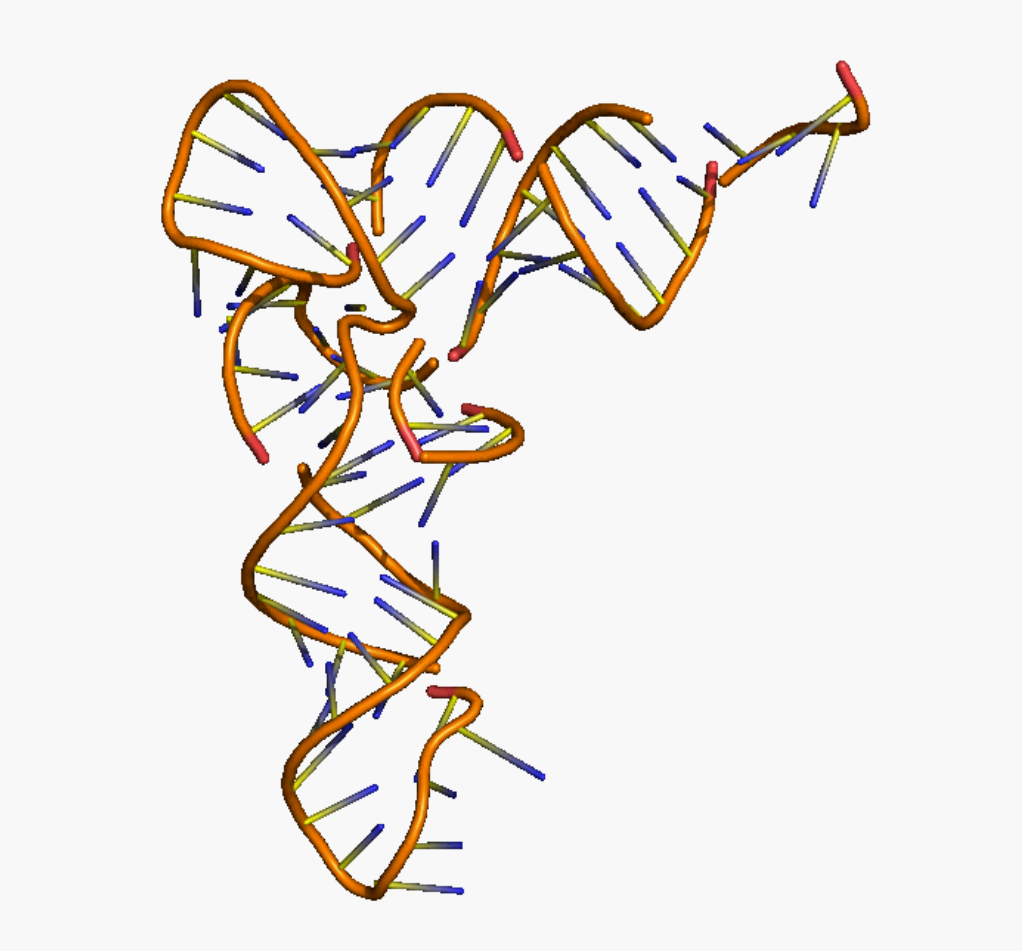
How it works



Template Structure

Full-atomic Matches

Structure assembly



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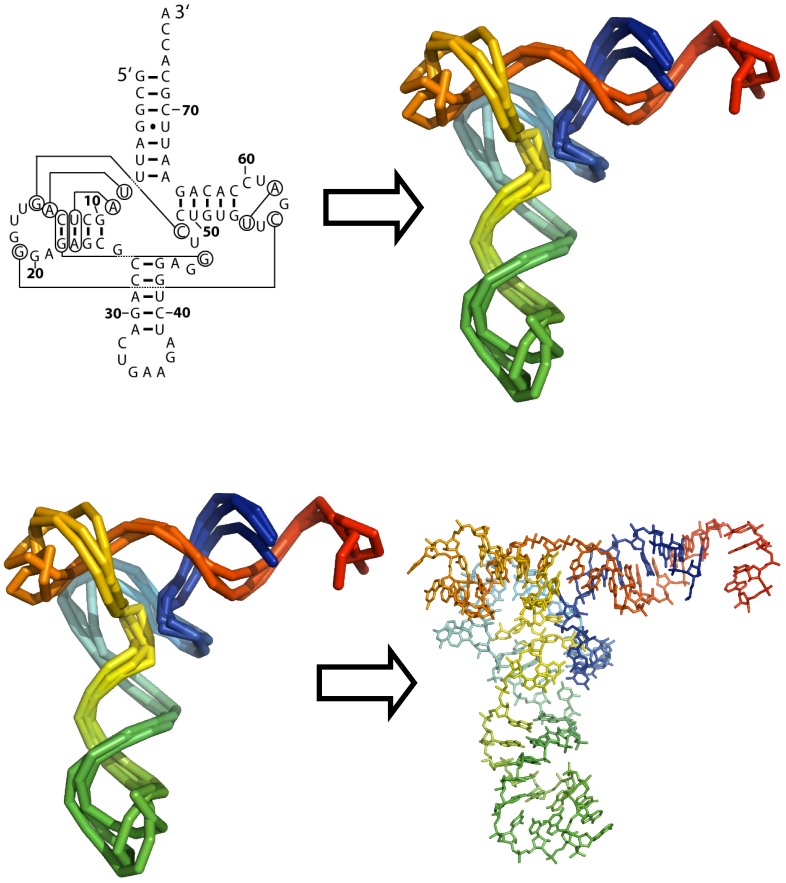
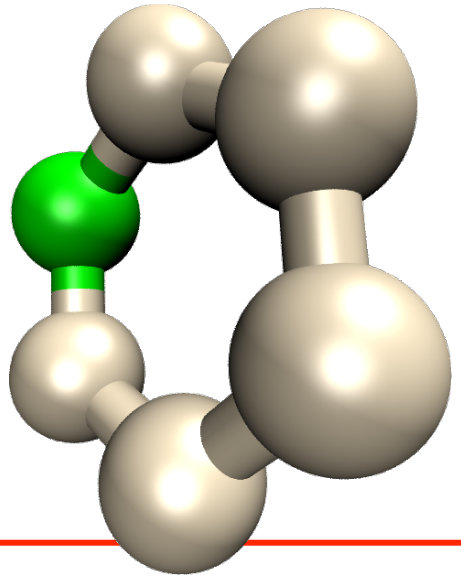
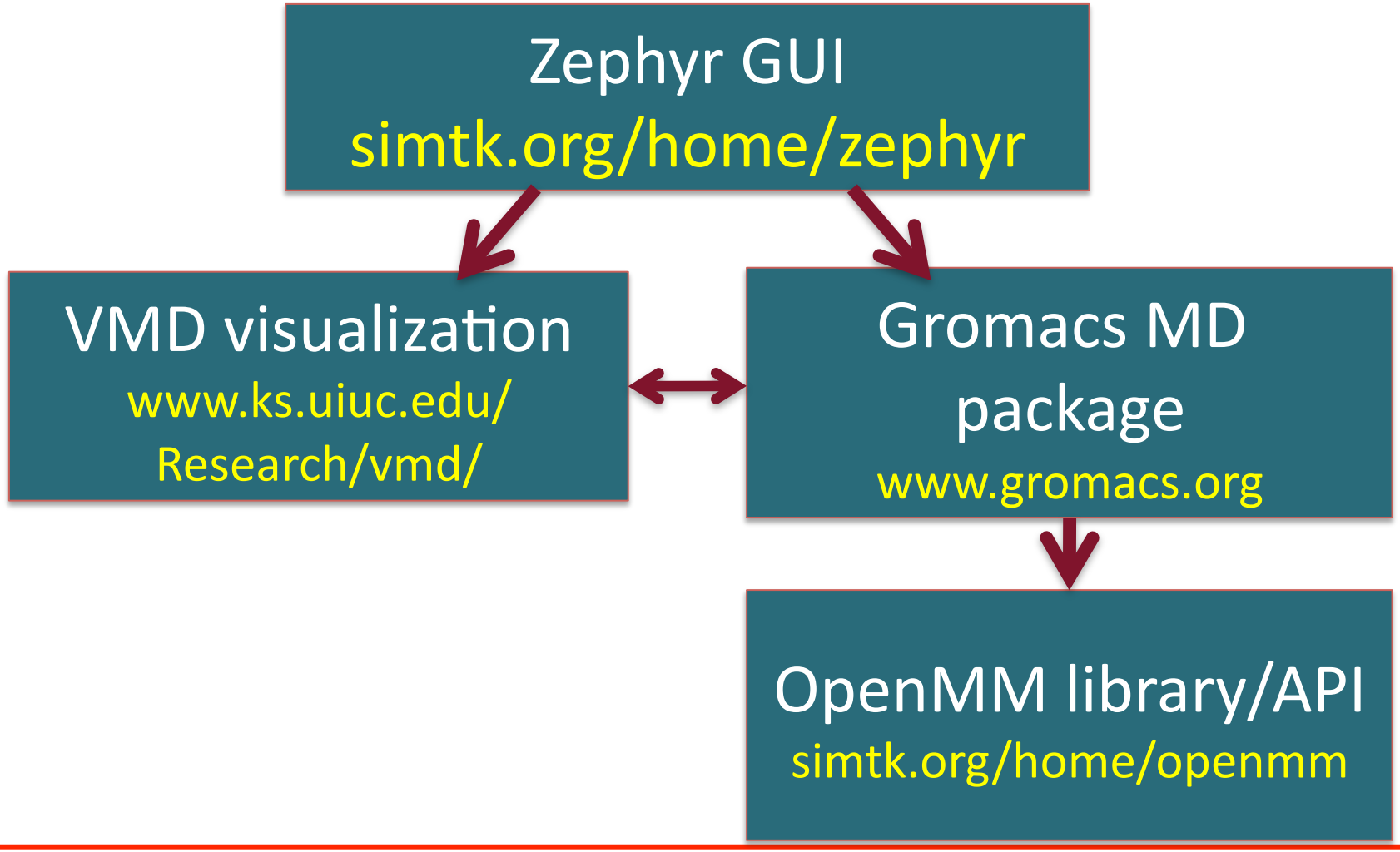


What is OpenMM Zephyr?

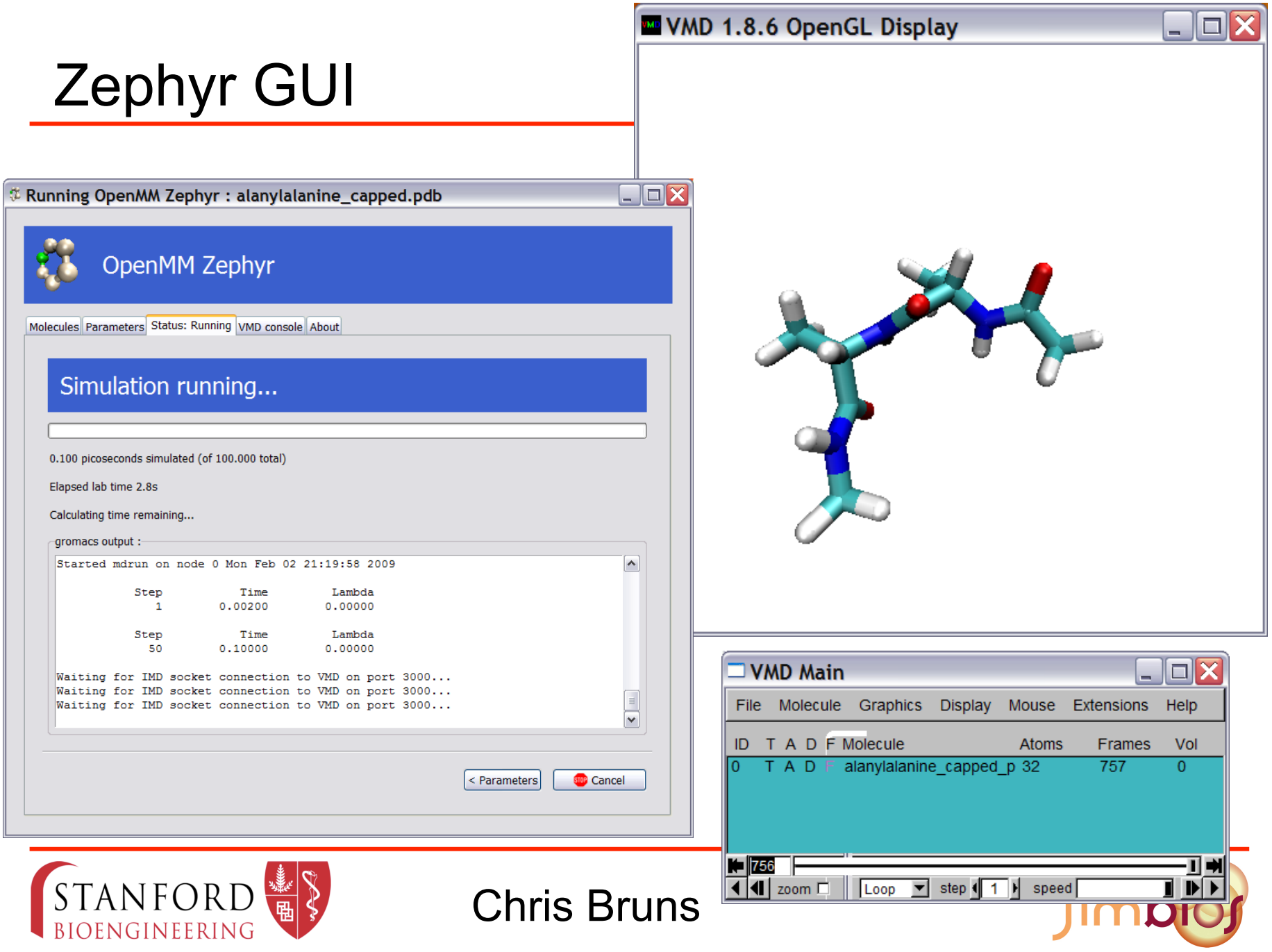
- Graphical user interface for running accelerated molecular dynamics simulations on high performance computer architectures, e.g., graphics processing cards (GPUs)
- Automates running of molecular dynamics programs, e.g., gromacs
- Vision of OpenMM Zephyr being a learning tool



Zephyr is a GUI layer on OpenMM, Gromacs, and VMD



Zephyr GUI



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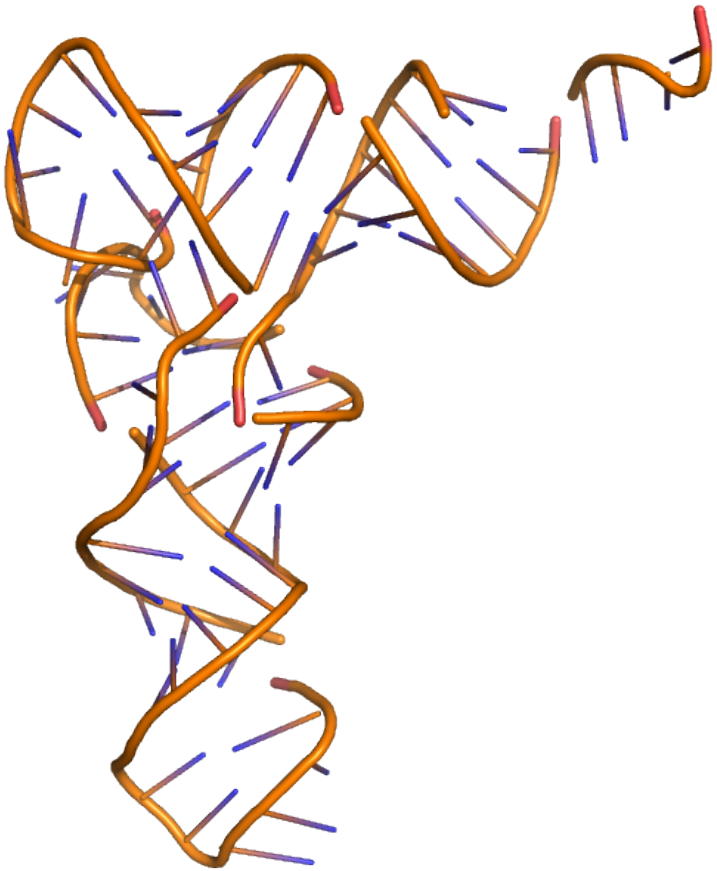
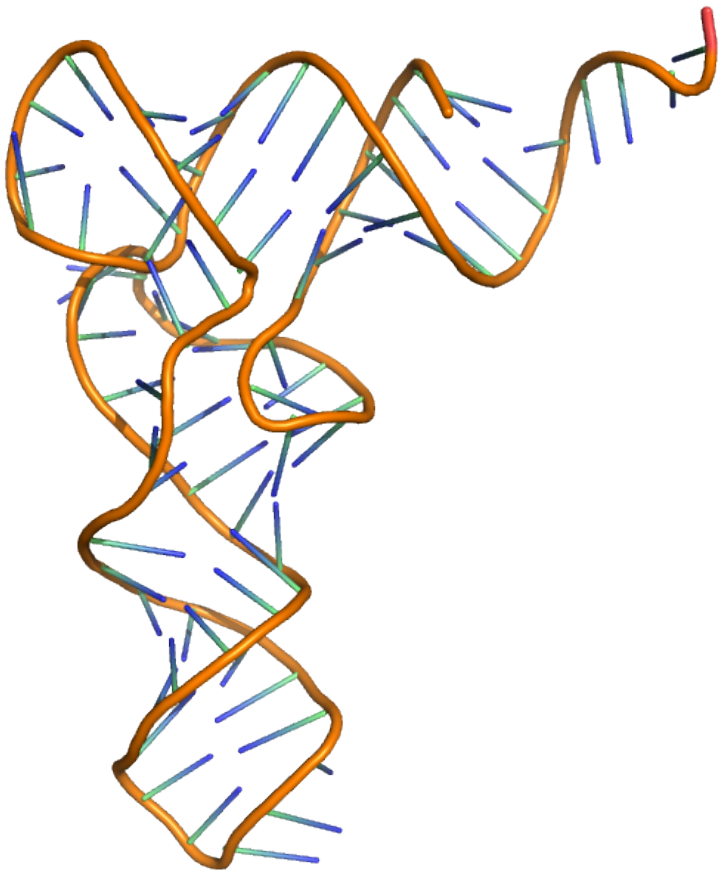
jimbios

Reducing gaps

Before minimization:



After minimization



A: Run these gromacs programs

OR

B: Click "Simulate" button in Zephyr

INPUT:
PDB structure file

.pdb

pdb2gmx

force field parameters

.top .gro

editconf

.top

minimize energy

grompp

.tpr

mdrun

simulation parameters

.gro

molecular dynamics

grompp

.mdp

.tpr

mdrun

GBSA parameters

.agb

.pdb .trr **OUTPUT: structure and trajectory**

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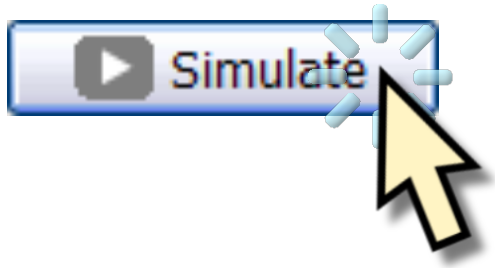
INPUT:
PDB structure file

.pdb



.pdb .trr **OUTPUT: structure and trajectory**

Chris Bruns simbios

Zephyr Design Principles

1. Discoverability
   - Not a black box
   - Learn molecular dynamics by investigating simulation interface
2. Convention
   - Harvest best practices of experts for default work flow
3. Feedback
   - Reveal when things go wrong
   - Reveal when things go right

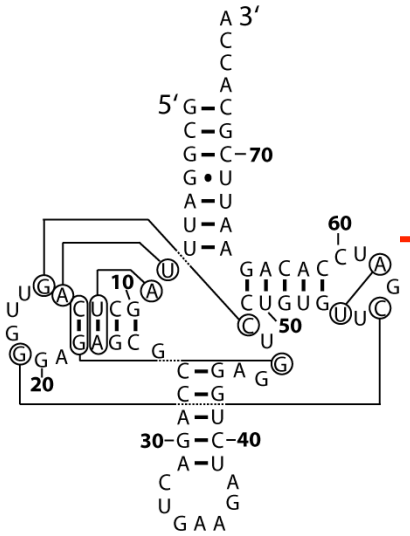
Zephyr & Role in RNA Modeling

- Molecular dynamics
- Final step of a 3D structure modeling pipeline

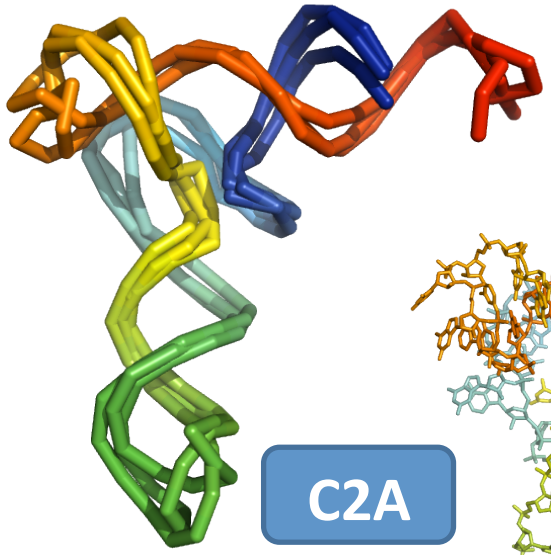
Current Zephyr Restrictions

- Windows (XP or Vista), Mac, Linux beta
- 32 bit
- Implicit solvent only
- Amber96 force field only
- Standard protein/RNA/DNA molecules only
- For GPU accelerated dynamics:
  - must have supported GPU and drivers

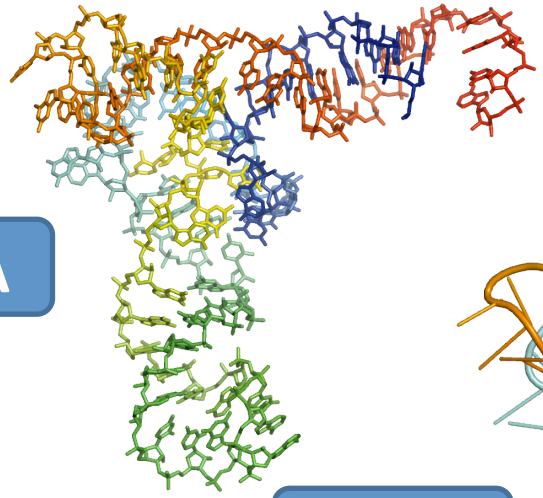
Conclusion



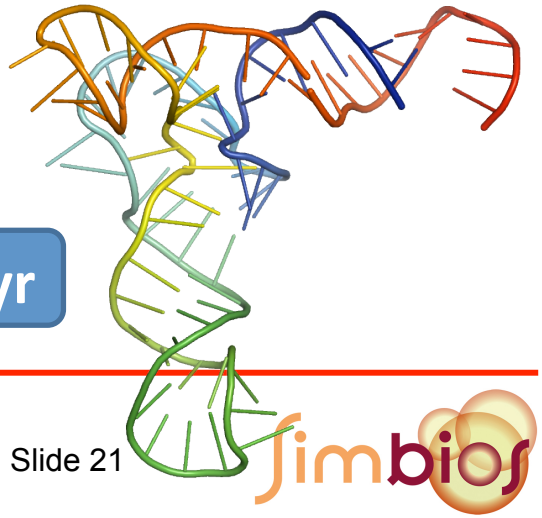
NAST



C2A



Zephyr



- 975 residue RNA.
- Secondary structure computed from predictions by program like Mfold/Vienna.
- 10M steps to equilibrate:
  - 6.2M at 0K
  - 3.8M at 300K
- ~3M steps / day.
- 4 days computation total (one cpu).
- SAXS scattering curve for this model fits experiment.

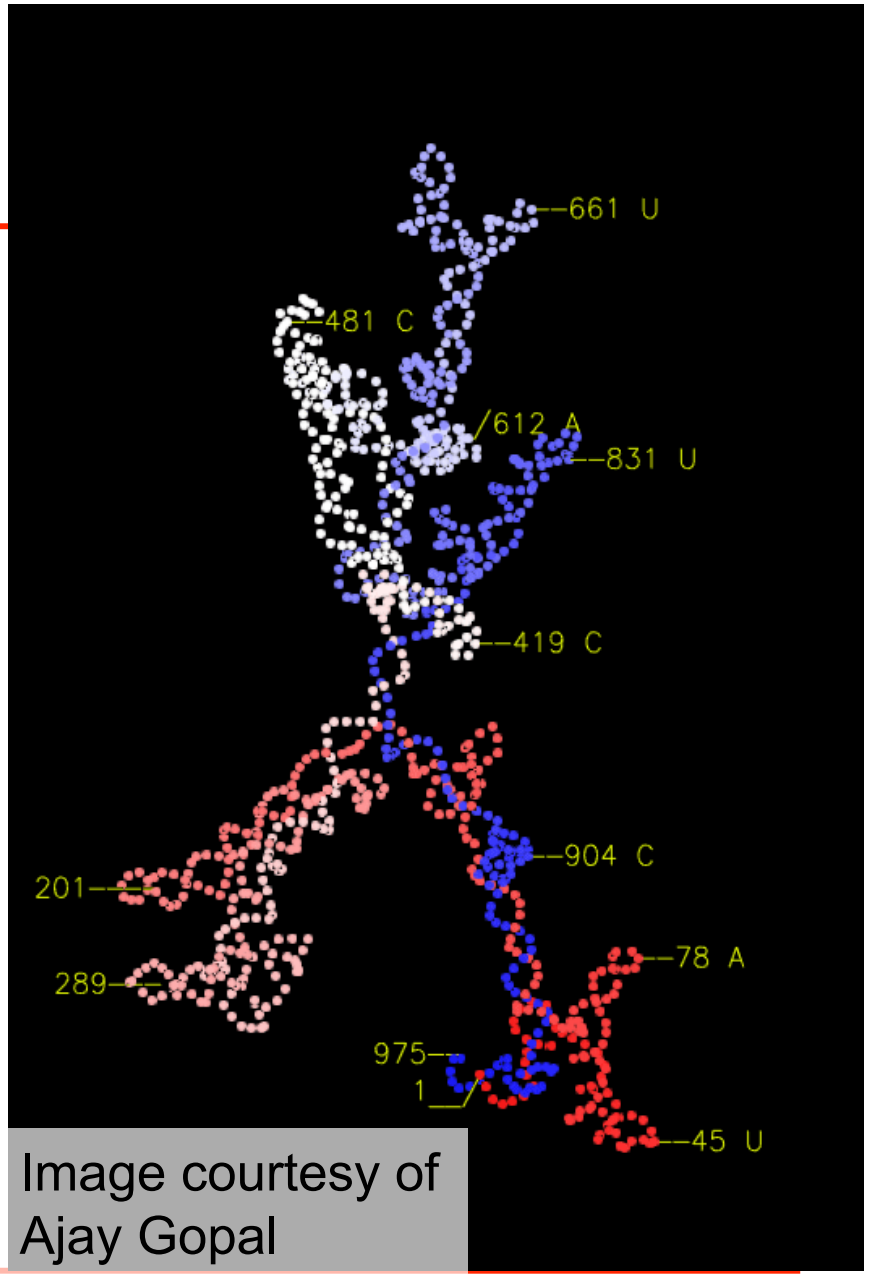


Image courtesy of Ajay Gopal