



Structural modeling with RNABuilder

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Presented at

Biophysical Society





Overview

- What is RNABuilder?
- Turning base-pairing contacts into 3D structure
- Multiple-template threading
- Morphing large complexes

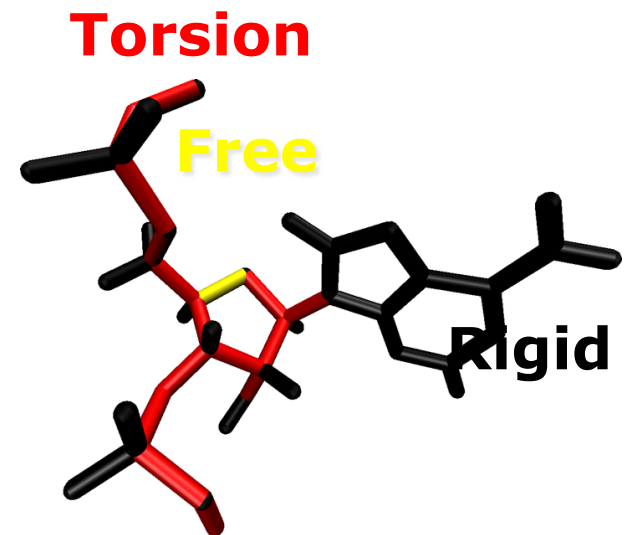


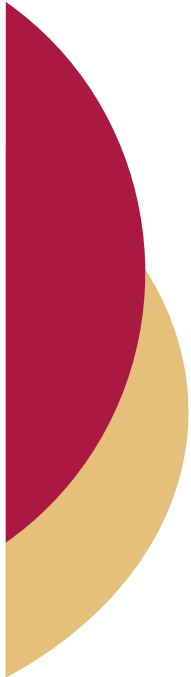
RNABuilder basics

- Works in internal coordinates
- Can apply any observed base-pairing interaction
- Collision detecting spheres approximately recover sterics

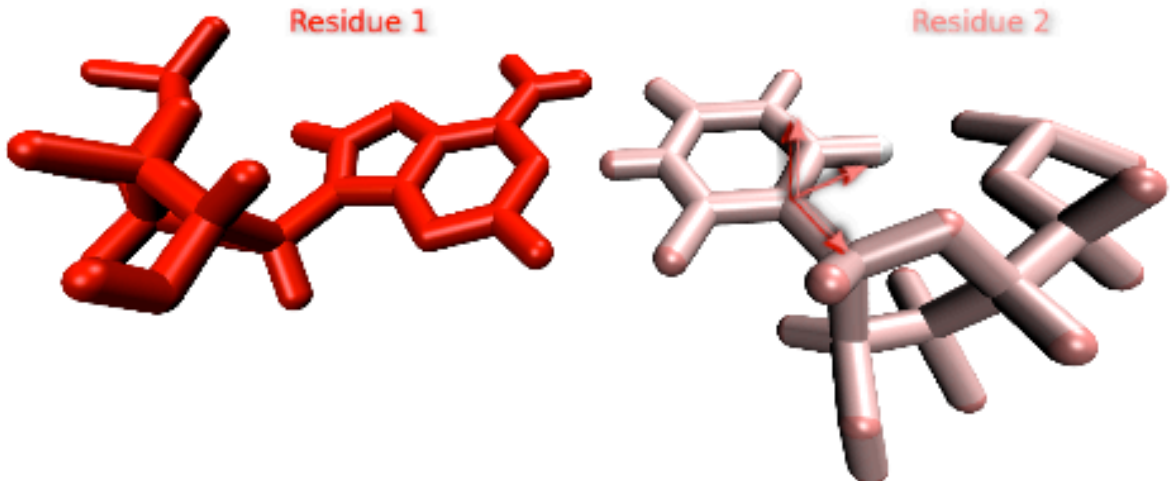
Internal coordinates lets you choose bond mobilities

- For each stretch of residues, you decide:
 - **Free:** All variable (bond lengths, angles, and dihedrals)
 - **Torsion:** Only dihedrals can vary
 - **Rigid:** All fixed.

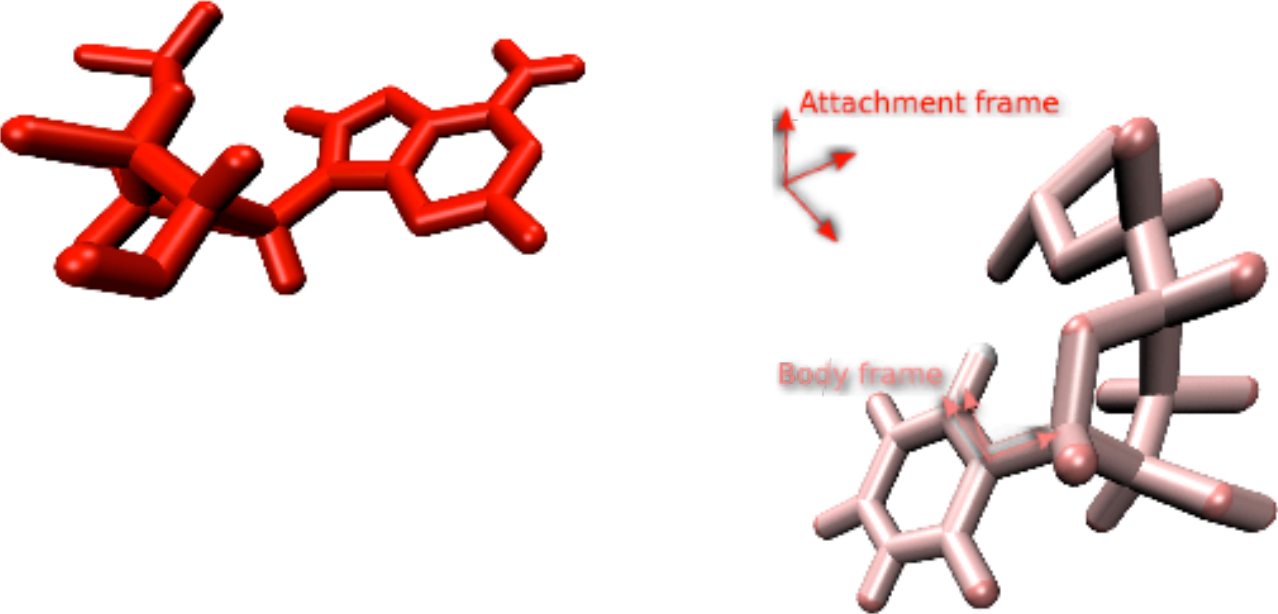


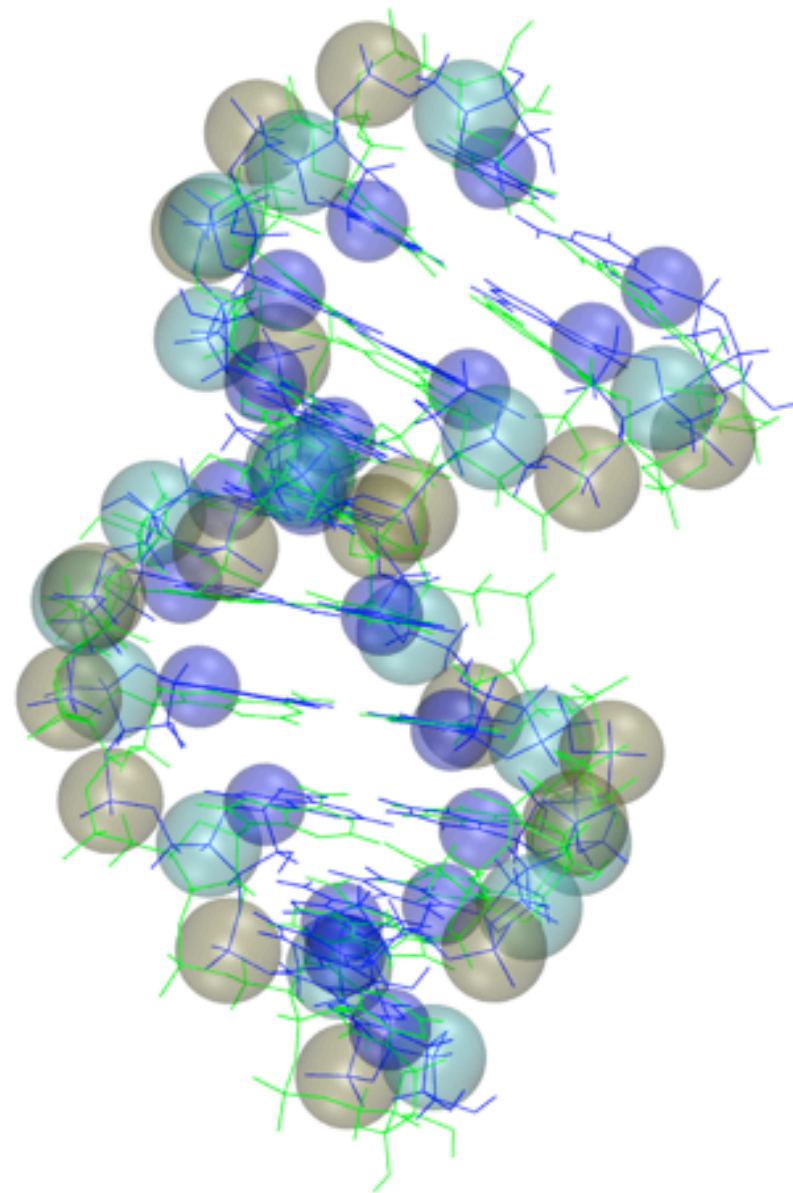
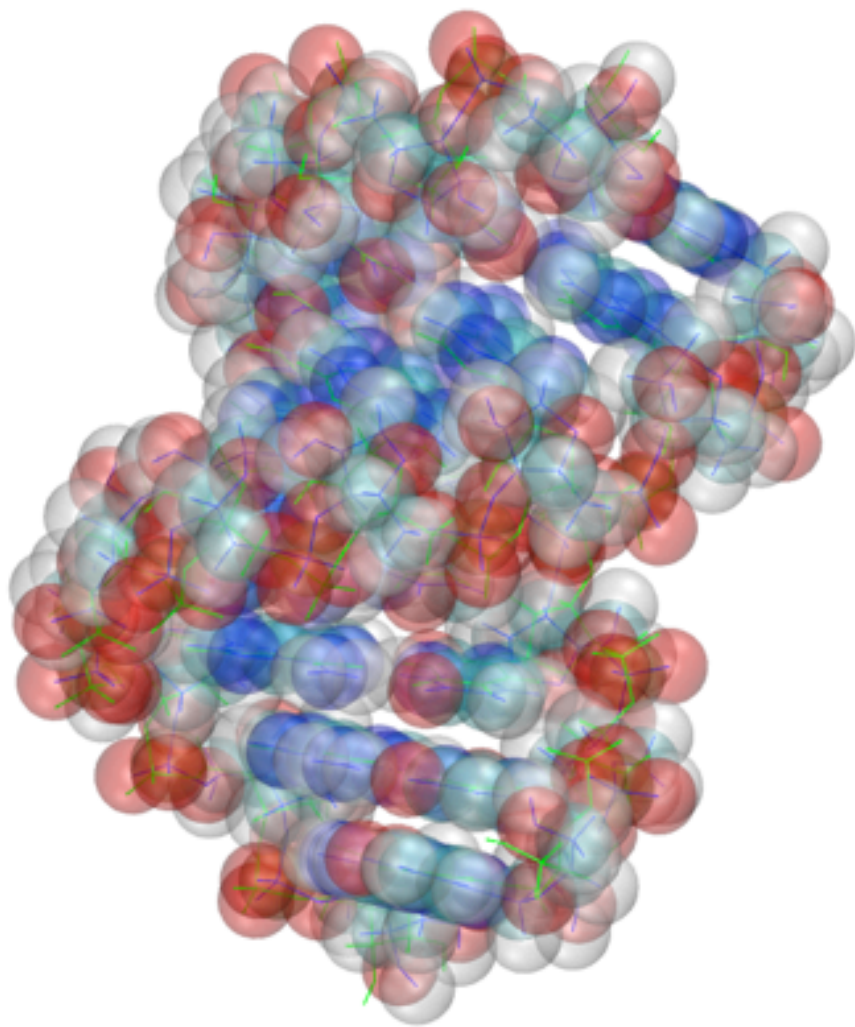


A



B

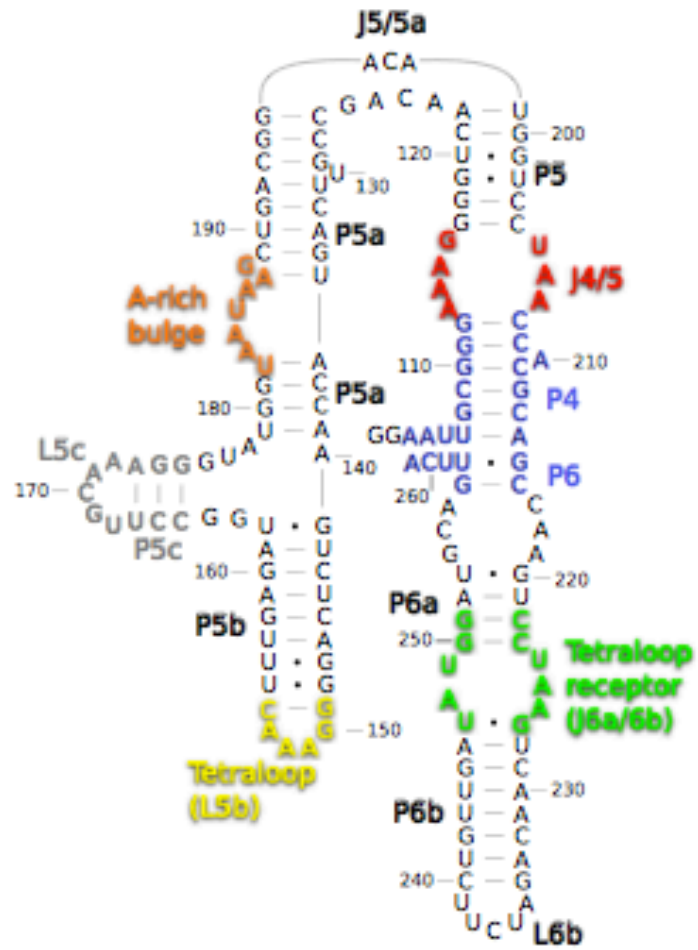


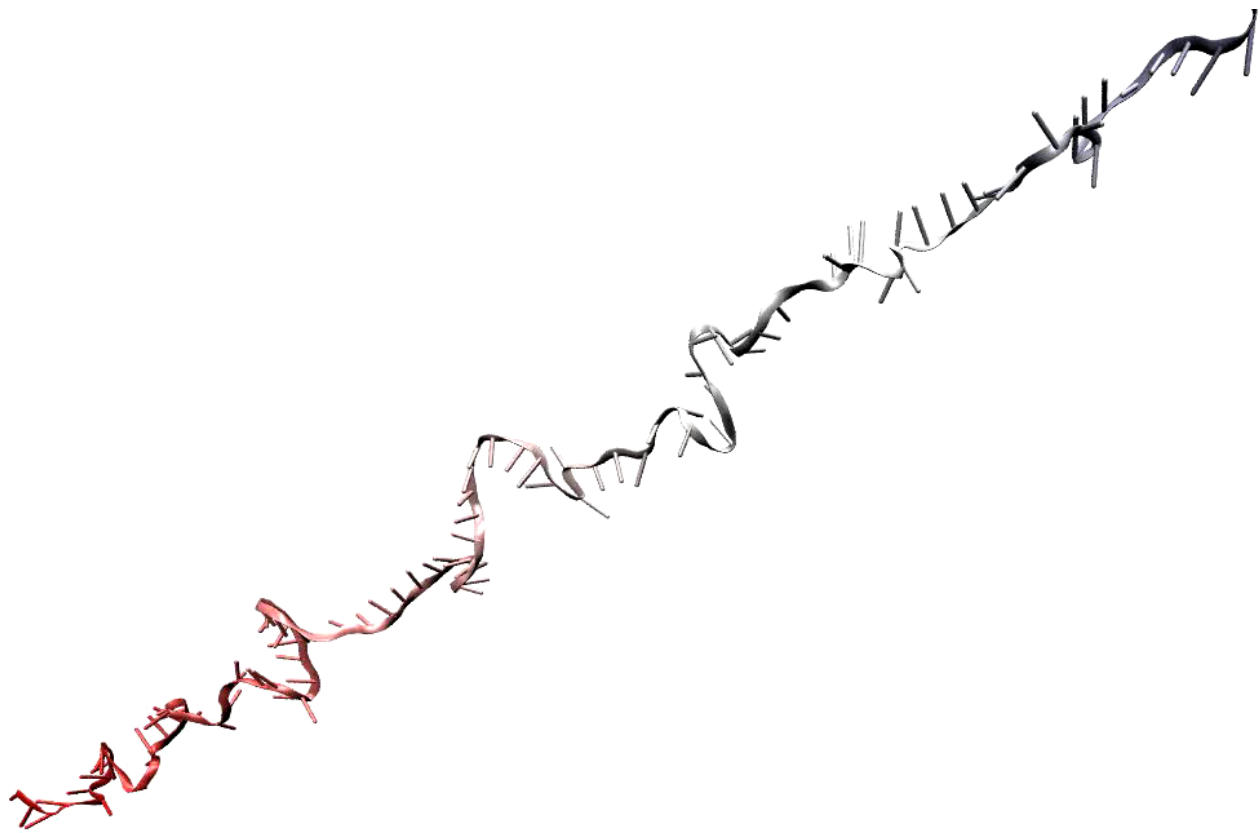




Turning base pairs into 3D structure

- Crystallography is hard
- Base pairing contacts can be obtained by cheap experiments or theory
- We did this for P4P6 ..



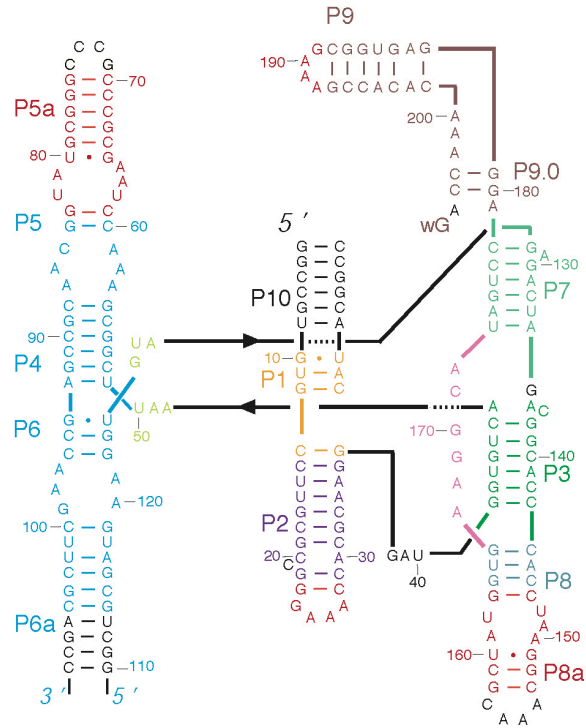




Threading RNA onto multiple templates

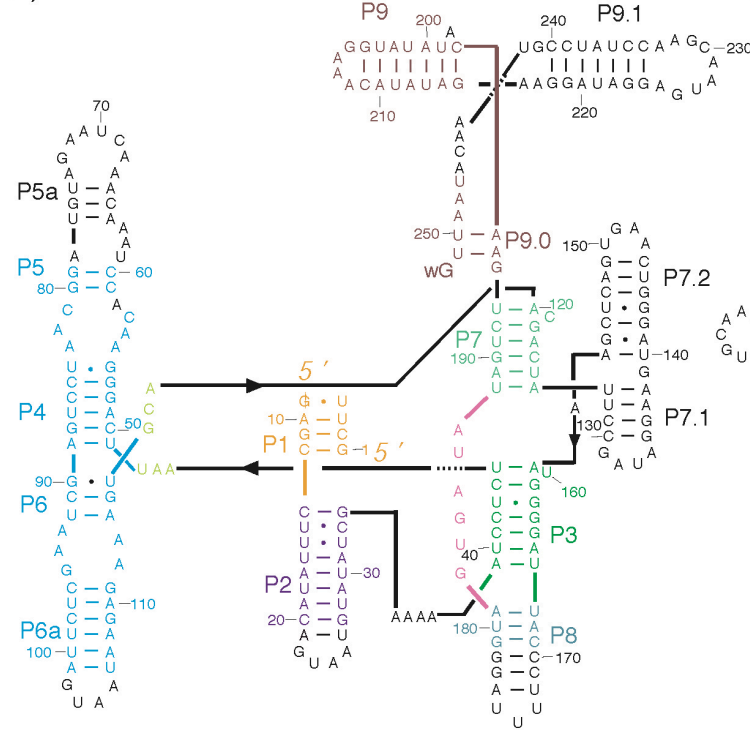
- Threading: the structural matching of a RNA sequence onto “template” molecules from the same or different species
- We will take an Azoarcus group I intron sequence and thread it onto template fragments from Twort and Tetrahymena
 - Structure much larger than Molecular Dynamics can handle
 - Inserted regions (with no template) can be modeled using our base pairing forces.
 - Can use multiple target fragments

A)



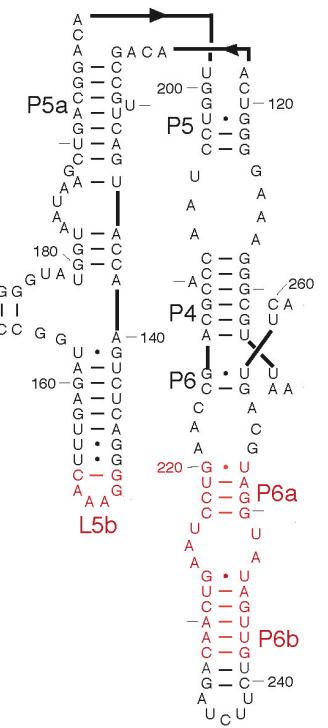
Azoarcus

B)

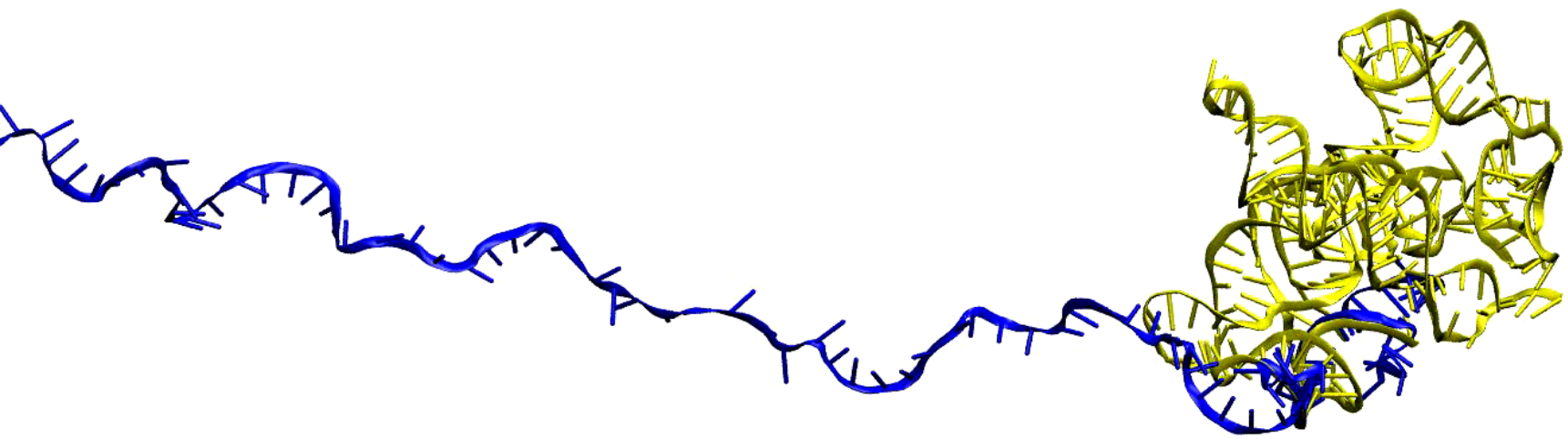


Twort

C)



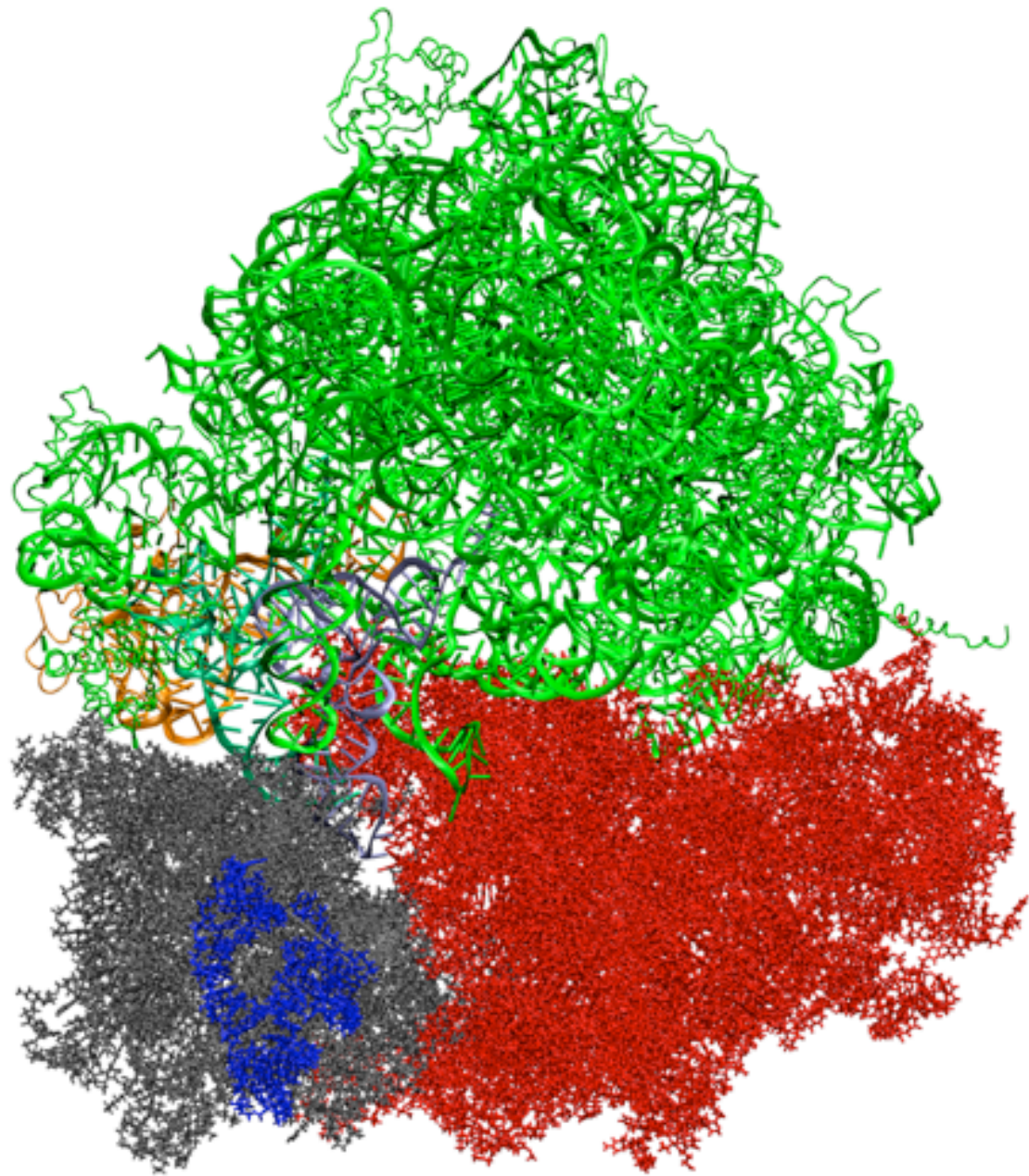
Tetrahymena P4P6

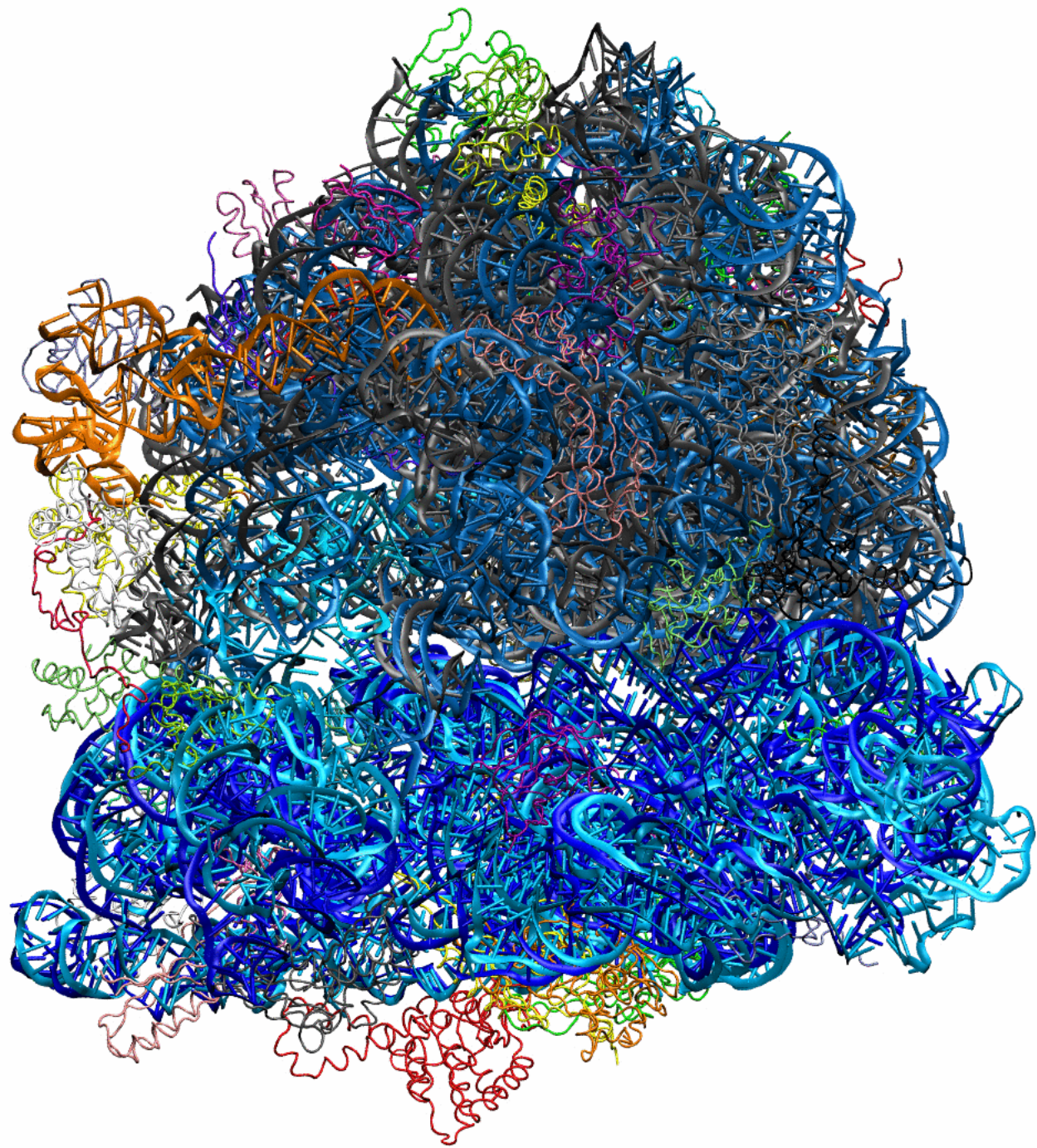




Morphing the ribosome

- We can break the complex into rigid blocks
- One block can contain multiple molecules, likewise one molecule can span multiple blocks, connected with a flexible hinge
- Threading forces align the blocks with a target structure
- The tRNAs are held in by base pairing forces and adjust as the subunits move







Conclusions

- RNABuilder technology
 - Internal coordinate mechanics
 - Base-wise force field
 - Approximate sterics
- Turns 2D contacts into 3D structure
- Can do multiple-template threading
- Can morph large complexes


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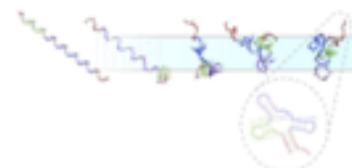
Advanced

Downloads & Source Code

This project has no public downloads, but makes [source code](#) available.

RNABuilder Project Overview

Description This toolkit contains RNABuilder and associated programs.



RNABuilder constructs structural models of RNA by enforcing user-provided base pairing interactions and other structural constraints. Key to the algorithm's effectiveness is its ability to enforce a folding pathway that is automatically computed or provided by the user. Its speed arises from its use of multi-resolution techniques such as coarse grained force fields and selective rigidification of groups of atoms.

The user is required to write the contacts.dat input file specifying the sequence, base pairs, and any of the other available constraints, forces, and options.

RNABuilder produces trajectory files in PDB format. These show the trajectory as the RNA folds from some initial configuration to one that satisfies the user supplied constraints. The last frame in this trajectory is typically the most interesting for structure prediction, although for dynamical studies the trajectory files are the more useful ones.

Available Downloads and Their Potential Uses We provide the RNABuilder package which allows the user to model RNA structures as described.

Purpose/Synopsis Easily build RNA structures and sample their dynamics

Audience Structural biologists wishing to create models of RNA structures and sample their conformational dynamics

Project Lead



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Distribution

- available from SimTK.org
- contact me scflores@stanford.edu
- Simbios runs RNA modeling workshops -- sign up SimbiosFeedback@stanford.edu



Acknowledgements

- Russ Altman, Chris Bruns, Peter Eastman, Jack Middleton
- Yaqi Wan, Rick Russell